

Volume 6 / Number 10 / 2012

ISSN 1840-2291

HealthMED

Journal of Society for development in new net environment in B&H



HealthMED journal with impact factor indexed in:
Thomson Reuters ISI web of Science,
Science Citation Index-Expanded, Scopus, Embase
EBSCO Academic Search Premier, Index Copernicus, getCITED



design by Mirza Basic

HealthMED

Journal of Society for development in new net environment in B&H

EDITORIAL BOARD

Editor-in-chief	Mensura Kudumovic
Execute Editor	Mostafa Nejati
Associate Editor	Azra Kudumovic
Technical Editor	Eldin Huremovic
Cover design	Mirza Basic

Members

Paul Andrew Bourne (Jamaica)
 Xiuxiang Liu (China)
 Nicolas Zdanowicz (Belgique)
 Farah Mustafa (Pakistan)
 Yann Meunier (USA)
 Suresh Vatsyayann (New Zealand)
 Maizirwan Mel (Malaysia)
 Budimka Novakovic (Serbia)
 Daa Eldin Abdel Hameed Mohamad (Egypt)
 Zmago Turk (Slovenia)
 Chao Chen (Canada)
 Farid Ljuca (Bosnia & Herzegovina)
 Sukrija Zvizdic (Bosnia & Herzegovina)
 Damir Marjanovic (Bosnia & Herzegovina)
 Emina Nakas-Icindic (Bosnia & Herzegovina)
 Aida Hasanovic (Bosnia & Herzegovina)
 Bozo Banjanin (Bosnia & Herzegovina)
 Gordana Manic (Bosnia & Herzegovina)

Address of the Sarajevo, Bolnicka BB

Editorial Board healthmedjournal@gmail.com
 http://www.healthmedjournal.com

Published by DRUNPP, Sarajevo

Volume 6 Number 10, 2012

ISSN 1840-2291

HealthMED journal with impact factor indexed in:

- Thomson Reuters ISI web of Science,
- Science Citation Index-Expanded,
- Scopus,
- EBSCO Academic Search Premier,
- EMBASE
- Index Copernicus,
- getCITED, and etc.

Sadržaj / Table of Contents

Basic assistance for mental health in Northeast Brazil.....	3244
<i>Modesto Leite Rolim Neto, Alberto Olavo Advincula Reis, José Cezario de Almeida, Nadia Nara Rolim Lima, Saulo Araújo Texeira, Marina Lucena de Aguiar Ferreira</i>	
The study on physiological indexes of exam anxiety in medical students	3248
<i>Abbas Mosoudzadeh, Nasrin Bali-Lashak, Sara Asadpour, Reza Alizadeh-Navaei</i>	
Arterial elasticity measurement in patients with Behcet's disease	3255
<i>Hakan Ucar, Kemal Karaagac, Osman Akin Serdar, Zeynel Abidin Yetgin, Yusuf Akturk, Esra Ugurlu Karaagac, Hayriye Saricaoglu</i>	
The effect of memory reinforcement on creating dependency in male mature mice using conditioned place preference (CPP) method	3261
<i>Ebrahim Hosseini, Mahmoud Vessal, Sanaz Bahaadini, Maryam Rafieirad</i>	
A prospective trial of epidural versus intravenous meperidine analgesia during labor: Effects on perinatal and maternal outcome	3268
<i>Feyza Yayci, Eyup Yayci, Sibel Devrim, Meltem Ince Gul, Melek Gura</i>	
An ex vivo comparison of three electronic apex locators.....	3275
<i>Joanna Baginska, Ewa Linczuk, Bartłomiej Botulinski, Anna Kierklo</i>	
The effect of caffeic acid phenethyl ester on QT interval in cirrhotic rats	3281
<i>Mahin Dianat, Samira Saadat Fard, Mohammad Badavi, Akram Ahangarpour</i>	
Examining the relation between sociotropic and autonomic and problem solving abilities of nursing students	3286
<i>Birsan Altay, Huriye Demet Cabar, Bilge Bal Ozkaptan, Kubra Gumus</i>	
Children's mental health in northeast Brazil: Vulnerability and public policies	3298
<i>Modesto Leite Rolim Neto, Alberto Olavo Advincula Reis, Jose Cezario de Almeida, Marina Lucena de Aguiar Ferreira, Nadia Nara Rolim Lima</i>	

Sadržaj / Table of Contents

Study subclinical Hepatitis A infection in ambulatory patients, with nonspecific abdominal complaints in Mofid hospital of Tehran Iran.....	3302	Improvement of anxiety resources scale of school-age children with oncological disease under condition of illness and hospitalization.....	3378
<i>Fariba Shirvani, Naimeh Taslimi, Abodlah Karimi, Mohammad Rahbar</i>		<i>Selver Guler, Huriye Demet Cabar</i>	
Body image dissatisfaction and risk factors among female adolescents: A sample from Turkey.....	3307	Ethical performance in delivery of sexual and reproductive health services: A Delphi study focused on the right of confidentiality	3385
<i>Perim Turker, Murat Bas, Mendane Saka, Sinem Metin</i>		<i>Tahmineh Farajkhoda, Robab Latifnejad Roudsari, Mahmoud Abbasi</i>	
Mothers' knowledge, attitude, and practice: The performance of the nationwide integrated maternal health care project	3316	Assessment of kinesthetic awareness and fine motor dexterity in music students with performance-related hand disorders	3995
<i>Forouzan Akrami, Gohar Mohammadi, Mohammad Esmaeil Motlagh, Ali Ramezankhani, Shahrzad Valafar</i>		<i>Zeliha Baskurt, Ferdi Baskurt, Bilge Kara</i>	
Clopidogrel resistance in patients with type 2 Diabetes Mellitus: A comparison between oral antidiabetic agents and insulin.....	3323	Burnout syndrome among special education professionals	3403
<i>Zuhal Ariturk, Habib Cil, Ercan Gunduz, Celal Yavuz, Hasan Kaya, Faruk Ertas, Mustafa Oylumlu, Serdar Soydinc</i>		<i>Nikola Petkovic, Dragana Macesic Petrovic, Vasilije Balos, Miroslav Misic, Milos Djordjevic</i>	
Circulating levels of Homocysteine, Zinc, Iron and Copper in pregnant women with pre-eclampsia	3329	The level of awareness regarding conflict and violence in university students and the affective factors in Turkey	3413
<i>Zoleikha Atarod, Hamed Roohanizadeh, Marzieh Saberi, Seyyed Abbas Hashemi, Mehran Fazli</i>		<i>Seyda Dulgerler, Oguz Polat, Serap Yildirim, Serap Ozer</i>	
Risk of depression and anxiety in high school students and factors affecting it	3333	Subtypes of Interstitial cells of Cajal in normal and inflamed appendix in children.....	3418
<i>Zehra Tezvaran, Hulya Akan, Oguzhan Zahmacioglu</i>		<i>Dragoljub V Zivanovic, Mirjana Abramovic, Goran Radenkovic, Andjelka Slavkovic, Zoran Marjanovic, Verica Avramovic, Zlatko Djuric</i>	
Effects of intraoperative skin surface warming on postanesthetic recovery and shivering: A prospective, randomized, clinical trial.....	3340	The effect of intravenous pamidronate treatment for type i osteogenesis imperfecta patients have on their bone mineral density, fracture rate, and mobility	3425
<i>Salih Yildirim, Canan Baran Unal, Isa Dongel, Cevdet Duger, Ali Feyzullah Sahin, Idris Ersan</i>		<i>Zekeriya Oztemur, Hayati Ozturk, Esra Circi, Okay Bulut, Serdar Uner, Ahmet Altun, Gunduz Tezeren</i>	
Continuing education of intensive and emergency units nurses during clinical shifts	3346	Quality of family interactions and mental development of preschool children	3430
<i>Abbasali Ebrahimian, Nader Khalesi, Maedeh Tourdeh</i>		<i>Radmila Milovanovic, Gordana Budimir-Ninkovic</i>	
Attitudes of nursing students towards older people in Turkey	3351	The knowledge of teenagers about breast self-examination.....	3440
<i>Bilge Bal Ozkaptan, Birsan Altay, Huriye Demet Cabar</i>		<i>Huriye Demet Cabar, Dilay Argun Acil, Birsan Altay, Yelda Guler</i>	
Conceptual skill in physicians: An overlooked basic competency	3359	Analysis of implementation of the strategic management concept in the healthcare system of Serbia	3448
<i>Khajavi Abdoljavad, Vatankhah Soudabeh, Maleki Mohammad Reza, Barati Ahmad, Alami Ali, Heyrani Ali</i>		<i>Marko M. Mihic, Vladimir Lj. Obradovic, Marija Lj. Todorovic, Dejan C. Petrovic</i>	
The effects of self-perceived fatigue on functional mobility and balance in the community-dwelling elderly.....	3366	Effect of cigarette smoking on nasal mucociliary transport rate: Rhinoscintigraphic evaluation with using 99mTc-macroaggregated albumin.....	3458
<i>Zeliha Baskurt, Ferdi Baskurt, Celal Haydar Demir</i>		<i>Zeki Dostbil, Yusuf Dag, Abdurrahman Abakay, Salih Bakir, Cengizhan Sezgi, Ozlem Abakay, Hadice Sen</i>	
Nutritional status and possible causes of obesity in preschool children.....	3372	Frequency of ischemic stroke subtypes in relation to risk factors for ischemic stroke	3463
<i>Biljana Ilic, Zoran Igrutinovic, Mile Despotovic, Hristos Aleksopoulos, Svetlana Milovanovic, Slavica Markovic</i>		<i>Natasa Turanjanin, Mirjana Jovicevic, Ksenija Bozic, Marija Zarkov</i>	

Sadržaj / Table of Contents

Contraception use and attitudes of women and health care providers.....	3469
<i>Aleksandra Kapamadzija, Tihomir Vejnovic, Slobodana Mihaldzic Tubic, Radojka Ratkovic, Sladjana Koledin, Gordana Radeka, Vesna Kopitovic</i>	
Human ischemia modified albumin can be a predictive biomarker for the detection of peripheral ischemia duration	3478
<i>Celal Yavuz, Ahmet Caliskan, Suleyman Yazici, Oguz Karahan, Orkut Guclu, Sinan Demirtas</i>	
Case study: school experience of children with attention deficit hyperactivity disorder.....	3482
<i>Olivera Knezevic-Florice, Sladjana Zukovic, Stefan Ninkovic</i>	
Thromboelastographic comparison of the effects of different fluid preloading regimens delivered before spinal anesthesia.....	3488
<i>Irsat Ozen, Turkan Tugal, Mustafa Said Aydogan, Mehmet Ali Erdogan, Hamza Nakir, Nurcin Gulhas, Huseyin Ilksen Toprak, Mehmet Ozcan Ersoy</i>	
The reasons for sharing needle using and syringe among injection drug users in the city of Ahvaz: A qualitative study	3494
<i>Morteza Mansourian, Mahnaz Solhi, Tahereh Dehdari, Mohamad Hosain Taghdisi, Fereshteh Zamani-Alavijeh, Hadi Rahimzadeh Barzoki, Hamid Asayesh</i>	
Surgical treatment of retroperitoneal Pelvic tumors.....	3501
<i>Ljiljana Ivanovic, Srdjan Djurdjevic, Mirjana Bogavac, Dragan Nikolic, Marijana Basta-Nikolic</i>	
Serum homocysteine, folate and B₁₂ concentration in patients with coronary artery disease: A case-control study	3506
<i>Seyyed Farzad Jalali, Amir Saeed Hosseini, Zeinab Shirvani Farsani, Ali Bijani</i>	
Radiographic interpretation of the abnormalities of the follicles of impacted teeth.....	3512
<i>Branko Mihailovic, Milan Miladinovic, Milos Duka, Zoran Vlahovic, Nebojsa Mitic, Dejan Dubovina</i>	
Psychic vulnerability and the increase of crack addiction in Brazil	3517
<i>Jose Cezario de Almeida, Alberto Olavo Advincula Reis, Luiz Carlos de Abreu, Modesto Leite Rolim Neto</i>	
Endoscopic management of non-variceal upper gastrointestinal bleeding.....	3519
<i>Praveen Kumar Yadav, Zhan-Ju Liu</i>	
Evaluation of computer workstation ergonomics and prevalence of the musculoskeletal symptoms - A cross sectional study of Macedonian office workers	3532
<i>Viktorija Prodanovska-Stojcevska, Jovica Jovanovic, Tanja Jovanovska, Rozalinda Isjanovska</i>	
Comparative analysis of three different short tandem repeat multiplex system approaches in fingerprint DNA analysis.....	3538
<i>Anida Causevic-Ramosevac, Lejla Kovacevic, Dzenisa Buljugic, Mirela Dzehverovic, Jasmina Cakar, Damir Marjanovic</i>	
Instructions for the authors.....	3544

Basic assistance for mental health in Northeast Brazil

Modesto Leite Rolim Neto¹, Alberto Olavo Advincula Reis², Jose Cezario de Almeida³, Nadia Nara Rolim Lima⁴, Saulo Araújo Texeira⁴, Marina Lucena de Aguiar Ferreira⁴

¹ Faculty of Medicine of Federal University of Ceara - UFC, Juazeiro do Norte, CE, Brazil,

² Faculty of Public Health of University of Sao Paulo - USP, Sao Paulo, SP, Brazil,

³ Faculty of Medicine of Federal Campina Grande University - UFCG, Cajazeiras, PB, Brazil,

⁴ Technology to Information, narrativity, Society and Plural Identities Research Group - CNPq/UFC, Juazeiro do Norte, CE, Brazil.

Abstract

Introduction: Brazilian northeast region is historically affected by socioeconomic problems that made this region more needful for strategies regarding to psychiatric disorders assistance.

Methods: This study includes original analysis based on data of secondary level health assistance, extracted from Brazil's Hospitalar Information System, Basic Assistance Information System and Brazilian Institute of Geographic and Statistics.

Results: Between 2008 and 2010, more than two hundred million dollars were spent by Brazilian federal government to achieve better quality in the assistance for mental health in Northeast. The service network responsible for the treatment of mental disorders in primary care involves a wide range of professionals and establishments.

Conclusion: In northeastern Brazil, socioeconomic and geographic conditions contribute to a particular state of vulnerability for the development of psychopathologies. The association of primary care and an integrated network of public health, however, have improved the attention to mental disorders in this region.

Key words: Basic Assistance, Mental health, Northeast Brazil.

Background

In Brazil, the fifth world's largest country in territory extension, there are completely different regions with different profiles of mental disorders and, mainly, unequal coverage for psychosocial care¹. Brazilian northeast region is historically affected by socioeconomic problems, such as income concentration, archaic rural economy, dry weather and principally lack of efficient social-

based governmental policies. This reality made this region more needful for strategies regarding to psychiatric disorders assistance².

Brazilian Federal Constitution was promulgated in 1988, creating a public health care system (Sistema Único de Saúde – SUS). This fact determined institutional conditions to establish new health policies, including those oriented for mental health attention³. Brazilian laws were unveiled to ensure the free transit of people with mental disorders, consolidating an open and community-based model of mental health care⁴. This model is based in a network of services composed by the Centers for Psychosocial Assistance, the Therapeutic Residential Services, the Centers for Living and Culture and the specialty unities in general hospitals⁵.

Nowadays, the primary care strategies in Brazil seeks to improve health and quality of life, prioritizing actions aimed at preventing and promoting health in a comprehensive and continuous in country⁶. It has some fundamental principles: integrity, gratuity, quality, equity and social participation⁷. Family health program (Estratégia de Saúde da Família – ESF), as well as the skills of the multidisciplinary team consists in a duty to mobilize the capabilities and resources of the patient and the community, emphasizing the role of each individual as the protagonist in the solution of their problems⁸, and seeking recognition of the needs of the community, both learned from the establishment of a social bond with this, and through permanent contact with the environment in which territorial inserts, allowing the evaluation of more complex matters, including, health mental⁹.

Innovative experiences have been conducted, starting from the association between mental health and primary care, and have achieved consi-

derable success¹⁰. Although not precisely outlined, widely recognized actions to assist people with psychological distress were created in the sphere of family health care¹¹. One example is the development of actions which contributed to organize groups and activities related to the community, as the theoretical support, and regarding to the influence of social factors in those disorders¹². Is important to highlight the actions that promote an early identification of mental disorders, what should occur at this level of attention¹³.

This study aims to contextualize mental health and primary health assistance in Brazil, to describe and analyze the development status of mental health public policies, focusing the northeast region of the country and the population of children and adolescents (under the age of 19).

Methods

This article analyzes the evolution process of mental health and its care in Brazil, notably in country's northeast region and for the age-group of children and adolescents. We surveyed original data from official sources and revised studies regarding this subject in order to understand the processes involving mental health in one of the country's poorest regions.

We included, in this study, original analysis based on data of secondary level health assistance, extracted from Brazil's following databases: Hospital Information System (Sistema de Informações Hospitalares – SIS/SUS), Basic Assistance Information System (Sistema de Informação de Atenção Básica – SIAB). We also searched data from Brazilian Institute of Geographic and Statistics (Instituto Brasileiro de Geografia e Estatística – IBGE), notably those about socioeconomic indices and population amount. Information contained in these systems is publicly available on internet and refers to all nine states involved in our research, which compose the northeast region of Brazil. Official databanks have also information about all Brazilian regions, although we have discarded these additional data.

Original data about mental health and, in a more specific way, children and adolescent mental health, were complemented by a careful review of published articles. This analysis involved the

following subjects: primary and secondary health assistance models which give support to mental health, psychiatric reform, public policies and services destined to public health system users. These studies were published between 2003 and 2011 in indexed journals. We did not restrictions about language. A general reading was performed to obtain an overview if these scientific publications. This work is based, overall, in information that comes from Brazilian Ministry of Health (Ministério da Saúde do Brasil) and available on internet.

Results

Northeast is Brazil's third larger region in geographic area. Nowadays, more than 49 million people live in Northeast region, what corresponds to almost 30% of total Brazilian population, representing the second larger population, only surpassed by the Southeast region of the country, the richest and most industrialized area of Brazil.

Official investments to improve the care for mental health in northeast Brazil have increased along the years, specially concerning to national government¹⁴. Between 2008 and 2010, more than two hundred million dollars were spent by Brazilian federal government to achieve better quality in the assistance for mental health in this Brazilian region. Table 1 shows the amounts spent in this area along the last three years.

Table 1. Investment in mental healthcare: Northeast Brazil¹⁵

Year	Amount
2008	US\$ 66,977,700.00
2009	US\$ 70,750,400.00
2010	US\$ 74,900,700.00
Total	US\$ 212,633,800.00

This information shows a better distribution of resources, which has occurred in Brazilian public policies, early centralized in South and Southeast regions, and also how these public actions are oriented to these important disturbs, that are responsible for an important deficit of patients' quality of life¹⁶.

According to database of secondary level health care, which involves specialty centers, clinics and hospitals, in 2005 and 2006, Northeast region was at the second position in number of hospitalization due to psychiatric illnesses, following the Southeast

region. In the five following years, Northeast region occupied the third place, led by South and Southeast regions¹⁵. Yet analyzing data from secondary level, we see that these hospitalizations are more centralized in urban areas than in rural ones in a proportion of 3: 1, for the same referred period¹⁶.

In secondary attention, based on data about results of public health care policies in Brazil, we can highlight the performance of northeast region between 2002 and 2011 regarding to the expressive increase of the Centers for Psychosocial Assistance (Centros de Assistência Psicossocial – CAPS). One index that measures the public assistance for mental health in Brazil is the rate of CAPS unities per 100.000 inhabitants. Northeast region had the largest increase of this index in the referred period, as seen on table 2.

Table 2. Mental health assistance coverage in Northeast Brazil between 2002 and 2011¹⁷

Year	Psychosocial Assistance Centers / 100.000 inhabitants
2002	0.12
2011	0.83
2002-2011	591 %

Despite of these huge investments directed to care for mental health disorders, they still provoking substantial losses. Between 2008 and 2011, 470 deaths were registered due directly to mental disorders in northeast Brazil. Pernambuco was the state with the highest number of deaths and also presents the lowest coverage of CAPS between the surveyed states¹⁸. It is important to highlight that Bahia and Ceará, although have good coverage indicators (CAPS unities per 100.000 inhabitants), present high numbers of deaths in the period, respectively, 75 and 71 cases. This shows that CAPS creation is not sufficient to improve health indicators¹⁹. Training of health professionals involved in the treatment of these patients still extremely important.

We can also infer a substantial progress in care of mental disorders in children and adolescent in the states of northeast region. The considerable increase in the number of Centers for Psychosocial Assistance specialized in children and adolescent care (Centros de Atenção Psicossocial Infantil – CAPSi) demonstrates this phenomenon. Today there are 34 of these secondary attention unities in northeast region²⁰. But this coverage growth does

not occur uniformly within the region and there has been centralization of services in some states, such as Ceará and Bahia. This fact is extremely detrimental to the performance of health policies and, consequently, its users tend to not receive appropriate care. Therefore, these children and adolescents are exposed to a greater burden of risk factors and have a small amount of local support and treatment of their disorders²¹.

The service network responsible for the treatment of mental disorders in primary care involves a wide range of professionals and establishments from the Community Health Agent (Agente Comunitário de Saúde – ACS) to the secondary attention centers for family health (Núcleo de Assistência à Saúde da Família – NASF). In 2011, across the northeast region, ACS are present in 1,790 cities, involving approximately 40% of healthcare professionals and ensuring a coverage of 87.03% of the population. The number of NASF unities in the northeast Brazil, in the same year, reached approximately 48% of total²².

Conclusion

The national mental health policies have evolved, leading to changes, even when slight, in the profile of services and management of patients. It is undeniable that the association of primary care and the creation of an integrated network of care contribute greatly to the appropriateness of actions in mental health, valuing the multidisciplinary care of the subject in psychological distress and gradually abandoning the position of asylum care. However, it is unquestionably the persistence of failure in addressing the psychiatric patients, whether in the face of the diagnosis, treatment or rehabilitation, or by insufficient professional training, resource scarcity or lack of healthcare coverage. Government has lead important and undeniable progresses in public policies for mental health and these actions already can be inferred by the improvement in several indices, which demonstrate a strong rearrange of psychosocial care, especially in northeast region.

In northeastern Brazil, socioeconomic and geographic conditions contribute to a particular state of vulnerability for the development of psychopathologies. In general, this region follows a national

trend of expanding primary care and decreasing the availability for psychiatric beds, with a notable decentralization of the South-Southeast in benefit of North and Northeast regions. Literature presents few studies about mental disorders in northeast Brazil as a whole. The consequence is the poor availability of data and absence of an actual epidemiological profile, making the adequacy of health policy and evaluating the effectiveness of these actions with the target population.

However, is important to seek innovations for the management of patients with psychopathologies and for the improvement of the attention coverage. Some challenges remain in the field of mental health, such as improving support network, expanding diagnostic and therapeutic resources, encouraging social reintegration of the psychiatric patient, promoting joint approach to mental and socioeconomic status, training health professionals regarding to the autonomy of the subject individuals and mental patients.

Acknowledgements

This study was supported by grants the Ceará Federal University – UFC.

References

1. Silveira DP, Vieira ALS. *Mental health and primary care: analysis of a local experience. Cienc Saude Coletiva.* 2009; 14: 139-148.
2. Andrade SR, Büchele F, Gevaerd D. *Salud mental en servicios básicos de salud en Brasil. Enfermería Global* 2007; 6: 1-12.
3. Ministério da Saúde (Brasil). *Saúde mental no SUS: acesso ao tratamento e mudança do modelo de atenção.* Brasília: MS, 2006.
4. Tanaka OY, Ribeiro EL. *Mental health in primary care: ways to reach an integral care. Cienc Saude Coletiva.* 2009; 14: 477-486.
5. Ministério da Saúde (Brasil). *Portaria nº 1.169, de 7 de julho de 2005.* Brasília: MS, 2005.
6. Figueiredo MD, Campos RO. *Mental health in the primary care system of Campinas, SP: network or spider's web? Cienc.saudecoletiva* 2009; 14: 129-138.
7. Neves HG, Lucchese R, Munari DB. *Mental health in primary attention: needed constitution of competences. Rev. bras. enferm.* 2010; 63: 666-670.
8. Antonacci MH, Pinho LB. *Living with mental illness: the family perspective on primary care. Rev Gaúcha Enferm.* 2011; 32: 136-42.
9. Kessler RC. *The effects of stressful life events on depression. Annu Rev Psychol.* 1997; 48: 191.
10. Kendler KS, Gardner CO, Prescott CA. *Personality and the experience of environmental adversity. Psychol Med.* 2003; 33: 1193-1202.
11. World Health Organization. *The Global Burden of Disease: 2004 (Update 2008).* Geneva: WHO, 2008.
12. Lopes CS, Foerstein E, Chor D. *Eventos de vida produtores de estresse e transtornos mentais comuns: resultados do Estudo Pró-Saúde. Cad Saude Publica.* 2003; 19: 1713-20.
13. Ministério da Saúde (Brasil), Secretaria de Atenção à Saúde. *Saúde mental no SUS: acesso ao tratamento e mudança do modelo de atenção, Projetos, Programas e Relatórios Série C.* Brasília: MS, 2007.
14. Ministério da Saúde (Brasil), Secretaria de Atenção à Saúde, Departamento de Atenção Básica. *Cadernos de Atenção Básica, Textos Básicos Série B.* Brasília: MS, 2009.
15. DATASUS. Ministério da Saúde/Secretaria de Atenção à Saúde (SAS): *Sistema de Informações Hospitalares do SUS (SIH/SUS).* Brasília: MS, 2011.
16. Ministério da Saúde (Brasil), Secretaria de Atenção à Saúde. *Saúde mental e atenção básica: o vínculo e o diálogo necessários.* Brasília: MS, 2006.
17. DATASUS. Ministério da Saúde/Secretaria de Atenção à Saúde (SAS): *Sistema de Informações sobre Mortalidade (SIM/SUS).* Brasília: MS, 2011.
18. DATASUS. Ministério da Saúde/Secretaria de Atenção à Saúde (SAS): *Sistema de Informações Hospitalares (SIH/SUS).* Brasília: MS, 2011.
19. World Health Organization. *Primary prevention of mental, neurological and psychosocial disorders.* Geneva: WHO, 1998.
20. Collins PY, Patel V, Joestl SS, March D, Insel TR, Daar AS. *Grand challenges in global mental health. Nature.* 2011; 475: 27-30.
21. Reinaldo AMS. *Mental health in the basic attention as a historic process of community psychiatric evolution. Esc Anna Nery Rev Enferm* 2008; 12: 173 - 8.
22. Ferriolli SHT, Marturano EM, Puntel LP. *Family context and child mental health problems in the Family Health Program. Rev. Saúde Pública* 2007; 41: 251-259.

Corresponding Author
Modesto Leite Rolim Neto,
Universidade Federal do Ceara,
Juazeiro do Norte – CE,
Brazil,
E-mail: modestorolim@yahoo.com.br

The study on physiological indexes of exam anxiety in medical students

Abbas Mosoudzadeh¹, Nasrin Bali-Lashak¹, Sara Asadpour², Reza Alizadeh-Navaei³

¹ Psychiatry and Behavioral sciences research center, Mazandaran University of Medical Sciences, Iran,

² Tehran university of Medical Sciences, Iran,

³ Mazandaran University of Medical Sciences, Iran.

Abstract

Background and Objective: Exams are used as the most important tool for the educational progress in all of the educational levels. Success or failure in an exam usually has a crucial effect in a person's future; consequently it brings about anxiety for most of the people's potentiality. The purpose of this study is to assess the physiological indices of anxiety in the medical students.

Material and methods: This analytical study was carried out on 46 medical students of Mazandaran University of Medical Sciences. To measure physiologic indices, including blood pressure, pulse, and temperature were performed on students before and after physiological exam and also blood test for the study of blood indices (cortisol and CBC) before exam was performed and *spiel burger* trait-state anxiety questionnaire was used to assess the anxiety rate. Statistical studies were done by descriptive statistics and paired t-test.

Findings: From physiological indices, rate of heartbeat increased significantly ($P=0.01$) after exam. The study of blood indexes also indicated that cortisol level and the other blood indices except (eosinophil, monocyte and lymphocyte) were normal. According to assessment of *spiel burger* questionnaire, the relation of trait – anxiety was significant ($P=0.02$) before and after exam in students. So that 4% of the students had strong trait-anxiety (hidden) before the exam and 11% of them had strong trait-anxiety after the exam.

Conclusion: The study of physiological indices of test anxiety in medical students indicated a significant difference on trait-anxiety (hidden) before and after exam, and difference was also significant on tachycardia of test subjects after exams. Along this way, the education of contrastive guide lines seems essential in student's anxiety reduction.

Key words: Physiological indices, exam anxiety, Medical students.

Introduction

Exam anxiety is excessive worry about the function in an exam. It is an unpleasant emotional reaction to the assessment situation. This emotion is determined by mental feeling from tension, anxiety and automatic nervous system excitement (1). Response to stress is due to activity of different axes such as hypothalamus axis, hypophysis adrenal (2).

Exam anxiety is a kind of mental preoccupation that mostly leads to negative cognitive assessment, lack of concentration and unpleasant physiological reactions (3). Ergene expresses exam anxiety as a scientific elements and concept for a series of conceptual, physiological and behavioral responses that accompanies worrying about negative repercussions or assessing situations (4).

According to the results of the different research, the outbreak rate of exam anxiety has been reported from 10% to 30% (5). In addition, emotional concept of exam anxiety accompanies with physical signs and tension that leads to digestive disorders, increase in heartbeat, blood pressure and hypothermia (6-8).

In a test that was carried out on 11 graduates, it was observed that students who had more stress before the exam, had cortisol increase. Students, who got lower grades, had more stress and higher cortisol level (9).

Psychological studies of the blood samples from 37 medical students before and during exam indicated that medical college exams are adequately stressful to change the production of blood cells including increase in neutrophil and heat oblast while there is reduction in eosinophil, lymphocyte, monocyte and basophile. On the other hand, stress can change the parameters of blood cells in healthy people (10).

In a study carried out to assess the anxiety rate of the morphological and physiological effects of the chronic saline administration, signs from corti-

sol level increase, thymus and spleen suppression, and cognitive activities have been observed that are stress signs (11).

In addition to the carried out studies, many case reports were done. One case report carried out on a 48-year-old patient indicated that anxiety increase caused the rise and release of adrenal simpatico hormones, and heartbeat and systole pressure rises (12).

In a far-sighted study that dealt with the stress rate and educational function of freshmen at medical university, 121 students were surveyed before the start of the class and again 8 month later. The results indicated that the academic data before and during university did not have a significant relation with stress responses (13).

Another study compared emotional and physiological responses and assessed their relational control with individual characters. In that assessment, physiological responses included heart system activity, adrenocortical system and body immune system. Study was done on 11 women and 12 men. The results indicated that people with higher self confidence had more flexibility and adaptability to the situations than people with lower self confidence (14).

In a study, which examined the temperature, the (oral) temperature average in medical students before the exam was 108 degrees Fahrenheit that was higher than the lab conditions. This indicates the emotional hyperthermia among students and the temperature before the exam was practically same among the students with high grades and the students with low grades (15).

Various studies examined the effect of stress such as exam stress on activity of different parts of human body including automatic nervous system and increase in pulse rate (16-18).

About the effect of exam stress on the axis activity of hypothalamus, hypophysis and adrenal (cortisol changes), several studies were carried out in Iran and abroad (19-22). However, most of the studies worked only on one of the physiological factors, while exam anxiety causes various physiological responses in human. Assessment and measurement of these responses provides the possibility of the assessment of conditions (initiators), (predisposes) and (maintainers).

Anxiety tests are created in many body parts, but 4 body parts have more sensitivity. These

parts include heart and blood vessels, axis of hypophysis – adrenal of blood cells and temperature control mechanism (23). Studying medicine is often associated with prolonged state of having to cope with multiple stressors (24). Therefore, with current study, we not only examine these indexes for recognition of conditions (initiators), (predisposes) and (maintainers), and possibility of confronting with them, but also gain crucial results.

Material and Methods

This was a descriptive study that 46 medical students of Mazandaran medical university were chosen in 2008 to participate in the study. Consequently and explanatory meeting was held, in which test subjects were informed from the project works, the ideal goals and the administrative steps. Then each of the test subjects received one ID code that was identified with this code until the end of the test.

Students were chosen randomly and according to a study recall. Samples of 46 students gained according to the sample selection in assurance limit of 95% and ratio of effect size to SD is 90%.

In the current study, measurement of anxiety hyperthermia was examined to assess the temperature control mechanism.

Test subjects' temperature rate was measured and recorded through the oral thermometer before entering the meeting. The same procedure was carried out after the exam. Then to measure the blood pressure, each student's blood pressure was recorded in an auditory way, after that heartbeat was recorded for 3 minutes and a half, and the same procedure was done after the test, too.

Blood – sampling was done only in one-step (level) because cortisol rate does not change until long time and students refused the blood – sampling after the exam. In the study, blood indexes, hemoglobin rate, Hematocrit, Hematoblast, Neutrophil, Eosinophil, Monocyte and lymphocyte. To achieve this goal, 10 ml of blood was taken from vein Z hours before the test at the exam salon. In order to prevent the fall of blood pressure, test subjects were given a glass of diet soda each to drink after blood sampling. Blood was gathered in the plastic containers with anti-clotting materials and was placed into ice container. Then the samples were transferred to a physiological lab. In addition

on, immediately after transfer to Zare hospital lab, the samples were under centrifuge with 1000 rpm for then minutes.

Student's anxiety rate was measured before and after the exam with the use of spiel Berger trait – state anxiety questionnaires (25). The above-mentioned questionnaire included 40 articles that 20 are related to the hidden anxiety. Stability of the above – mentioned scales were according to norm – finding study for the clear anxiety was 91% and for the hidden anxiety was 90%.

The clear and hidden anxiety of test subjects was classified into six levels according to the earned marks – low level (20 to 31), normal to down (31 to 42), normal to up (43 to 52), almost serious (53 to 62), serious (63 to 74) and too serious (73 and more).

This questionnaire had 40 questions with multiple choices of (almost) never – sometimes – often- almost always). For the state – anxiety, mean score and deviation standard were respectively 41.807 and 10.98. For the trait – anxiety, mean score and divination standard were respectively A2.165 and 9.77. For the final change, mood description and subject score were used.

It should be mentioned that for the observation of the medical principles before the start of this study and after holding the explanatory meeting, the volunteer students were chosen at first and then the subjects were asked to give letters of satisfaction for cooperation in this project.

Finally, the raw data analyzed using SPSS software, to see if the statistical sample is normal; kolmogorov – smirnov (KS) test was used, as well. Statistical test of paired sample tests were used due to normality of society. Pierson coefficient correlation was used to determine the relation between the variables.

Findings

From the total 46 under study subjects, 41% were boys and 59% were girls.

Table No.1 shows correlation rate to studied variables before and after exam, about hyperthermia rate of anxiety after the normality determination by the KS test. Subjects' average temperature changes before and after exam was more than (-0.07) in male subjects and less than (0.02) in the female subjects .but this difference was not

significant statistically ($P=0.56$) and hyperthermia changes of anxiety were not also significant in all of the subjects ($P= 0.82$).

Table 1. Correlation coefficient of parameter before and after exam

Parameters	Y	Sig (2-tailed)
Hyperthermia	0.33	0.8227
Systole pressure	0.247	0.098
Diastole pressure	0.152	0.313
Heartbeat	0.377	

The current study indicated that the mean of changes of systole blood pressure was not statistically significant ($P= 0.3$) in all the students before and after the exam. In addition, the difference between girls and boys from the view of change rate in male students before and after exam was less and it was more in female students. However, the difference of these two groups was not statistically significant ($P=0.38$).

Considering the changes in diastole blood pressure, the mean of changes in the boy subjects was less (1.5) and the rate of changes in diastole blood pressure was more (74), in the girl subjects. Nevertheless, this difference was not statistically significant ($P=0.63$). The mean of changes in diastole blood pressure was not statistically significant ($P=0.3$) in all of the students before and after the exam.

Pierson test (Table 1) showed the rate of changes in the heartbeat before and after exam was significant in all of the students ($P=0.01$, $r=0.37$). The mean of heartbeat changes was (5.4) in male group and it was (0.07) in the female subjects and the difference was statistically significant ($P=0.013$).

The study of blood indexes indicated that the cortisol rate and other blood indexes (except Eosinophil , monocyte and lymphocyte) was normal, and the difference was significant ($P=0.16$) in these two materials.

Table 2 indicates the difference of boys and girls from the view of anxiety level with the studied components by the spiel Berger trait –state questionnaire. The mean of the trait anxiety questions before and after the exam was less than 0.11 for boy students and it was more (-0.16) for girl subjects and the difference was not statistically significant ($P=0.4$); the mean of trait – anxiety questions was not statistically significant ($P=0.66$) before and after exam for all of the students.

Table 2. The difference of boys and girls from the view of anxiety level with the studied components

Parameter	Before the exam M $\pm$ SD	After the exam	Sig (2-tailed)
Trait –anxiety	2.22 $\pm$ 0.791	2.29 $\pm$ 1.078	0.667
State –anxiety	2.23 $\pm$ 0.792	2.17 $\pm$ 0.972	0.781

The mean of state-anxiety questions was less for boy subjects (0.23) before and after the exam and it was more for girl subjects (-0.08), and the difference was not statistically significant ($P=0.37$).

The mean of state – anxiety questions was not statistically significant ($P=0.78$) before and after the exam for all of the students.

The data of table 3 indicates that correlation coefficient of the trait – anxiety was significant before and after the exam through the Pierson test. *Table 3. Correlation coefficient of parameters after and before the exam*

Parameter	R	Sig (2-tailed)
Trait-anxiety	0.36	0.02
Trait – anxiety	0.21	0.18

Based on the findings of table 4, regarding anxiety level of (hidden) trait –anxiety rate before the exam, the most of frequency rate (48.9%) was in the level of average to down (42-32) before the exam, and the most of frequency rate (45%) was in the level of average to down. The least of frequency rate in the hidden anxiety before the exam

was related to almost serious anxiety (4.4%) that increased to (11.1%) after the exam.

Table 5 indicates that in study of questionnaire of (trait-state) anxiety, 71%.of students had before – the – exam – anxiety of low and average to down that the state – anxiety of this group decreased to 69% after the exam and almost 2% of the subjects had serious state anxiety before and after exam.

Discussion

The results of this study indicated that the hyperthermia rate of anxiety in medical students does not change before and after the exam. This result is identical to the results of the other researchers such as Comunian(6) and Gjesme(7). They showed that exam anxiety causes tension and increases hyperthermia.

In addition, in the Muldoon's study (26), temperature degree of 22 subjects during 15 and 60 minutes before the annual psychological exam was 6% more than this number during 2 or 3 minutes before or after the exam.

Table 4. Frequency distribution of trait anxiety for the subjects

Parameters	Trait-anxiety before the exam		Trait –anxiety after the exam	
	Frequency	Percent	Frequency	Percent
Low	9	20	9	21.4
Average to down	22	48.9	19	45.2
Average to up	12	26.7	7	16.7
Almost sever	2	4.4	5	11.9
Severe	0	0	2	4.8
Total	45	100	42	100

Table 5. Frequency distribution of anxiety for the subjects

Parameters	Trait-anxiety before the exam		Trait –anxiety after the exam	
	Frequency	Percent	Frequency	Percent
Low	8	17.8	10	22.8
Average to down	24	52.3	19	45.2
Average to up	12	26.7	8	19
Almost serious	0	0	4	9.5
Severe	1	2.2	1	2.4
Total	45	100	42	100

These findings indicate that despite the response appearance to anxiety in all physiological systems, it is the most suitable of all, considering the performance ability, decrease of pessimism and determination of temperature increase rate.

The statistical analysis indicated that there is a significant relation between the rate of heartbeat changes and exam anxiety in all of the students before and after exam. When there is stress, heartbeat increase and pulse are the physiological response of body; consequently, the achievement to such a result is justifiable, fuller and et al. (27) also indicated that psychological aspects such as character structure influence on heart response rate and heartbeat changes.

The current study also demonstrated that the average of heartbeat changes in the group of female students was more than the group of male students that such a difference has been confirmed in various studies (28-30).

However, such a result is predictable because girls are usually more emotional and emotional people show more sensitivity to issues such as an exam. Because the cortisol density is measured to assess anxiety response of hypophysis adrenal axis and hypophysis axis –adrenal – is influenced by new factors and negative emotions, it is mentioned as a crucial index for anxiety (10).

The results of the carried out studies on cortisol, before the subjects' exam indicated that its rate in both genders (boys and girls) was normal. In as much as the cortisol rate is rhythmic, most researches that have been done since 1980 and later have reported the increase in cortisol rate before and during the exam while almost none of them have not measured the cortisol rate before and after the exam (31).

Some current researches demonstrated that a few minutes after anxiety, MCH and RDW change in number of red blood cells, hematocrit and hemoglobin after the anxiety gained from the solution of the problem 50 that increase has been reported in number of red blood cells, hematocrit and hemoglobin (10).

Some researches indicated that anxiety has a negative effect on the immune system and indexes but these effects will appear on the long-term, while its short term influence, based on the carried-out research, is increase in the activity of the

white blood cells (32), that the white blood cells were studied in this research. The results obtained from the blood indexes showed in the current study that the whole blood indexes were normal except eosinophil, monocyte and lymphocyte before the exam. While the research results of Qureshi and et.al (10) showed that exams incur change in the production of blood cells (increase in neutrophil and platelet and decrease in (eosinophil, monocyte, lymphocyte and busophil).

The current study results showed that the rate of systole and diastole changes was not statistically significant in the medical students. This result contradicts with the results of other researchers such as Liberty and et.al (8), because they showed that the exam anxiety in subjects accompanied with the increase in the heartbeat and blood pressure. And also a research that was carried out by Nourjah and et.al (32) on 237 students, distinguished that systolic and diastole blood pressure of the first and last exam has changed compared to the normal conditions and it has increased. In addition, the changes were statistically significant. The contradiction in the current research results with the after researches might be due to the difference in the number of samples, educational major, sampling location and society or the time of project performance.

In this research, the difference of trait anxiety rate with spiel Berger questionnaire was statistically significant that corresponds with the study of Keogh and et.al (33). In this research, the exam anxiety was called trait anxiety that examines reflect when they are under cognitive changes and this study is correspondent with a research carried out by Paragament and et.al (34). In the current study, it has also been determined that the mean of trait and state before and after the exam was less in male students and was more in female students that showed similarity with the study of Zeidner and et.al (35). Moreover, Ferrando and et.al (36), because they gained the female anxiety rate more than the males in the analysis of the gender role in the exam anxiety, while the study contrasted with the study carried out by Mwamwedna and et.al (37).

From all of the findings as confirmation for the results of the similar studies, it can be concluded that the exam anxiety is effective on the physiological indexes (heartbeat changes) and their trait anxiety was significant before and after the exam.

Therefore, the education of contrastive guidelines seems necessary for the decrease of the student anxiety.

References

- Guida, FV, Ludlow, LH. A cross- cultural study of anxiety. *Lowth* 1989; 20; 178- 190.
- Rohleder N, Schommer NC, hellhammer DH, Engel R, Kirschbaum C. Sex differences in glucocorticoid of proinflammatory cytokine production after psychosocial stress. *Psychosom Med* 2001; 63(6):966-72.
- Sarason IG. *Stress and anxiety*. 2nd ed, New York, Hemisphere/ Hastead, 1975.
- Ergene T. Effective intervention of test anxiety reduction. *School Psychology* 2002;4: 313- 328.
- McRenolds RA, Morris, RJ, Kratochwill, TR. *Cognitive- Behavioral Approaches in Educational Setting*. 1983: New York, Guilford Press.
- Comunian AL. Anxiety, cognitive interference and school performance of Italian children. *Psychol Rep* 1993; 73 (3pt 1): 747- 54
- Gjesme T. Worry and emotionality components of test anxiety in relation to situational and personality determinants. *Psychol Rep* 1983; 52(1): 267-80.
- Liebert RM, Morris LW. Cognitive and emotional components of test anxiety: a distinction and some initial data *Psychol Rep* 1967; 20(3):975-8.
- Ng V, koh D, Chia SE. Examination stress, salivary cortisol, and academic performance. *Psychol Rep* 2003; 93(3 Pt 2): 1133-4.
- Qureshi Faiyaz, Jane Alam, masood Ahmad Khan and Ghazala Sheraz Effect of Examination stress on blood cell parameters of students in a Pakistani medical college. *J Ayub Med Coll Abbottabad* 2002; 14(1):20-22
- Kondashevskaya MV, Nikolskaya KA. Problem of controls in physiology and pharmacology: psychophysiological and morphofunctional effects of chronic saline administration. *Biology Bulletin* 2008; 3:56- 63.
- Deva C, Bansal S, Gombar S. Ventricular Tachycardia encountered in the pre-induction period in an anxious patient case reports 2000.
- Stewart SM, Lam TH, Beston CL, et al. A Prospective Analysis of Stress and Academic Performance in the first two years of Medical School. *Med Educ* 1999; 33(4): 243- 50.
- Institute of psychology, university of Regensburg, federal republic of Germany psychological and physiological. Responses during an exam and their relation to personality characteristics. *Psychoneuroendocrinology* 1997; 22(6):423-41
- Universidad de los ande, merida, Venezuela Emotional hyperthermia and performance in humans. *Physiol Behav* 1995; 58(3): 615-8.
- Flin TV, England BY. Social economics of childhood glucocorticoid Stress response and health. *Am J phys Anthropol*. 1997; 102 (1): 33-53
- Rohrmann S, Netter P, Hennig R, Hodapp V. Repression- Sensitization, gender, and discrepancies in psychobiological reactions to examination Stress. *Anxie Stress Cop*, 2003. 16(3): 321- 329.
- Sakuragi S, Sugiyama Y. Interactive effects of task difficulty and personality on mood and heart rate variability. *J Physiol Anthropol Appl Humman Sci*. 2004; 23(3):81-91
- Al-Ayadhi LY. Neurohormonal changes in medical students during academic stress. *Ann Saudi Med* 2005, 25(1): 36-40
- Lacey K, Zaharia MD, Griffiths J, Ravindran AV, Merali Z, Anisman H. A prospective study of neuroendocrine and immune alterations associated with the stress of an oral academic examination among graduate students. *Psychoneuroendocrinology* 2000; 25(4):339-56.
- Krahwinkel T, Nastali S, Azrak B, Willershausen B. the effect of examination stress conditions on the cortisol content of saliva a study of students from clinical semesters *Eur J Med Res* 2004; 9(5) 256- 60.
- Harris A, Martin BJ. Increased abdominal pain during final examinations. *Dig Dis Sci* 1994; 39(1): 104- 8.
- Spangler G. psychological and physiological responses during an exam and their relation to Personality characteristics. *Psychoneuronendocrinology* 1997; 22(6):423- 41.
- Jevtic M, Backovic D, Zivojinovic-Ilic J, Maksimovic M, Bjelanovic J. Burnout syndrome in medical students during clinical training. *HealthMED* 2012; 6(2):571-577
- Spielberger C D, Vagg PR. *Test anxiety: theory, assessment and treatment*. Taylord Franeis Washangton, DC,US;XV.(1995).
- Muldoon, M.F., Herbert, T.B. Patterson, et al. Effects of acute psychological stress on serum lipid levels, hemoconcentration, and blood viscosity. *Archives of internal medicine* 1995; 155:615- 620.

27. Fuller B. *The effects of stress anxiety and coping style on hearth rate variability. Inter journal of psychophysiology* 1992; 12:81- 86.
28. Kudielka BM, Buske- kirschbaum A, hellhammer DH, Kirschbaum C. *Differential heart rate reactivity and recovery after psychosocial stress (TSST) in healthy children younger adults, and elderly adults: the impact of age and gender. Int J Behave Med* 2004; 11(2): 116-21.
29. Lindfores P, Lundberg U. *Is low cortisol an indicator of positive health? Stress and Health* 2002; 18: 153-160.
30. Polk DE, Cohen S, Doyle WJ, Skoner DP, Kirschbaum C, *State and triat affect as predictors of salivary cortisol in healthy adults. Psychoneuroendocrinology.* 2005; 30(3): 261-72.
31. Maes M, Vander Planken M, Van gastel A, et al. *Influence of academic examination stress on hematological measurements in subjectively healthy volunteers. Psych Research* 1998; 80:201- 212.
32. Noorjah P, Gharegozli Z. *The survey of exam induced stress on blood pressure in students of dormitory Hesarak. Basic Medical Sciences* 2002; 15(1):32-42. [Persian]
33. Koegh E, French CC. *Test anxiety evaluative stress and susceptibility to distraction from threat. European journal of personality* 2001; 15(2) 123- 41.
34. Paragament KJ. *The psychology of religion and coping.* New York: Guilford press; 1997.
35. Zeidner M, Safir MP. *Sex, ethnic and social differences in test anxiety among Israeli adolescents. J Genet Psychol* 1989; 150(2): 175- 85.
36. Fernando PJ, Varea MD, Lorenzo U. *A psychometric study of the test anxiety scale for children in a Spanish sample. Pers Individ Dif* 1999; 27(1):37- 44.
37. Mac Donald SA. *The prevalence and effects of test anxiety in school children Educational psychology* 2001; 21: 89- 101.

Corresponding Author

Nasrin Bali-Lashak,

Psychiatry and Behavioral sciences research,

Mazandaran University of Medical Sciences,

Sari,

Iran,

E-mail: nbali57@yahoo.com

Arterial elasticity measurement in patients with Behcet's disease

Hakan Ucar², Kemal Karaagac¹, Osman Akin Serdar³, Zeynel Abidin Yetgin², Yusuf Akturk⁴, Esra Ugurlu Karaagac⁵, Hayriye Saricaoglu⁶

¹ Bursa Postgraduate Hospital, Department of Cardiology, Turkey,

² Bursa Sevket Yilmaz Postgraduate Hospital, Department of Cardiology, Turkey,

³ Uludag University Faculty of Medicine, Department of Cardiology, Turkey,

⁴ Bursa Acibadem hospital, Department of Cardiology, Turkey,

⁵ Bursa Bahar hospital, Department of Biochemistry, Turkey,

⁶ Uludag University Faculty of Medicine, Department of Dermatology, Turkey.

Abstract

Behcet's syndrome is a chronic, multisystem disorder characterized by recurrent oral and genital ulceration, skin lesions and uveitis. In addition, 25% of patients develop vascular complications, which may include superficial thrombophlebitis, deep vein and arterial thrombosis and arterial aneurysm formation. Pulse wave velocity (PWV) is an important factor in determining cardiovascular mortality and morbidity. It is an index of arterial wall stiffness and inversely related to the arterial distensibility. In this study we investigated the arterial distensibility in Behcet's Disease (BD) by PWV. We studied 50 patients with BD and 20 healthy subjects without known cardiovascular disease. Arterial distensibility was assessed by All patients underwent pulse wave analysis (HDI/Pulse Wave model CR-2000) to determine large and small vessel compliances. Large arterial elastisite index (LAEI) and small arterial elastisite index (SAEI) of the radial artery were determined from an internal algorithm based on diastolic decay features of the calibrated radial pulse contour using a modified Windkessel model. The mean ages, systolic blood pressure, diastolic blood pressure, large arterial elastisite index (LAE), small arterial elastisite index (SAE) of Behcet's disease and control subjects were 37 ± 8.323 and 37 ± 7.984 years, 125.8 ± 3 and 124.3 ± 11.4 mmHg, 68.5 ± 7.7 and 68.5 ± 7.7 mmHg, 13.3 ± 3.6 and 13.6 ± 3.64 mL/mm Hg X 10, 5.2 ± 2.43 and 6.01 ± 2.6 mL/mm Hg X 100 respectively. Differences between all parameters studied were not found to be statistically significant ($p > 0.05$). Furthermore, in patients group there were no significant correlation between disease duration and LAEI(C1) and SAEI(C2) ($p = 0.267$

and $p = 0.456$, respectively). Eventually, no significant correlation was shown between increase in systemic involvement, LAEI and SAEI values ($p = 0.447$ and $p = 0.345$, respectively).

In this study, it was shown that Behcet's disease did not change arterial stiffness parameters used as a strong indicator of atherosclerosis. Further, it was determined that disease duration and increase in systemic involvement did not alter arterial stiffness parameters.

Key words: Behcet disease, endothelial dysfunction, arterial stiffness.

Introduction

Behcet's Disease (BD) is a chronic, multi-system disorder characterized by recurrent oral and genital ulceration, skin lesions and uveitis¹. A wide spectrum of clinical features is observed, including involvement of the ophthalmic, musculoskeletal, vascular, central nervous, and gastrointestinal systems. Diverse vascular complications, such as deep vein thrombosis, myocardial infarction, arterial aneurysm, and arterial thrombus formation have been noted in patients with BD in about 20% to 35% of cases, predominantly in male patients and those with venous lesions².

The etiologic mechanisms underlying vascular disease in Behcet's syndrome are not well understood. Histopathologic studies have demonstrated that the predominant lesion is vasculitis, affecting both the vessel wall and perivascular tissues¹. The histopathological features are mainly characterized by vasculitis, with prominent neutrophil and monocyte infiltration in perivascular lesions with or without fibrin deposition in the vessel wall³. Although the

pathogenic mechanism of vascular involvement in BD is under investigation, endothelial cell dysfunction is thought to play an important role in the development of these lesions⁴⁻⁵. Endothelial dysfunction leading to abnormal coagulation or fibrolytic activity and impaired brachial artery flow-mediated dilatation has been demonstrated in BD. Because flow-mediated dilatation is endothelium-dependent and is largely controlled by the release of endothelial nitric oxide (NO), an impairment in endothelium-dependent flow-mediated dilatation suggests a decreased endothelial NO activity⁶. This lack of activity may contribute to the vascular lesions often seen in BD. In addition, endothelial NO has been found to directly regulate large artery stiffness *in vivo*⁷⁻⁸. Arterial stiffness is a reliable and strong independent predictor of subsequent cardiovascular events and mortality, it may be closely related to the process of atherosclerosis⁹⁻¹⁰. Since stiffened arteries transmit pulse waves faster than do the more elastic blood vessels, pulse wave velocity (PWV) is an ideal indicator of arterial stiffness. In addition, arterial abnormalities may be attributed to functional changes like endothelial dysfunction and also structural alterations such as atherosclerosis¹¹⁻¹². Acute systemic inflammation and chronic systemic vasculitis are noted to be associated with endothelial dysfunction¹³⁻¹⁴. Moreover, inflammation is known to be an important risk factor for future cardiovascular events¹⁵.

This study investigated the arterial stiffness of different arterial regions in BD patients and we then assessed whether arterial stiffness was affected by the clinical parameters of BD.

Patients and Methods

This study included 50 patients with BD who fulfilled the International Study Group (ISG) criteria¹⁶, along with 20 healthy controls matched to the patients for age, sex, blood pressure, heart rate, height, and total cholesterol and glucose levels. The frequency of smokers, if any, was also taken into account. Exclusion criteria were a previous history of coronary artery disease, myocardial infarction or stroke, arrhythmias, infectious diseases, neoplasm, renal or liver failure, alcohol abuse, and smoking or recent smoking history (quit smoking during the previous 12 months). Hypertension (defined by

blood pressure > 140/90 mm Hg or the current use of antihypertensive medications), history of high hyperlipidemia (LDL cholesterol > 160mg/dL) or obesity (body mass index > 30 kg/m²) and diabetes mellitus (fasting glucose $\geq$ 140mg/dL) were also considered as exclusion criteria.

At examination, the presence of two or more of the following Behcet's clinical features was considered as active disease: oral ulceration, genital ulceration, skin lesions, ocular lesions, active major vessel disease, and active major organ involvement including active gastrointestinal or neurological lesions. During the course of the disease, the presence of one or more of the following clinical features defined severe disease¹⁷: posterior uveitis or retinal vasculitis, gastrointestinal ulcerations with bleeding or perforation, major organ involvement, and major vessel involvement. In addition, BD patients with venous or arterial occlusive diseases or arterial aneurysm were considered as having vascular lesions; however, those with superficial thrombophlebitis were not considered as such. The duration of the disease in the BD group was calculated from the time from which the ISG criteria were fulfilled to the time of examination. The mean of this time period was 5.6 ± 4.1 years.

Using standard laboratory methods, the levels of total cholesterol and glucose were measured with fasting blood samples from all subjects. The study was approved by the Hospital Ethics Committee, and informed and written consent was obtained from each subject.

Measurements of PWV

PWV was measured in the morning with the patient in a supine position after 15 minutes of bed rest in a quiet room, following 12-hour abstinence from smoking, alcohol and coffee consumption. A single trained observer performed all the measurements. All patients underwent pulse wave analysis (HDI/Pulse Wave model CR-2000) to determine large arterial elastisite index (LAEI, C1) and small artery elastisite index (SAEI, C2). Large (C1) and small (C2) vessel compliances of the radial artery were determined from an internal algorithm based on diastolic decay features of the calibrated radial pulse contour using a modified Windkessel model.

Statistical analysis

Statistics were obtained using the ready-to-use program of SPSS version 13.0. Two independent variables were compared by means of the Student's *t*-test. If normality assumption was violated non-parametric Man-Whitney U was used for continuous variables. The categorical data were analysed using the chi-square test, Bivariate correlations between two continuous variables were evaluated using the Pearson correlation coefficient when indicated. All of the values are expressed as mean±standard deviation; $p < 0.05$ was accepted as statistically significant.

Results

Clinical and biochemical characteristics. The mean time of disease duration was 5.6 ± 4.1 years. Table 1 summarises Clinical features of 50 patients with Behcet's disease. Oral aphthae (in 29 patients, %42), genital ulcers (in 5 patients, %10), erythema nodosum (in 7 patients, %14), uveitis (in 9 patients, %18), arthritis (in 17 patients, 34%), thrombophlebitis (in 2 patient, %4), and neurologic involvement (in 2 patient, %4) were detected over the entire disease duration. were detected over the entire disease duration. Thirty-two of the patients were on therapy with colchicine, four were on immunosuppressive therapy, and eighteen were on corticosteroid.

Table 2 summarises clinical features and cardiovascular variables of the study group. No differences between patients with BD and controls were found for mean age, sex ratio, height, systolic and diastolic blood pressure, serum glucose, and cholesterol levels, large arterial elastisite index(LAE), small arterial elastisite index(SAE). Furthermore, in patients group there were no significant correlation between disease duration and indeces of arterial elastisite (LAEI - SAEI) ($p=0,267$ and $p=0,456$, respectively)(figure 1-2). Eventually, no significant correlation was shown between increase in systemic involvement and LAEI and SAEI values ($p=0,447$ and $p=0,345$, respectively)(figure 3-4).

Table 1. Clinical features of patients with Behcet's disease

Clinical features	Number of patients %
Oral ulcerations	29 (%42)
Genital ulcerations	5 (%10)
Erythema nodosum-like lesions	7 (%14)
Ocular lesions	9 (%18)
Peripheral arthritis	17 (%34)
Thrombophlebitis	2 (%4)
Central nervous system lesions	2 (%4)
Active disease	10 (%20)
Severe disease	8 (%16)
Immunosuppressant use	5 (%10)
Corticosteroid use	18 (%36)
Cholsisin	32 (%64)

Table 2. Comparisons of the demographic data, laboratory values and cardiovascular parameters between patients with Behcet's disease and the controls

	Behcet's group (n: 50)	Control group (n: 20)	p value
Age (year)	$37 \pm 8,323$	$37 \pm 7,98$	NS
Gender (man/female)	25/25	11/14	NS
Height (cm)	$1,65 \pm 0,008$	$1,64 \pm 0,008$	NS
Weight (kg)	$67,48 \pm 12,6$	$70,4 \pm 13,1$	NS
Body mass index(kg/m ²)	$24,48 \pm 4,2$	$25,8 \pm 3,2$	NS
Systolic BP (mm Hg)	$120,5 \pm 9,7$	$124,3 \pm 11,4$	NS
Diastolic BP (mm Hg)	$68,5 \pm 7,7$	$72,3 \pm 8,1$	NS
Serum glucose (mg/dL)	$85,2 \pm 9,5$	$80,9 \pm 12,4$	NS
Triglyceride(mg/dL)	$110,04 \pm 27,06$	$107,2 \pm 35,8$	NS
Total cholesterol (mg/dL)	$166,8 \pm 26,5$	$176,8 \pm 33,1$	NS
HDL-cholesterol (mg/dL)	$48,6 \pm 5,2$	$51,9 \pm 10,6$	NS
LDL-cholesterol (mg/dL)	$96,9 \pm 23,4$	$102,3 \pm 25,5$	NS
LAEI(C1)(cm ³ mmHg ⁻¹)	$13,3 \pm 3,16$	$13,6 \pm 3,64$	0,45
SAEI(C2)(cm ³ mmHg ⁻¹)	$5,2 \pm 2,43$	$6,01 \pm 2,6$	0,21

NS, nonsignificant; HDL, high-density lipoprotein; LDL, low-density lipoprotein; BMI, body mass index; BP, blood pressure; LAE, (C1): large arterial elastisite index(large vessel compliance),; SAE, (C2): small arterial elastisite index(large vessel compliance), Data are expressed as means±SD

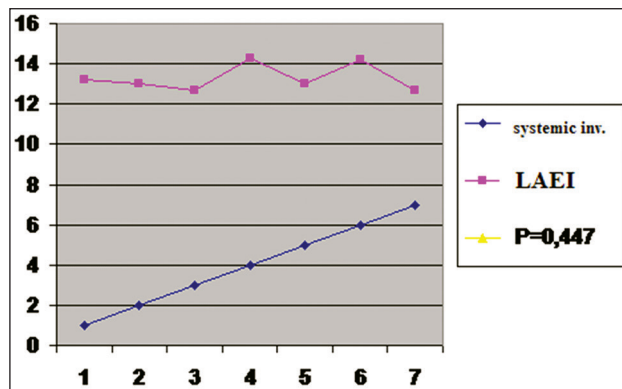


Figure 1. Comparison the number of the systems that are effected by Behçet's disease with LAEI, LAEI: Large Arterial Elastisite İndex ($\text{cm}^3\text{-mmHg}^{-1}$)

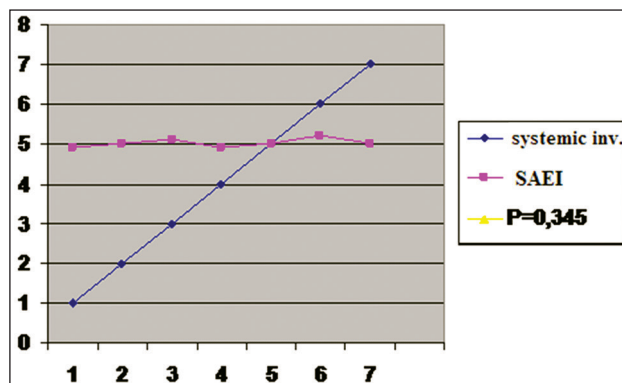


Figure 2. Comparison the number of the systems that are effected by Behçet's disease with SAEI, SAEI: Small Arterial Elastisite İndex ($\text{cm}^3\text{-mmHg}^{-1}$)

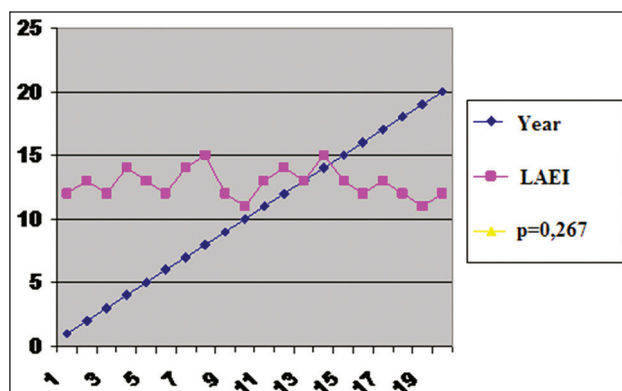


Figure 3. Comparison the duration of Behçet's disease with LAEI
LAEI: Large Arterial Elastisite İndex ($\text{cm}^3\text{-mmHg}^{-1}$)

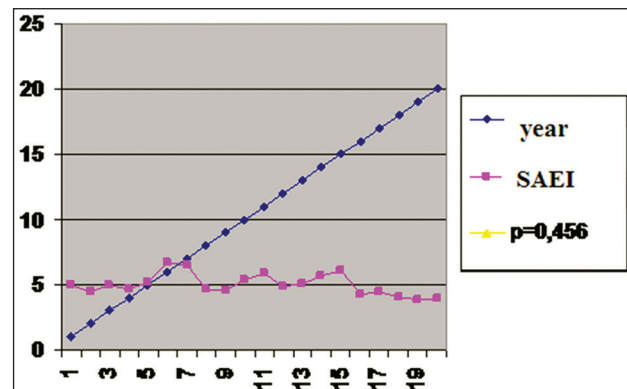


Figure 4. Comparison the duration of Behçet's disease with SAEI
SAEI: Small Arterial Elastisite İndex ($\text{cm}^3\text{-mmHg}^{-1}$)

Discussion

Behçet's disease is a chronic inflammatory vasculitis. Vascular involvement is one of the major complications of Behçet's disease, during the course of the disease. Venous involvement is more often than arterial involvement. Approximately 30% of patients seen vascular complications such as venous thrombosis and arterial thrombosis¹⁸. Despite uncertainty in the pathogenic mechanism of vascular lesions in BD, vascular endothelial dysfunction has been recognized in BD and is thought to play an important role in the vascular lesions⁵⁻¹⁹⁻²⁰⁻²¹. Acute systemic inflammation and chronic systemic vasculitis are associated with endothelial dysfunction¹³⁻¹⁴. Moreover, inflammation is an important risk factor for future cardiovascular events¹⁵. In this study, we evaluated the tendency to atherosclerosis of patients with BD. Significant differences were not found for large artery elasticity index (LAEI) and small artery elasticity index (SAEI) values which were used as arterial elasticity parameters between Behçet's patients and controls. In patients group there were no significant correlation between disease duration, increase in systemic involvement and arterial stiffness indexes.

An investigation made in Turkey by Kurum et al²² supports our results. In this study they found no significant difference about arterial stiffness of patients with Behçet's disease when compared to healthy subjects. Their measurements were made by a device that measures carotis-femoral pulse wave velocity automatically, Complior Colson (France). PWV measurements were made using parameters

‘pulse transit time’ and ‘distance’. Unlike to our study they did not compare the duration of the disease and the number of the organ systems involved. The most important restrictive factor of their study was the small number of patients.

Chang et al²³ reported different values of arterial stiffness in patients with Behcet’s disease in South Korea, but this difference was not statistically significant. They measured arterial stiffness of carotid, femoral, brachial and dorsalis pedis artery using an automated device (VP-2000, Colin Co Ltd., Japan). In their study they found different arterial stiffness values for particularly male patients, patients with severe disease, patients with vascular lesions and patients using immunosuppressive drugs but they also reported that this difference was not statistically significant. There was not significant difference between patient group and control group about the duration of the disease. Only patients who were older and who had higher blood pressure values were found to have different arterial stiffness values and this was statistically significant. Thus, this study supports the results of our study.

In another study in South Korea Moo-Yong Rhee et al²⁴ reported significantly different values of arterial stiffness for patients with Behcet’s Disease. In this study they also measured Carotid intima media thickness (C-IMT). Unlike to stiffness there was no difference about the C-IMT between two groups. The measurements were made from the common carotid artery using the device (Sequoia 512, Acuson, Mountain View, CA, USA) that contains 8 MHz linear transducer. They used “distensibility coefficient” (DC), stiffness index” (β) and “elastic modulus” (Einc) as arterial stiffness parameters. When compared to our study there were more patients with severe systemic involvement and active disease in their study. For this reason we can say that patients with active disease may have more arterial involvement as they found significantly different arterial stiffness values in their study. On the other hand as the forms of Behcet’s Disease may differ according to different geographical regions, arterial stiffness parameters may also differ. This may be caused by the difference of genetic characteristics of patients.

In conclusion, in our study we found that arterial stiffness parameters did not change in patients with Behcet’s Disease. As a result we can say that

endothelial dysfunction has no significant effects on arterial atherosclerosis in patients with Behcet’s Disease or endothelial dysfunction may not reach a significant level in patients with Behcet’s Disease unlike to our estimations. Randomized, larger and multicenter studies investigating the same parameters using the same devices will be more guiding to our results.

References

1. Sakane T, Takeno M, Suzuki N, Inaba G. Behcet’s disease. *N Engl J Med* 1999; 341: 1284–1291.
2. Kural-Seyahi E, Fresko I, Seyahi N, Ozyazgan Y, Mat C, Hamuryudan V, Yurdakul S, Yazici H. The long-term mortality and morbidity of Behcet syndrome: a 2-decade outcome survey of 387 patients followed at a dedicated center. *Medicine (Baltimore)* 2003; 82: 60-76
3. Jorizzo JL, Abernethy JL, White WL, Mangelsdorf HC, Zouboulis CC, Sarica R, Gaffney K, Mat C, Yazici H, al Ialaan A, Assad-Khalil SH, Kaneko F, Frederick Jorizzo EA. Mucocutaneous criteria for the diagnosis of Behcet’s disease: an analysis of clinicopathologic data from multiple international centers. *J Am Acad Dermatol* 1995; 32: 968-76
4. Hampton KK, Chamberlain MA, Menon DK, Davies JA. Coagulation and fibrinolytic activity in Behcet’s disease. *Thromb Haemost* 1991; 66: 292-4
5. Haznedaroglu IC, Ozcebe OI, Ozdemir O, Celik I, Dundar SV, Kirazli S. Impaired haemostatic kinetics and endothelial function in Behcet’s disease. *J Intern Med* 1996; 240: 181-7
6. Joannides R, Haefeli WE, Linder L, Richard V, Bakkali EH, Thuillez C, Luscher TF. Nitric oxide is responsible for flow-dependent dilatation of human peripheral conduit arteries in vivo. *Circulation* 1995; 91: 1314-9
7. Wilkinson IB, Qasem A, McEniery CM, Webb DJ, Avolio AP, Cockcroft JR. Nitric oxide regulates local arterial distensibility in vivo. *Circulation* 2002; 105: 213-7
8. Kinlay S, Creager MA, Fukumoto M, Hikita H, Fang JC, Selwyn AP, Ganz P. Endothelium-derived nitric oxide regulates arterial elasticity in human arteries in vivo. *Hypertension* 2001; 38: 1049-53
9. Laurent S, Boutouyrie P, Asmar R, Gautier I, Laloux B, Guize L, Ducimetiere P, Benetos A. Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. *Hypertension* 2001; 37: 1236-41

10. Kim YK, Kim D. The relation of pulse wave velocity with Framingham Risk Score and SCORE Risk Score. *Korean Circ J* 2005; 35: 22-9
11. Booth AD, Wallace S, McEniery CM, Yasmin, Brown J, Jayne DR, Wilkinson IB. Inflammation and arterial stiffness in systemic vasculitis: a model of vascular inflammation. *Arthritis Rheum* 2004; 50: 581-8
12. Klocke R, Cockcroft JR, Taylor GJ, Hall IR, Blake DR. Arterial stiffness and central blood pressure, as determined by pulse wave analysis, in rheumatoid arthritis. *Ann Rheum Dis* 2003; 62: 414-8
13. Hingorani AD, Cross J, Kharbanda RK, Mullen MJ, Bhagat K, Taylor M, Donald AE, Palacios M, Griffin GE, Deanfield JE, MacAllister RJ, Vallance P. Acute systemic inflammation impairs endothelium-dependent dilatation in humans. *Circulation* 2000; 102: 994-9
14. Raza K, Thambyrajah J, Townsend JN, Exley AR, Hortas C, Filer A, Carruthers DM, Bacon PA. Suppression of inflammation in primary systemic vasculitis restores vascular endothelial function: lessons for atherosclerotic disease? *Circulation* 2000; 102: 1470-2
15. Danesh J, Whincup P, Walker M, Lennon L, Thomson A, Appleby P, Gallimore JR, Pepys MB. Low grade inflammation and coronary heart disease: prospective study and updated meta-analyses. *BMJ* 2000; 321: 199-204
16. International Study Group for Behcet's Disease (ISGBD). Criteria for diagnosis of Behcet's disease. *Lancet* 1990; 335: 1078-80
17. Kim JU, Chang HK, Lee SS, Kim JW, Kim KT, Lee SW, Chung WT. Endothelial nitric oxide synthase gene polymorphisms in Behcet's disease and rheumatic diseases with vasculitis. *Ann Rheum Dis* 2003; 62: 1083-7
18. Koc Y, Gullu I, Akpek G, Akpolat T, Kansu E, Kiraz S, Batman F, Kansu T, Balkanci F, Akkaya S. Vascular involvement in Behcet's disease. *J Rheumatol* 1992; 19: 402-10
19. Chambers JC, Haskard DO, Kooner JS. Vascular endothelial function and oxidative stress mechanisms in patients with Behcet's syndrome. *J Am Coll Cardiol* 2001; 37: 517-20
20. Kayikcioglu M, Aksu K, Hasdemir C, Keser G, Turgan N, Kultursay H, Doganavsargil E. Endothelial functions in Behcet's disease. *Rheumatol Int* 2006; 26: 304-8
21. Alan S, Ulgen MS, Akdeniz S, Alan B, Toprak N (2004). Intima-media thickness and arterial distensibility in Behcet's disease. *Angiology* 55: 413-9
22. Turhan Kürüm, Mustafa Yildiz, Mehmet Soy, Gültaç Özbay. Arterial distensibility as determined by carotid-femoral pulse wave velocity in patients with Behçet's disease. *Clinical Rheumatology* 2005; 24: 134-138
23. H K Chang, S K Kim, S S Lee, M Y Rhee. Arterial stiffness in Behçet' disease: Increased regional pulse wave velocity values. *Ann Rheum Dis* 2006; 65: 415-41
24. Moo Yong Rhee, Hyun Kyu Chang, Seong Kyu Kim. Intima-media thickness and arterial stiffness of carotid artery in Korean patients with Behçet's disease. *J Korean Medical Sciences* 2007; 22: 387-392

Corresponding Author

Kemal Karaagac,
Bursa Yüksek İhtisas Eğitim ve Araştırma hastanesi,
Kardiyoloji Kliniği,
Yıldırım,
Bursa,
Turkey,
E-mail: drkaraagac2001@gmail.com

The effect of memory reinforcement on creating dependency in male mature mice using conditioned place preference (CPP) method

Ebrahim Hosseini¹, Mahmoud Vessal², Sanaz Bahaodini¹, Maryam Rafieirad³

¹ Department of Biology Science and Research Branch, Islamic Azad University, Fars, Iran,

² Department of Biochemistry, Science and Research Branch, Islamic Azad University, Fars, Iran,

³ Department of Biology, Izeh Branch, Islamic Azad University, Izeh, Iran.

Abstract

Addicting drugs such as morphine induce an uncontrolled desire in man for an over-consumption of the drug. They stimulate the brain compensative systems and, for a period of time, prevent the desensitization of the neuron sensitivity produced after administration and detoxification of the drug. The purpose of this investigation was to examine the effect of memory reinforcement produced by physostigmine in creating morphine dependency. Mature male mice (30-35g) were used as the experimental and the control groups. The experimental groups included a morphine treated group, a physostigmine group and one with physostigmine + morphine treatment, respectively. Morphine was used for dependency and physostigmine for memory reinforcement studies. CPP method was used to estimate dependency. No meaningful difference was obtained between the control and the physostigmine groups in preferring a special location to receive the drug. However, there was a meaningful difference ($P < 0.05$) between the control and the morphine groups in preferring the place for drug reception and also a significant enhancement in physostigmine + morphine group in preferring a certain location to receive the drug. It was suggested that physostigmine may directly stimulate the nicotinic and muscarinic receptors of acetylcholine upon inhibition of the choline esterase enzyme, thereby interfering with acetylcholine metabolism and reinforcing the induced morphine dependent CPP.

Key words: Memory, Reinforcement, Morphine dependency, Physostigmine, CPP method.

Introduction

Memory as one of the basic cognitive functions and learning are the most developed functions of the nervous system [1, 2]. Different experiments show that the brain cholinergic system activities play a major role in memory and learning process [3, 4]. Different studies demonstrate that the destruction of hippocampus, which is enriched with cholinergic neurons, leads to the destruction of the animals' long term memory and could be recovered using drugs that stimulate acetylcholine production [3]. Physostigmine is a parasympathomimetic drug and a cholinesterase inhibitor preventing acetylcholine degradation. It is obtained from Calabar bean and stimulates the nicotinic and muscarinic receptors directly through inhibition of acetylcholine catabolism [5]. Physostigmine crosses the blood brain barrier easily and is used to treat the adverse effects of excessive consumption of atropine, scopolamine and other anticholinergic drugs on the central nervous system (CNS).

Morphine and its derivatives, generally known as opioids, decrease responses to stimuli, attenuate CNS activity, influence mood changes and decrease anxiety, therefore their abuse has increased tremendously. They perform their tasks through attachment to opioid receptors [6]. Morphine and other addicting drugs produce great impulses in producing uncontrolled desire to consume the drugs overtly [7]. Such addicting drugs excessively stimulate the brain's compensative systems such as dopaminergic mesolimbic systems, and the increased jollity produced by such drugs is due to the intensive activity of this part of CNS [8]. Since the brain enjoyment system becomes more resistant by increasing the consumption of the drug, it has to increase the drug consumption further to re-

ach a natural balanced state and resume enjoyment [9]. If the drug consumption is stopped, the brain enjoyment system activity, which has become resistant now, motivates the addict to continue the drug consumption [10]. Apparently, dopamine mesolimbic compensative system depends less on the pleasure reward than the desire and consequently its hyper function in the addict leads to excessive desire in drug consumption [11].

Nucleus accumbens (NAC) has important roles in compensative, competition, joy, drug and pseudo drug effects and is considered as a part of brain compensative system [12]. NAC with Ventral Tegmental Area (VTA) are the first parts which are influenced by narcotics such as morphine. Drugs consolidate dopamine activity in NAC which reinforces the neuron activity in VTA through dopamine neural adjustment in processing confirmatory signals [13].

Conditioning is a type of association learning observed in two distinct classic and operant forms and is one of the easiest types of learning [14]. Among empirical methods which are used for evaluating compensative effect of addicting drugs in animal experiments, CPP method that shows the conditioned local preference process is considered as the most famous empirical method to study the compensative effects of different drugs [15].

Considering the effects of morphine and other addicting drugs on social and physical behavior and its effect on cellular and molecular activity of the brain, it seems that discovering the factors causing drug dependency is one of the methods in preventing addiction. Also, studying the factors that increase dependency helps researchers to prevent addiction and dependency. Therefore, the main aim of this research is to study the effect of memory reinforcement in creating morphine dependency in male mature mice using CPP method.

Materials and Method

This study was performed on a total of 60 mature male 85-day old albino mice, weighing 30-35 grams. They were divided into 5 groups of 12 rats each including the control or the treatment- free group, witness group receiving only distilled water subcutaneously and 3 experimental groups receiving by the same route either morphine, physostigmine or morphine + physostigmine. The research protocols were

according to the international regulations devised to support laboratory animals and was approved by the ethics committee of the university. The drugs used were obtained from Iran Daru Company. A Plexi-glas box of 15cm × 30cm × 15cm divided into two equal parts and a central section as a corridor was used for the CPP method. One part of the box had white floor and walls and the other had black floor and walls. There were pre-conditional, conditional, and post-conditional steps in performing CPP.

In the pre-conditional step, all of the mice were put into the box for 10 minutes without injection for a day where they could move into the two compartments of the box without any restriction. The time remaining in each compartment was recorded. It was found that the animals did not have any preference for either compartment and statistically they were present 50% of the time in each compartment and if an animal preferred one of the compartments 90% of the time, it was excluded from the investigation. At the beginning of the experiment the mice were put in the white or the black compartment of the box at random and the time they remained in the compartments was recorded. On the day of CPP experiment, the animals were put in the compartment that they were during the pre-conditioned period.

During the conditional step that lasted for 8 days, the control group did not receive any treatment and the witness group received 1 ml of distilled water subcutaneously, while the morphine group was given 10 mg/kg body weight morphine through the same route. According to several studies, this is the best dose to create psychic dependency in the CPP method. The animals were put immediately and randomly in the white or the black side of the box for 30 minutes without letting them move to the other side by closing the opening between the two sections. This procedure was repeated for 8 days and it was assumed that the animals remain in the same colored compartments that were assigned to them until conditioning occurred.

The physostigmine receiving group took the optimum dose of 0.1mg/kg of drug subcutaneously and after 5 minutes which is the necessary time for the maximum effect of the drug, they were transferred to the drug conjugate part and were kept there for 30 minutes. The physostigmine + morphine group were also firstly given 0.1 mg/kg

physostigmine subcutaneously and after 5 minutes, followed by 10mg/kg of morphine subcutaneously. They were then transferred immediately to the drug conjugate part to remain there for 30 minutes. This group was compared with the morphine and the control groups. In all of the groups, the time remaining in the drug conjugate part was recorded to evaluate the desire of the animals to that part on the day of CPP experiment.

In the post-conditional step that included the fourth and the ninth day, animals were kept in the same part of the box as the pre-conditional days and allowed to move freely for 10 minutes as in the pre-conditional day and the time that each animal stayed in each part was recorded to find out, in spite of the training, if memory enhancing drugs have any effect on the morphine dependency of the animals. The data were statistically analyzed by Anova and independent Student's t- test using SPSS version 18.

Results

The results showed that in the pre-conditional step in the CPP method, the mice did not have any location preference statistically and were present 50% of the time in each compartment of the box (Table 1). Also the results demonstrated that there

was no difference between the mean passed time in the stimuli conjugate part in both the control and the witness groups during the experimental days (days 4th and 9th) compared to the pre-conditional time. It means that none of the animals preferred to remain in the part that they had stayed during the conditional step (Table 2).

As noted from Table 2, there was no significant difference in the mean time spent in a given part between the experimental group treated with physostigmine and the control group during the experiment days (fourth & ninth days) compared with the preconditional day (the 1st day).

Statistical analyses showed that the morphine group had a significantly higher time spent in a given part of the box during the test days compared with the first preconditional day as well as compared with the control group ($p < 0.05$). Also the physostigmine+morphine group had a statistically significant increase in the mean time spent in a given compartment compared with the control and the morphine groups.

Discussion

The results showed that there was no meaningful variation in the mean time spent in a given part between the groups treated with physostigmine com-

Table 1. Mean and standard deviation of the animal presence in the two compartments of the box during the pre-conditional step (in seconds)

number	animal presence in the box			
	black side		white side	
	mean	std. deviation	mean	std. deviation
96	303	4.23	294	6.02

Table 2. Mean and standard deviation of time elapsed in different days between research groups (in seconds)

Hypodermic injection	groups	number	mean and standard deviation of time spent in stimuli conjugated part		
			pre-conditional	test (fourth day)	test (ninth day)
distilled water	control	12	4.23240±	2.17249±	1.45239±
	witness	12	2.47248±	2.13247±	2.15248±
physostigmine	control	12	4.23240±	2.17249±	1.45239±
	physostigmine	12	1.93246±	3.97242±	2.18246±
morphine	control	12	4.23240±	2.17249±	1.45239±
	morphine	12	1.74238±	381±4.64*	376±4.71*
physostigmine + morphine	control	12	4.23240±	2.17249±	1.45239±
	combined injection	12	4.28241±	450±4.64*	448±4.55*

* $P < 0.05$

pared to the control group during the experimental days (fourth and ninth) and the first day (pre-conditional) because the creation of CPP is specific for certain drugs that are stimulatory and addictive and physostigmine does not belong to such a group [16, 17]. However, there was a meaningful increase at $P < 0.05$ level in the mean time spent in a given compartment by the morphine group on the experimental days (days fourth and ninth) compared to the first day (pre-conditional) compared to the control group. The results reveal that morphine can create CPP or local preference in animals due to behavioral dependency.

Chronic consumption of morphine induces several changes in CNS that lead to drug dependent behavioral changes causing the activation of the dopaminergic neurons in VTA which have an important role in the neural formation of addiction [18, 19]. The dopaminergic path from VTA to NAC is a critical area for the promotion of psychic dependency to narcotics [20]. Since morphine removes pain, it has beneficial medical use, but because of its effect on mood variation and on decreasing anxiety, it has been significantly abused [6]. Morphine and similar drugs have strong compensative characteristics and humans and animals learn the methods to anticipate the sources of addicting drugs which will lead to an increase urge for the drugs. Since this has a great effect on the hyperactivity of the brain compensative system, the consumption of these drugs is increased [8].

The results also showed that there was a meaningful increase at $P < 0.05$ level in the time spent in a compartment in the experimental group treated with physostigmine +morphine during the experimental days (the fourth and the ninth days) compared to the first day (pre-conditional) when compared with the experimental group treated with morphine alone.

Most observations reveal that the neural cause of frequent and habitual use of addicting drugs is due to a long term memory process which is accompanied by the involvement of dopaminergic neurons of the prefrontal cortex (PFC) of the mid-brain [21, 22, and 23]. Addicting drugs and compensative response influence behavior through an increase in dopamine level of NAC [24].

In addition to NAC, amygdala and PFC have also important roles in the compensative response and the compensative dependency memory [22, 25].

PFC has roles in the memory and in guiding the organism towards the target [26, 27, and 28]. Acetylcholine released in the synaptic spaces of the brain has the main role in memory and learning and electrophysiological studies demonstrate that the response of cholinergic interneurons to sensational stimulation triggers learning and the compensative behavior [3, 29]. Acetylcholine is a neurotransmitter which is degraded by cholinesterase after its release in the synaptic cleft [30].

Investigations demonstrate that an inter-amygdala injection of physostigmine, an efficient anticholinesterase drug, leads to a significant increase in inducing CPP with morphine through an increase in acetylcholine [31]. Nicotine as an agonist of the nicotinic receptor enhances the acetylcholine induced CPP with morphine in the rat, while an antagonist of the nicotinic receptor, mecamylamine, inhibits the induced CPP with morphine [31]. Another study indicates that galantamine, an inhibitor of cholinesterase enzyme similar to physostigmine, reduces cigarette addiction through an increase in acetylcholine [32]. Donepezil, an inhibitor of acetylcholine esterase enzyme also increases acetylcholine in the brain and stimulates dopaminergic neurons in VTA upon stimulating muscarinic receptors critical for the compensative stimulation in the rat [33, 34].

Studies show that physostigmine or nicotine injections, as agonists of nicotinic receptors, to the CA1 region of hippocampus, elevates the induced CPP with morphine while atropine as an antagonist of the muscarinic receptors of acetylcholine inverses the physostigmine effect on morphine response [35].

NAC and VTA are the first locations which are affected by narcotics and these drugs diminish dopamine activity in NAC by enhancing neuron activity in VTA through a neural adjustment of dopamine in processing the potentiating signals and leading to a searching behavior of the animal toward the drug when encountering the drug or the corresponding stimulus even after drug withdrawal [36].

A different study showed that the increased dopamine level in NAC, which emerges after electrical stimulation of the dorsolateral tegmental nucleus, is not observed in mice which are without muscarinic M5 receptors of acetylcholine [37]. M5 receptor stimulation which is expressed in VTA neurons is responsible for long term release

of dopamine in NAC after stimulating dorsoventral tegmental nuclei [34].

Another study shows that the M1 muscarinic receptor of acetylcholine has a time dependency role in morphine dependency memory [38]. It is suggested that pharmacologic inhibition of central M5 receptor leads to providing a way to treat addiction and opioid dependency. NAC is an important part of the brain that is involved in the compensative process and jolliness stimulation [39, 40, and 41]. Opioids cause the brain to respond to compensation through stimulation of dopamine release in VTA and NAC [42].

CPP is an effective method to search the path that leads to the elucidation of the compensative effects of addiction drugs [43]. Electrophysiological studies show that cholinergic interneuron response to sensational stimulation triggers the learning and compensative behaviors [44].

Inter-amigdala injection of physostigmine leads to enhancement of CPP induction with morphine [31]. The study shows that acetylcholine which is released in VTA has a stimulatory action on the activity of dopaminergic neurons [45].

It has been shown that reciprocal injection of cholinesterase enzyme inhibitors, such as physostigmine or nicotine as acetylcholine agonists to hippocampus or amigdala, enhances morphine dependency CPP [46] in the mice which do not have the muscarinic M5 receptors, and reduces the morphine compensative effect and CPP production [47]. Investigators show that atropine or micamilamine blocks the muscarinic or nicotinic receptors in the dorsal part of hippocampus or amigdalia and prevents CPP production by morphine [49, 50]. Some studies indicate that central nicotinic receptors facilitate the enhancement of the compensative processes [49, 50 and 51].

Considering the present investigation, it seems that memory enhancement leads to an increased psychic dependency toward narcotics in animals and it is suggested that similar investigations should be performed in humans.

Acknowledgement

The authors wish to thank the Research Vice Chancellor of Shiraz University of Medical Sciences for his cooperation in this research.

References

1. Spoehr, K. *Human Learning and Memory*. COGS 1560, CRN 21190. 2008, <http://cog.brown.edu/~spoehr/>.
2. Arsic S, Eminovic F, Stankovic I, Jankovic S, Despotovic M. *The Role of Executive Functions at Dyscalculia*. *HealthMED*. 2012; 6(1): 314-318.
3. Hasselmo Michael E. *The Role of Acetylcholine in Learning and Memory*. *Curr Opin Neurobiol*. 2006; 16(6): 710-715.
4. Tan H, Liu N, Wilson FA, Ma Y. *Effects of scopolamine on morphine-induced conditioned place preference in mice*. *Addict Biol*. 2007; 12(3-4): 463-469.
5. Davis KL, Mohs RC, Tinklenberg JR, Pfefferbaum A, Hollister LE, Kopell BS. *Physostigmine: improvement of long-term memory processes in normal humans*. *Science*. 1978; 201(4352): 272-4.
6. Lingford-Hughes AR, Welch S, Nutt DJ; *British Association for Psychopharmacology*. *Evidence-based guidelines for the pharmacological management of substance misuse, addiction and comorbidity: recommendations from the British Association for Psychopharmacology*. *J Psychopharmacol*. 2004; 18(3): 293-335.
7. Kosten TR, George TP. *The neurobiology of opioid dependence: implications for treatment*. *Sci Pract Perspect*. 2002; 1(1): 13-20.
8. McDonald J, Lambert G. *Opioid mechanisms and opioids drugs*. *Anaesthesia and intensive care medicine* 2008; 9: 33-37.
9. Rogacheva A, Laatikainen T, Patja K, Paavola M, Tossavainen K, Vartiainen E. *Smoking and related factors of the social environment among adolescents in the Republic of Karelia, Russia in 1995 and 2004*. *Eur J Public Health*. 2008; 18(6): 630-636.
10. Thomas YF, Schnur P, Iguchi MY. *Behavioral and economic perspectives in drug abuse research*. *Drug Alcohol Depend*. 2007; 90 Suppl 1: S1-3. Epub 2007 Jun 5.
11. Ni X, Yan H, Chen S, Liu Z. *Factors influencing internet addiction in a sample of freshmen university students in China*. *Cyberpsychol Behav*. 2009; 12(3): 327-330.
12. Nicola SM, Taha SA, Kim SW, Fields HL. *Nucleus accumbens dopamine release is necessary and sufficient to promote the behavioral response to reward-predictive cues*. *Neuroscience*. 2005; 135(4): 1025-33.
13. Rezayof A, Golhasani-Keshtan F, Haeri-Rohani A, Zarrindast MR. *Morphine-induced place preference: involvement of the central amygdala NMDA receptors*. *Brain Res*. 2007; 1133(1): 34-41.

14. Shimosato K, Ohkuma S. Simultaneous monitoring of conditioned place preference and locomotor sensitization following repeated administration of cocaine and methamphetamine. *Pharmacol Biochem Behav.* 2000; 66(2): 285-292.
15. Carr GD, Fibiger HC, Phillips AG. Conditioned place preference as a measure of drug reward. In: Liebman JM, Cooper SJ (eds) *The neuropharmacological basis of reward*. Clarendon Press, Oxford, 1989, 264-319.
16. Tzschentke TM, Schmidt WJ. N-methyl-D-aspartic acid-receptor antagonists block morphine-induced conditioned place preference in rats. *Neurosci Lett.* 1995; 193(1): 37-40.
17. Maldonado R, Blendy JA, Tzavara E, Gass P, Roques BP, Hanoune J, Schütz G. Reduction of morphine abstinence in mice with a mutation in the gene encoding CREB. *Science.* 1996; 273(5275): 657-659.
18. Nestler EJ. Historical review: Molecular and cellular mechanisms of opiate and cocaine addiction. *Trends Pharmacol Sci.* 2004; 25(4): 210-218.
19. Spiga S, Serra GP, Puddu MC, Foddai M, Diana M. Morphine withdrawal-induced abnormalities in the VTA: confocal laser scanning microscopy. *Eur J Neurosci.* 2003; 17(3): 605-612.
20. Manzanedo C, Aguilar MA, Rodríguez-Arias M, Miñarro J. Effects of dopamine antagonists with different receptor blockade profiles on morphine-induced place preference in male mice. *Behav Brain Res.* 2001; 121(1-2): 189-197.
21. Hyman SE. Addiction: a disease of learning and memory. *Am J Psychiatry.* 2005; 162(8): 1414-22.
22. Everitt BJ, Cardinal RN, Parkinson JA, Robbins TW. Appetitive behavior: impact of amygdala-dependent mechanisms of emotional learning. *Ann N Y Acad Sci.* 2003; 985: 233-50.
23. Everitt BJ, Robbins TW. Neural systems of reinforcement for drug addiction: from actions to habits to compulsion. *Nat Neurosci.* 2005; 8(11): 1481-9.
24. Waldhoer M, Bartlett SE, Whistler JL. Opioid receptors. *Annu Rev Biochem.* 2004; 73: 953-90.
25. Kalivas PW, Volkow N, Seamans J. Unmanageable motivation in addiction: pathology in prefrontal-accumbens glutamate transmission. *Neuron.* 2005; 45(5): 647-50.
26. Kringelbach ML. The human orbitofrontal cortex: linking reward to hedonic experience. *Nat Rev Neurosci.* 2005; 6: 691-702.
27. Miller EK, Cohen JD. An integrative theory of prefrontal cortex function. *Annu Rev Neurosci.* 2001; 24: 167-202.
28. Rolls ET. The functions of the orbitofrontal cortex. *Brain Cogn.* 2004; 55(1): 11-29.
29. Zhou FM, Wilson CJ, Dani JA. Cholinergic interneuron characteristics and nicotinic properties in the striatum. *J Neurobiol.* 2002; 53: 590-605.
30. Tzschentke TM. *Prog. Neurobiol.* 1998; 56, 613-672.
31. Zarrindast MR, Fattahi Z, Rostami P, Rezayof A. Role of the cholinergic system in the rat basolateral amygdala on morphine-induced conditioned place preference. *Pharmacol Biochem Behav.* 2005; 82(1): 1-10.
32. Diehl A, Nakovics H, Croissant B, Smolka MN, Ba-tra A, Mann K. Galantamine reduces smoking in alcohol-dependent patients: a randomized, placebo-controlled trial. *Int J Clin Pharmacol Ther.* 2006; 44(12): 614-22.
33. Giacobini E. Cholinesterase inhibitors: new roles and therapeutic alternatives. *Pharmacol Res.* 2004; 50(4): 433-40.
34. Yeomans JS, Takeuchi J, Baptista M, Flynn DD, Lepik K, Nobrega J, Fulton J, Ralph MR. Brain-stimulation reward thresholds raised by an antisense oligonucleotide for the M5 muscarinic receptor infused near dopamine cells. *J Neurosci.* 2000; 20(23): 8861-7.
35. Rezayof A, Zatali H, Haeri-Rohani A, Zarrindast MR. Dorsal hippocampal muscarinic and nicotinic receptors are involved in mediating morphine reward. *Behav Brain Res.* 2006; 166(2): 281-90.
36. Rezayof A, Darbandi N, Zarrindast MR. Nicotinic acetylcholine receptors of the ventral tegmental area are involved in mediating morphine-state-dependent learning. *Neurobiol Learn Mem.* 2008; 90(1): 255-60.
37. Forster GL, Blaha CD. Laterodorsal tegmental stimulation elicits dopamine efflux in the rat nucleus accumbens by activation of acetylcholine and glutamate receptors in the ventral tegmental area. *Eur J Neurosci.* 2000; 12(10): 3596-604.
38. Esmaeili B, Basseda Z, Dehpour AR. Antagonism of muscarinic M1 receptors by dicyclomine inhibits the consolidation of morphine-associated contextual memory. *Brain Res Bull.* 2008; 76(4): 380-7.
39. Breiter HC, Aharon I, Kahneman D, Dale A, Shizgal P. Functional imaging of neural responses to expectancy and experience of monetary gains and losses. *Neuron.* 2001; 30(2): 619-39.

40. Knutson B, Adams CM, Fong GW, Hommer D. Anticipation of increasing monetary reward selectively recruits nucleus accumbens. *J Neurosci.* 2001; 21(16): RC159.
41. Robinson TE, Berridge KC. Addiction. *Annu Rev Psychol.* 2003; 54: 25-53.
42. Kelley AE, Berridge KC. The neuroscience of natural rewards: relevance to addictive drugs. *J Neurosci.* 2002; 22(9): 3306-11.
43. Murtra P, Sheasby AM, Hunt SP, De Felipe CD. rewarding effects of opiates are absent in mice lacking the receptor for Substance P. *Nature* 2000; 405: 180-183.
44. Zhou FM, Wilson CJ, Dani JA. Cholinergic interneuron characteristics and nicotinic properties in the striatum. *J Neurobiol.* 2002; 53(4): 590-605.
45. Greba Q, Munro LJ, Kokkinidis L. The involvement of ventral tegmental area cholinergic muscarinic receptors in classically conditioned fear expression as measured with fear-potentiated startle. *Brain Res.* 2000; 870(1-2): 135-41.
46. Rezayof A, Golhasani-Keshtan F, Haeri-Rohani A, Zarrindast MR. Morphine-induced place preference: involvement of the central amygdala NMDA receptors. *Brain Res.* 2007 Feb 16; 1133(1): 34-41.
47. Basile AS, Fedorova I, Zapata A, Liu X, Shippenberg T, Duttaroy A, Yamada M, Wess J. Deletion of the M5 muscarinic acetylcholine receptor attenuates morphine reinforcement and withdrawal but not morphine analgesia. *Proc Natl Acad Sci U S A.* 2002; 99(17): 11452-7.
48. Rezayof A, Razavi S, Haeri-Rohani A, Rassouli Y, Zarrindast MR. GABA(A) receptors of hippocampal CA1 regions are involved in the acquisition and expression of morphine-induced place preference. *Eur Neuropsychopharmacol.* 2007; 17(1): 24-31.
49. Bevins RA, Palmatier MI. Extending the role of associative learning processes in nicotine addiction. *Behav Cogn Neurosci Rev.* 2004; 3(3): 143-58.
50. Nakahara D. Influence of nicotine on brain reward systems: study of intracranial self-stimulation. *Ann N Y Acad Sci.* 2004; 1025: 489-90.
51. Rezayof A, Zarrindast MR, Sahraei H, Haeri-Rohani A. Involvement of dopamine receptors of the dorsal hippocampus on the acquisition and expression of morphine-induced place preference in rats. *J Psychopharmacol.* 2003; 17(4): 415-23.

Corresponding Author

Ebrahim Hosseini,
 Department of Biology Science and Research Branch,
 Islamic Azad University,
 Fars,
 Iran,
 E-mail: ebrahim.hossini@miau.ac.ir

A prospective trial of epidural versus intravenous meperidine analgesia during labor: Effects on perinatal and maternal outcome

Feyza Yayci¹, Eyup Yayci², Sibel Devrim¹, Meltem Ince Gul¹, Melek Gura¹

¹ Department of Anesthesiology and Reanimation, Goztepe Training and Research Hospital, Istanbul, Turkey,

² Department of Obstetrics and Gynecology, Goztepe Training and Research Hospital, Istanbul, Turkey.

Abstract

Aim: The objective of this study was to investigate the effects of epidural analgesia and intravenous meperidine analgesia on neonatal blood gases and Apgar scores, as well as maternal hemodynamics and pain, and progress of labor.

Methods: Ninety ASA class I-II parturients between 17-36 years of age were included in this randomized trial. Study participants were divided into 3 groups (n=30 in each group). Epidural analgesia with bupivacaine via epidural catheter to group E was administered; while intravenous (IV) meperidine was given to group M. Group C was the control group who did not receive any analgesics. Demographic, hemodynamic, and perinatal parameters were compared.

Results: The systolic arterial pressure (SAP), diastolic arterial pressure (DAP), and respiratory rate (RR) values showed significant decrease in the group E ($p<0.05$) when compared with the baseline values. After between-group analyses, we found that the overall, SAP, DAP, and RR values of group E were significantly lower than those of the groups M and C ($p<0.05$). The PR values showed no significant difference during that period ($p>0.05$). The VRS values revealed a significant decrease in the group E beginning from the 15th minutes of analgesia, while the VRS values increased significantly in the first hour in the groups M and C ($p<0.05$). Concerning the progress of labor, the first stage of labor was prolonged in the group C ($p<0.05$), while the second stage labor was prolonged in the groups E and M ($p<0.01$). The difference between the study groups with regard to type of delivery was not significant ($p>0.05$). The Apgar scores and umbilical artery blood gases revealed no significant difference among the study groups. When parturients were queried within 24

h of delivery, 66% of women in the group E rated their satisfaction as good, compared with 20% of women in the group M ($p<0.01$).

Conclusion: According to findings of this study, neonatal Apgar scores and umbilical arterial blood gas values are similar in parturients receiving epidural analgesia, intravenous opioid analgesia and no analgesia. Epidural analgesia is a more effective method for pain relief during labor and delivery than intravenous opioid analgesia with no detrimental effects on the progress of labor.

Key words: Epidural analgesia, Labor analgesia, meperidine, perinatal outcome

Introduction

Epidural and parenteral opioid analgesia are commonly preferred methods for pain relief during labor and delivery. Although systemic opioids have long been used for labor analgesia, they have become less popular because of frequent maternal and neonatal side effects (1). Meperidine, synthesized in 1939, was first used in labor in the early 1940s. It is the most commonly used opioid worldwide, and although there are considerable doubts about its analgesic effectiveness and concerns about its potential maternal, fetal, and neonatal side effects, it has the virtue of familiarity and low cost in clinical practice (2). For systemic analgesia, meperidine has been most extensively studied and compared with neuraxial analgesia. It depresses fetal muscular activity, aortic blood flow, short-term heart rate variability, and oxygen saturation. In the newborn, it exacerbates acidosis and depresses Apgar scores, respiration, neurobehavioural score, muscle tone, and suckling. Neonatal acid-base status is not only better with epidural than with systemic opioid analgesia, it is also better than with no analgesia (3).

Labor pain can cause sympathetic stimulation leading to metabolic acidosis and a decrease in uteroplacental flow and fetal oxygenation. Regional anesthesia can prevent those effects, relieving pain and anxiety of the parturient, leading to a regular respiratory rate and amplitude, and decreased oxygen consumption and catecholamine release. On the other hand, Roberts SW Et al. (4) claim that regional anesthesia is associated with fetal acidemia, which is less frequent with epidural anesthesia compared to subarachnoid techniques. There are not many published data enlightening that controversy. In this prospective study, we investigated the effects of epidural analgesia and intravenous meperidine analgesia on perinatal and maternal outcome such as neonatal blood gases and Apgar scores, as well as maternal hemodynamics and pain, and progress of labor and delivery.

Materials and methods

After approval by the hospital ethics committee and written informed consent by the participants were obtained, 90 ASA class I-II (American Society of Anesthesiologists' classification I-II) parturients between 17-36 years of age were included in this randomized trial. Study participants were divided into 3 groups (n=30 in each group). Epidural analgesia with bupivacaine via epidural catheter to group E was administered; while intravenous (IV) meperidine was given to group M. Group C was the control group who did not receive any analgesics. Inclusion criteria were uncomplicated course of pregnancy, singleton pregnancy in cephalic presentation, cervical dilation of 3-5 cm and normal cardiotocographic findings. Cases with maternal systemic disorders, meconium-stained amniotic fluid and cephalopelvic disproportion, gestation less than 36 weeks, previous abdominal surgery or any contraindication to regional anesthesia were excluded. Baseline values of systolic and diastolic arterial pressures (SAP and DAP), pulse rate (PR), respiratory rate (RR), fetal heart rate (FHR), uterine contractions and degree of cervical dilation were recorded. Verbal Rating Score (VRS), by which the parturients scored their pain between 0 and 10 (0= no pain, 10 = worst possible pain) was used to evaluate the degree of pain and efficacy of analgesia. Oxytocin infusion of 6mU/min was started with increasing doses of 6 mU/min

every 40 min (to a maximum dose of 24 mU/min) until 3 contractions every 10 min were recorded. Uterine contractions and FHR were monitored with OMF-8100 J/R (Partocorder, Tokyo, Japan).

Women randomized to epidural analgesia (group E) received an intravenous bolus dose of crystalloid solution (20 mL/kg), after the analgesia was initiated through an epidural catheter inserted into the L4-5 interspace via 18G Tuohy needle with the patients in the sitting position, when cervical dilation was 3-5 cm. When VRS was 4-6 and 3 contractions in 10 minutes with the duration of 35-40 seconds were observed, analgesia was achieved with 12 mL of bupivacaine 0.25 % to a bilateral T-10 sensory level evaluated by pinprick test. Left uterine displacement was maintained to avoid aortocaval compression. SAP, DAP, PR, RR, VRS, FHR and levels of sensory and motor blockade were recorded in 5 minutes intervals for the first hour; 15 minutes intervals for the second hour and 30 minutes intervals for the following hours. Hypotension (20% decline from baseline) was treated by increased rate of fluid infusion and incremental intravenously bolus doses of ephedrine 5 mg at 1- minutes intervals until the pressure returned to normal. When the level of sensory analgesia decreased at least two segments, 6-8 mL of bupivacaine 0.25% was given as the incremental dose of local anesthetic. Cervical dilation, SAP, DAP, PR, RR, FHR values were recorded before and after each incremental dose.

Women randomized to intravenous analgesia (group M) received 50 mg of intravenously meperidine on cervical dilation of 4-5 cm. Additional 20 mg doses of meperidine were given on request, not exceeding 100mg in 2 h. The period between the first anesthetic dose and cervical dilation of 10 cm determined by an obstetrician was defined as the first stage of labor, while the period from 10 cm of cervical dilation until delivery was the second stage. Control group (group C) received no analgesics. For the groups M and C, SAP, DAP, PR, RR, FHR, cervical dilation, uterine contractions and VRS values were recorded as previously described for group E. Immediately after delivery of the infant, umbilical artery blood was sampled from a doubly-clamped segment of umbilical cord. Umbilical artery blood gases and Apgar scores at 1 and 5 minutes as well as duration of the stages of the labor were recorded. In addition, the quality of pain relief was assessed with

hin twenty-four hours after delivery using a four point descriptive scale of excellent, good, fair, or poor.

Data were presented as mean $\pm$ standard deviation or percentage, as appropriate. Statistical analyses were performed Statistica 7.0. Software (Statsoft, Inc., Tulsa, AR, USA). Demographic parameters, durations of labor stages I and II, umbilical arterial blood gases, and Apgar scores were compared with ANOVA-test. Changes over time in SAP, DAP, PR, RR, and VRS between and within the study groups, comparing values at each time point, were analyzed with repeated measures ANOVA followed by a post hoc Bonferroni test to identify significant differences. Apgar scores were compared with Mann-Whitney U test. The ratios of education, gravidity, parity, and quality of pain relief of the study groups were compared with χ^2 as appropriate. A P value of <0.05 was considered significant.

Results

All of the randomized parturients completed the study. There were no significant differences in the maternal demographic characteristics among the study groups ($p>0.05$) (Table 1). Overall, gravidity and parity of group C, was significantly higher from the groups E and M ($p<0.05$) (Tables 2 and 3).

Table 1. Demographics of groups M, E, and C. Overall, study groups were similar with regard to these values ($p>0.05$). Data were presented as mean $\pm$ SD and percentage as appropriate

	Group E (n=30)	Group M (n=30)	Group C (n=30)
Age (years)	23.4 $\pm$ 3.9	22.7 $\pm$ 3.6	24.7 $\pm$ 5.4
Weight (kg)	67.8 $\pm$ 10.0	68.2 $\pm$ 7.1	67.8 $\pm$ 7.5
Height (cm)	160.6 $\pm$ 5.6	157.1 $\pm$ 6.7	157.3 $\pm$ 5.6
Education			
Primary school, n (%)	20 (66.66%)	26 (86.66%)	29 (96.66%)
Secondary school, n (%)	5 (16.66%)	1 (3.33%)	0 (0%)
High school, n (%)	5 (16.66%)	3 (10.%)	1 (3.33%)

Table 2. Gravidity of study groups

Gravidity (n)	Group E (n=30)	Group M (n=30)	Group C (n=30)
1	16 (53.3%)	21 (70%)	11 (36.7%)
2	11 (36.7%)	7 (23.3%)	10 (33.3%)
3 $\leq$	3 (10%)	2 (6.7%)	9 (30%)

Table 3. Parity of study groups

Parity (n)	Group E (n=30)	Group M (n=30)	Group C (n=30)
0	20 (66.7%)	23 (76.7%)	11 (36.7%)
1	10 (33.3%)	5 (16.1%)	13 (43.3%)
2	0	2 (6.7%)	6 (20%)

When the hemodynamic parameters and RR within the first hour after analgesia were evaluated, the SAP, DAP, and RR values showed significant decrease in the group E ($p<0.05$) when compared with the baseline values (Figures. 1, 2, 3).

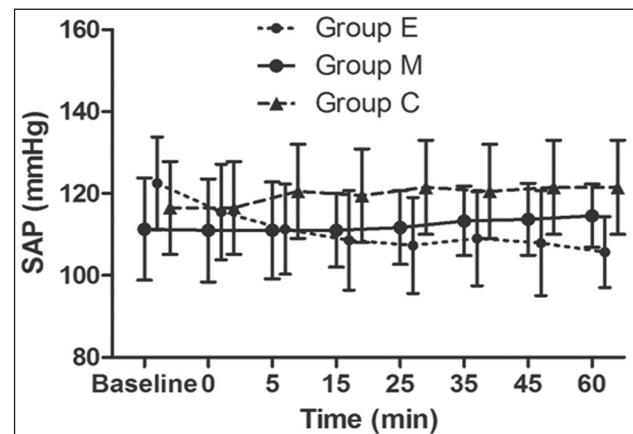


Figure 1. Systolic arterial pressure (SAP) of groups M, E, and C. Data were presented as mean $\pm$ SD. SAP values of group E were significantly lower than those of groups M and C from 0 min to 60 min ($p<0.05$)

After between-group analyses, we found that overall, SAP, DAP, and RR values of group E were significantly lower than those of the groups M and C ($p<0.05$). In the group E, 10% of the parturients

required treatment with ephedrine. The PR values showed no significant difference during that period ($p>0.05$) (Figure 4). Women who received epidural analgesia reported lower pain scores. The VRS values, as shown in Figure 5, revealed a significant decrease in the group E beginning from the 15th minutes of analgesia, while the VRS values increased significantly in the first hour in the groups M and C ($p<0.05$).

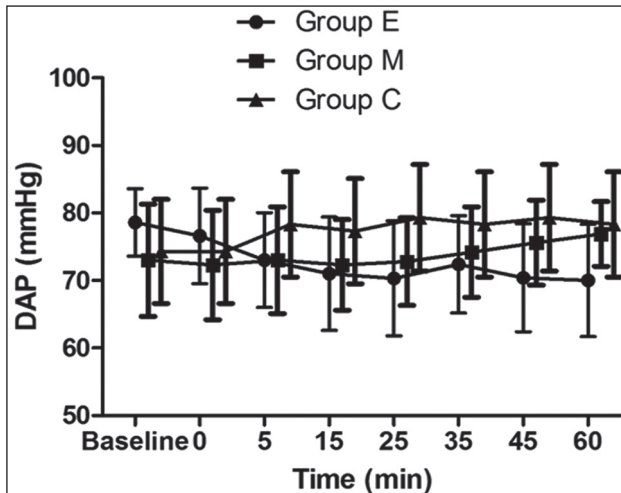


Figure 2. Diastolic arterial pressure (DAP) of groups M, E, and C. Data were presented as mean $\pm$ SD. DAP values of group E were significantly lower than those of groups M and C from 0 min to 60 min ($p<0.05$)

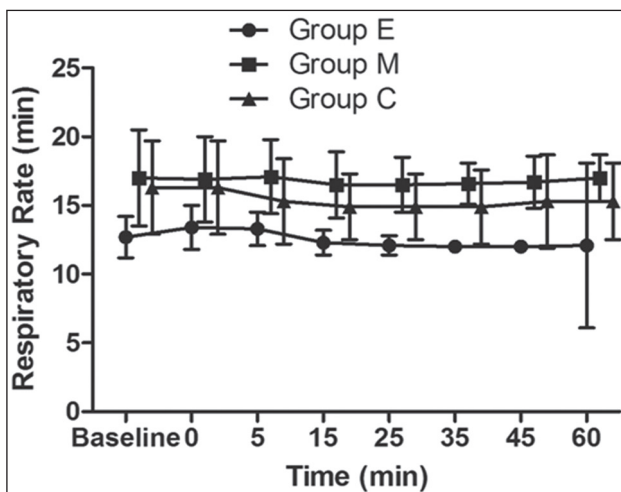


Figure 3. Respiratory rates (RR) of groups M, E, and C. Data were presented as mean $\pm$ SD. RR values of group E were significantly lower than those of groups M and C from 0 min to 60 min ($p<0.05$)

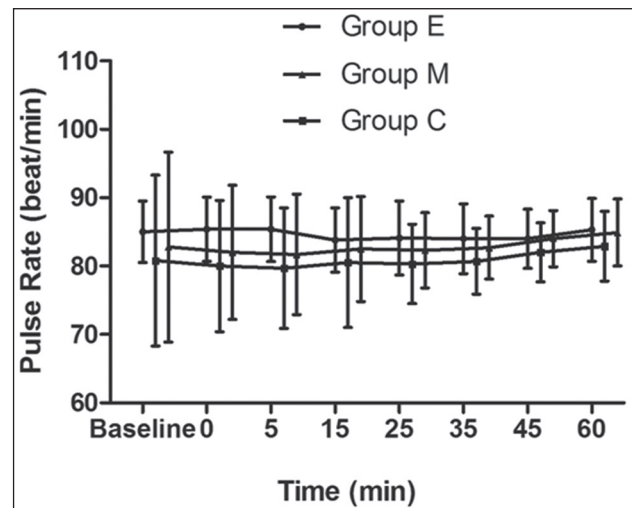


Figure 4. Pulse rate (PR) changes of groups M, E, and C. Data were presented as mean $\pm$ SD. Overall, study groups were similar with regard to heart rate values ($p>0.05$)

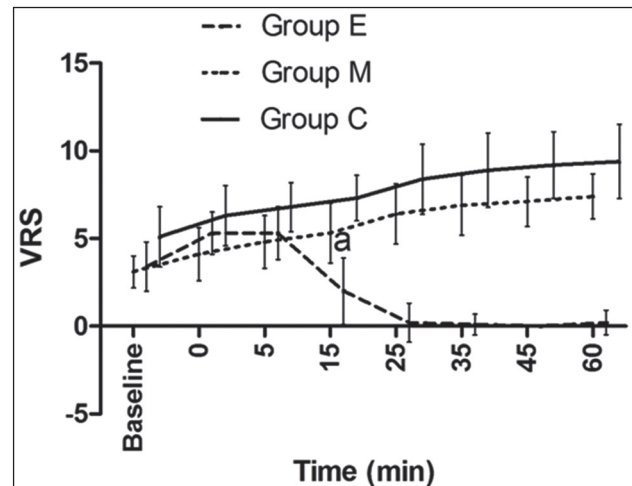


Figure 5. Verbal rating score (VRS) changes of groups M, E, and C. Data were presented as mean $\pm$ SD. ^a $P<0.05$ vs. groups M and C from 15 min to 60 min

Concerning the progress of labor, the first stage of labor was prolonged in the group C ($p<0.05$), while the second stage labor was prolonged in the groups E and M ($p<0.01$) (Figure 6). Cesarean section to one patient (3.3 %) and vacuum extraction to two patients (6.6 %) were performed in the group E, while all of the patients in the groups M and C had normal spontaneous vaginal delivery. The difference between the study groups with regard to type of delivery was not significant ($p>0.05$).

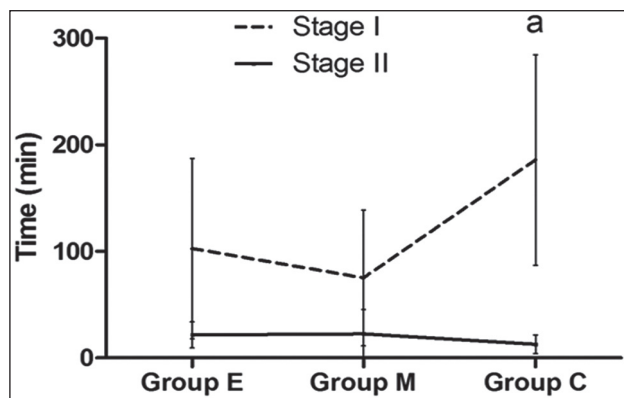


Figure 6. Duration of stages I and II of labor of groups E, M, and C. Data were presented as mean $\pm$ SD. ^a $P < 0.05$ vs. groups E and M

None of the neonates had depressed respiration on birth and there were no significant differences in the 1 and 5 minutes Apgar scores between the study groups ($p > 0.05$). The umbilical artery blood gases were summarized in Figure 7. Neonatal acidosis ($pH < 7.20$) was observed in 2 parturients in the group E (6.6%), while carbon dioxide tensions were normal (≥ 65 mmHg) in all the patients. Overall, the umbilical artery blood gas values did not differ significantly between the study groups ($p > 0.05$).

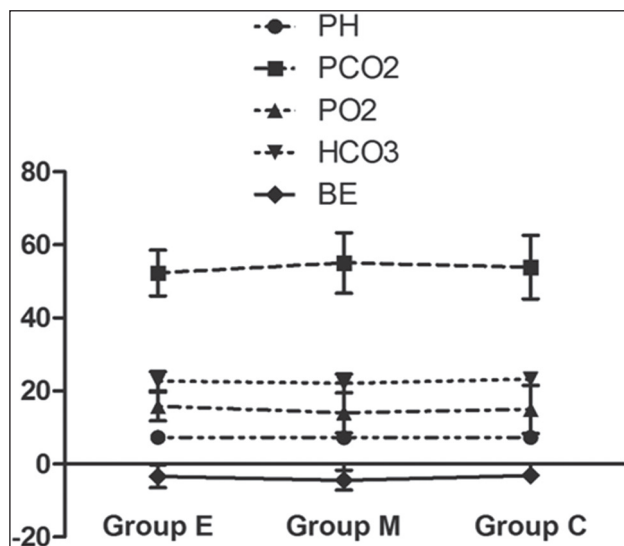


Figure 7. Blood gas values of groups M, E, and C. Data were presented as mean $\pm$ SD. Overall, study groups were similar with regard to these values ($p > 0.05$)

When parturients were queried within 24 h of delivery, 66% of women in the group E rated their satisfaction as good, compared with 20% of women in the group M ($p < 0.01$) (Figure 8).

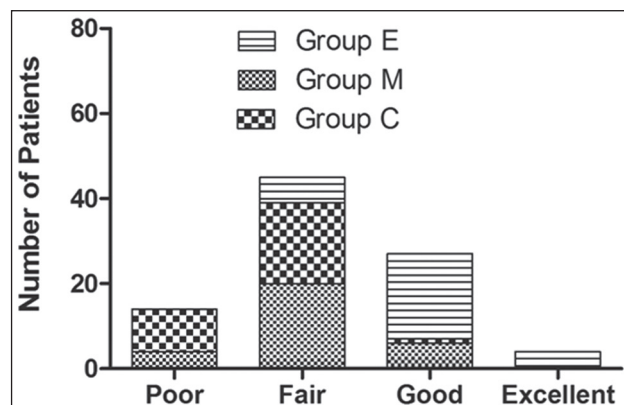


Figure 8. Ratios of patients' satisfaction of groups M, E, and C. Overall, patients' satisfaction of group E is better than groups M and C ($p < 0.05$)

Discussion

Primary findings of this study as neonatal blood gases and Apgar scores did not show significant change with epidural or intravenous labor analgesia when compared with no analgesia.

The major adverse effect of regional anesthesia and its sympathetic blockade is uteroplacental hypoperfusion that leads to an acute fall in intervillous blood flow with the potential for fetal acidemia. Antoine et al. (5) in a study of cesarean deliveries under epidural anesthesia found that 44% of patients suffered significant hypotension and they concluded that fetal acidosis was proportional to the severity of hypotension and the ephedrine dose. In a study by Sendag et al. (6) investigating the effects of lumbar epidural anesthesia on the Apgar score and acid-base status of the newborn, the mean umbilical artery blood pH was found to be significantly lower in the newborns exposed to lumbar epidural anesthesia. They concluded that lumbar epidural anesthesia was associated with lower umbilical arterial blood pH values, occasionally with severe fetal acidemia. Leveno KJ et al. (4) reported that regional anesthesia was associated with features of an acute respiratory type of fetal acidemia that was less frequent with epidural anesthesia compared to subarachnoid techniques. Repeated maternal administration of opioids such as meperidine results in significant fetal exposure and neonatal respiratory depression (7). El-Refaie et al. (8) investigated the effectiveness of meperidine, administered during the first stage of labor in patients with uterine dystocia. They found that the pH level of the umbilical cord arterial blood samples

were lower in the patients given meperidine than the control patients, although this difference was not reached statistical significance. For systemic analgesia, meperidine has been most extensively studied and compared with neuraxial analgesia. Alternatives have few advantages, remifentanyl being the most promising. Potentially serious side effects like maternal oxygen desaturation, sedation, and reduced fetal heart rates observed frequently during remifentanyl analgesia is thought to limit the use of remifentanyl in obstetrical practice (9). In a study comparing the analgesic efficacy of patient-controlled intravenous fentanyl, remifentanyl, and meperidine in labor, the results showed that none of those agents were particularly effective, overall satisfaction was greatest in the remifentanyl group and the neonatal outcomes were similar in all groups (10). Repeated maternal administration of opioids such as meperidine results in significant fetal exposure and neonatal respiratory depression. (11) During epidural analgesia, transient hyperventilation during, and hypoventilation between uterine contractions can be decreased, by this way, maternal PaCO₂ and PaO₂ may remain in normal ranges. In an unrandomized trial by Griffin et al. (12), the effect of analgesia on the incidence of hypoxemia during the second stage of labor was assessed. The lowest median incidence of desaturation (Spo₂<94%) was found in the extradural bupivacaine group, comparing with the groups of no analgesia, intravenous meperidine, epidural bupivacaine and fentanyl analgesia. It was concluded that there was no correlation between maternal oxygenation during the second stage of labor and measures of neonatal outcome including Apgar scores and umbilical artery and vein blood gases.

In our study, despite the higher rate of hypotension in epidural analgesia group, there were only 2 cases (6.6%) with umbilical artery blood pH levels of less than 7.20. Our results revealed that the Apgar scores and umbilical artery blood gases were in normal ranges in the study groups receiving epidural or intravenous analgesia or no analgesia. At the same time, the difference between the study groups with regard to type of delivery was not significant ($p>0.05$), with the cesarean section rate of 3.3%, and vacuum extraction rate of 6.6%. In an evaluation of cesarean delivery sponsored by American College of Obstetricians and Gynecologists, it was concluded that there

was an association between the use of epidural analgesia during labor and the risk of cesarean delivery (13). Sharma et al. (14) compared epidural analgesia to intravenous meperidine analgesia using patient-controlled devices to evaluate the effects of labor epidural analgesia, primarily on the rate of cesarean deliveries while minimizing limitations attributable to study design, and they found that cesarean deliveries did not increase in the epidural analgesia group. Sharma et al. (15) ended up with the same results in an individual patient meta-analysis of 2,703 women.

Although randomized trials have suggested that epidural labor analgesia increases instrumental vaginal delivery rates, this might be overcome by active management of labor or judicious use of oxytocin in the second stage (16). In our study, concerning the progress of labor, the first stage was prolonged in-group C while the second stage of labor was prolonged in both groups E and M. Patient satisfaction was much better with epidural analgesia, being consistent with the results of other studies.

In conclusion, the results of our study demonstrate that, neonatal Apgar scores and umbilical arterial blood gas values are similar in parturients receiving epidural analgesia, intravenous opioid analgesia and no analgesia. Epidural analgesia is a more effective method for pain relief during labor and delivery than intravenous opioid analgesia with no detrimental effects on the progress of labor.

References

1. Eyrton S, Ezri T. Options for systemic labor analgesia. *Curr Opin Anaesthesiol*. 2007 Jun; 20(3): 181-5.
2. R02 Bricker L, Lavender T. Parenteral opioids for labor pain relief: a systematic review. *Am J Obstet Gynecol*. 2002 May; 186(5 Suppl Nature): S94-109.
3. Reynolds F. Labour analgesia and the baby: good news is no news. *Int J Obstet Anesth*. 2011 Jan; 20(1): 38-50. Epub 2010 Dec 13.
4. Leveno KJ, Sidawi JE, Lucas MJ, Kelly MA. Fetal acidemia associated with regional anesthesia for elective cesarean delivery. *Obstet Gynecol*. 1995 Jan; 85(1): 79-83.
5. Antoine C, Young BK. Fetal lactic acidosis with epidural anesthesia. *Am J Obstet Gynecol*. 1982 Jan 1; 142(1): 55-9.

6. Sendağ F, Terek C, Oztekin K, Sağol S, Asena U. Comparison of epidural and general anaesthesia for elective caesarean delivery according to the effects of apgar scores and acid-base status. *Aust N Z J Obstet Gynaecol.* 1999 Nov; 39(4): 464-8.
7. Mattingly JE, D'Alessio J, Ramanathan J. Effects of obstetric analgesics and anesthetics on the neonate: a review. *Paediatr Drugs.* 2003; 5(9): 615-27.
8. El-Refaie TA, El-Said MM, Shoukry AA, Khafagy SM, El-Din AS, Badawy MM. Meperidine for uterine dystocia and its effect on duration of labor and neonatal acid-base status: a randomized clinical trial. *J Obstet Gynaecol Res.* 2012 Feb; 38(2): 383-9.
9. Volmanen P, Akural EI, Raudaskoski T, Alahuhta S. Remifentanyl in obstetric analgesia: a dose-finding study. *Anesth Analg.* 2002 Apr; 94(4): 913-7, table of contents.
10. Douma MR, Verwey RA, Kam-Endtz CE, van der Linden PD, Stienstra R. Obstetric analgesia: a comparison of patient-controlled meperidine, remifentanyl, and fentanyl in labour. *Br J Anaesth.* 2010 Feb; 104(2): 209-15.
11. Mattingly JE, D'Alessio J, Ramanathan J. Effects of obstetric analgesics and anesthetics on the neonate : a review. *Paediatr Drugs.* 2003; 5(9): 615-27.
12. Griffin RP, Reynolds F. Maternal hypoxaemia during labour and delivery: the influence of analgesia and effect on neonatal outcome. *Anaesthesia.* 1995 Feb; 50(2): 151-6.
13. ACOG committee opinion. No. 339: Analgesia and cesarean delivery rates. American College of Obstetricians and Gynecologists Committee on Obstetric Practice. *Obstet Gynecol.* 2006 Jun; 107(6): 1487-8.
14. Sharma SK, Alexander JM, Messick G, Bloom SL, McIntire DD, Wiley J, Leveno KJ. Cesarean delivery: a randomized trial of epidural analgesia versus intravenous meperidine analgesia during labor in nulliparous women. *Anesthesiology.* 2002 Mar; 96(3): 546-51.
15. Sharma SK, McIntire DD, Wiley J, Leveno KJ. Labor analgesia and cesarean delivery: an individual patient meta-analysis of nulliparous women. *Anesthesiology.* 2004 Jan; 100(1): 142-8; discussion 6A.
16. Impey L, MacQuillan K, Robson M. Epidural analgesia need not increase operative delivery rates. *Am J Obstet Gynecol.* 2000 Feb; 182(2): 358-63.

Corresponding Author

Feyza Yayci,
 Department of Anesthesiology and Reanimation,
 Goztepe Training and Research Hospital,
 Istanbul,
 Turkey,
 E-mail: yayci@yahoo.com

An ex vivo comparison of three electronic apex locators

Joanna Baginska¹, Ewa Linczuk¹, Bartłomiej Botulinski², Anna Kierklo²

¹ Department of Restorative Dentistry, Medical University of Białystok, Poland,

² Department of Dentistry Propaedeutic, Medical University of Białystok, Poland.

Abstract

Aim: The aim of the study was to evaluate *ex vivo* the accuracy of root canal measurements by three electronic apex locators.

Method: For the purpose of this *ex vivo* study, forty single root and single canal human teeth were prepared by cutting the crown to produce a flat surface for the precise reference point. Each canal was instrumented by the K-type file No. 10 until the file was visible at the apical foramen under 2.5x magnification and the control length (CL) was recorded with an endodontic ruler with a precision of 0.5 mm. Teeth were embedded in a plastic container filled with an alginate mold. The electronic length (EL) was established by three fifth-generation electronic apex locators: Rypex 5 (VDW GmbH, Munich, Germany), Locapex Five (Ionyx, Blanquefort, France) and Apex D.S.P. (Septodont, France). The measurements were taken three times by one operator until the devices signalized that the file reached the apical foramen. Differences between CL and EL were calculated and classified according to discrepancies in mm. Obtained data were analysed by the Pearson correlation coefficient and *t* test with 5% level of significance.

Results: The apical foramen was determined like CL in 70.5% of the specimens for Rypex 5, and in 62.5% and 57.5%, respectively, for Apex D.S.P. and Locapex Five. An analysis of Pearson's correlation coefficient revealed high levels of agreement between EL obtained by evaluated devices and CL. The *t* test showed no significant differences between CL and Rypex 5 ($p=0.6078$), however, such differences were shown for Apex D.S.P. and Locapex Five ($p=0.006$ and $p=0.0311$, respectively). For both units the mean EL was 0.2 mm shorter than the CL.

Conclusion: Under the condition of this *ex vivo* study, Rypex 5, Locapex Five and Apex D.S.P. EALs were found to be precise in determining the

tooth's apical foramen. Differences between direct visual measurements and electronic measurements observed in case of Apex D.S.P. and Locapex Five devices are not clinically significant.

Key words: electronic apex locators, canal working length, endodontic treatment, *ex vivo* study

Introduction

A key factor for successful endodontic treatment is a proper determination of the canal working length which should be maintained during canal shaping and filling procedures. Passing through apical foramen with the file leads to damage of the apical periodontal tissue and may be a cause of pain after the treatment, periapical inflammation or delayed healing of periodontal tissues. A too short working length is a cause of an incomplete canal debridement of bacteria left in the canal system.

Contemporary recommendations indicate an apical constriction (minor apical foramen) to be the most desirable end-point of canal preparation (1,2). An apical constriction is defined as being the narrowest portion of the canal system at its apical part. An average distance between an apical constriction and tooth's apex is 0.5-2 mm, but many variations in morphology are possible (1,3). Dentists have several methods for establishing the correct canal working length. The tactile method and paper point evaluation are known as less reliable and should be regarded as ancillary. For several years, radiography has been used for determining the working length. It is generally accepted that the end-point of preparation should be 0.5-1 mm shorter than the radiographic tooth apex (1,2). However, a radiological examination may contain errors due to distortions, artifacts and superimposition of dental structures it is not possible to provide x-ray examination in every situation (e.g. pregnancy), in addition the radiation dose for patients should be as low as possible. Currently, for determining canal

length electronic apex locators are recommended. There are many studies proving that the canal measurements provided electronically are more accurate than radiological ones (4-7).

The fundamental principles of electronic apex locators are: 1. there is a difference in the electrical conductivity between the canal and the tissues around the root apex, 2. the electrical resistance in the canal decreases from the coronal part to the apex, 3. the electrical resistance between the apical periodontal tissue and the oral mucosa is constant ($6,5\Omega$) (1). First-generation EALs were called resistance-based electronic apex locators. They were more accurate in dry canals than in those with pulp tissue, blood, pus or electrolytes (1). EAL regarded as second generation used 400-Hz alternating current and measured the variation in the impedance value. These devices allowed to provide measurements in wet environments, but due to the electrode being partially covered with insulating material they were not useful in narrow canals (1,8). Nowadays, second-generation units are not available on the market. At present, a large group called frequency EALs is used. Their principle of operation consists in comparing the resistance of currents with two or more markedly different frequencies. During the shift of the file in the canal the resistance decreases to a larger extent for the current with high frequency, and the maximum difference is recorded at the place of connection of the pulp and the periodontal tissue, e.g. at the apical constriction. In the third-generation units the currents are analysed simultaneously and the differences or the ratio of the impedance values are calculated. In the next generation devices the currents are emitted and analysed separately. In the fifth-generation apex locators the functional properties, such as the algorithm for calculating the properties of emitted currents, have been improved and a colour display to make the measurement easier to read has been added. Representatives of this group are Rypex 5 (VDW GmbH, Munich, Germany), Locapex Five (Ionyx, Blanquefort, France) and Apex D.S.P. (Septodont, France). The manufacturers reduced the size and weight of the Apex D.S.P. device so that it can be placed on the breast of a patient, which should facilitate the measurement, whereas a considerable shortening of the leads should prevent interference in the measurements (9). As compared to the first- and second-generation devices, the currently used

apex locators are characterised by the stability of the measurements in a wet environment, no influence of the pulp and periapical tissues' condition on the result, the possibility of taking the measurements also in teeth with a large diameter of the periapical foramen and no need of calibration (8).

The aim of the study was to evaluate *ex vivo* the accuracy of root canal measurements by three electronic apex locators.

Materials and Methods

The protocol of the present study was approved by the Bioethical Committee of the Medical University of Bialystok, Poland. For the purpose of this *ex vivo* study, forty single root and single canal human teeth with fully formed apices and without any symptoms of caries or canal treatment were selected. The teeth were extracted for periodontal or orthodontic reasons. After the extraction the teeth were stored in normal saline solution at room temperature. Every tooth was prepared by cutting the crown to produce a flat surface for the precise reference point and shaping canal's coronal part using Gates-Glidden burs #3 and #4 (Poldent, Warsaw, Poland). Canals were irrigated with 2.0 mL of 2% NaOCl. Each canal was instrumented by the K-type file No. 10 according to ISO (Poldent, Warsaw, Poland) until the file was visible at the apical foramen, the position of the file's tip was checked using the 2.5x magnifying loupes (SurgiTel, Michigan, USA). The silicon stop was set to a reference point, the file was removed and the control length (CL) was recorded with an endodontic ruler (VDW, Munich, Germany) with a precision of 0.5 mm. The next step was to embed the teeth in a plastic container filled with an alginate mold (Phase, Zermack, Italy). Next to the teeth a metal rod was inserted to be attached with the clip of electronic apex locators. Then the electronic length (EL) was established by three fifth-generation electronic apex locators: Rypex 5 (VDW GmbH, Munich, Germany), Locapex Five (Ionyx, Blanquefort, France) and Apex D.S.P. (Septodont, France). Devices are presented on Figures 1-3. The measurements were taken three times by one operator until the devices signaled that the file reached the apical foramen. In case of Rypex 5 it was when the last red field in enlarged image of the root end on LCD display was shown. Locapex Five has several

Table 1. Accuracy of electronic length measurements with Apex D.S.P., Locapex Five and Rypex 5 compared to control length measurements

	-1	-0.5	0	0.5	1	1.5
Apex D.S.P.	1 (2.5%)	11 (27.5%)	25 (62.5%)	2 (5%)	1 (2.5%)	0
Locapex Five	2 (5%)	10 (25%)	23 (57.5%)	4 (10%)	1 (2.5%)	0
Rypex 5	2 (5%)	5 (12.5%)	28 (70.5%)	3 (7.5%)	1 (2.5%)	1 (2.5%)

colour led lights indicating the file progression in the canal with the “apex” clearly marked in red. The Apex D.S.P. unit shows the depth of the endodontic file with five led lights distributed every 0.5-0.2 mm, the apical foramen position is indicated by red light which starts to flash if the file passes the apex. After reaching the apical foramen position, EL was measured similar to CL. For the next evaluation an average electronic length for each EAL was calculated. Differences between CL and EL were calculated and classified according to discrepancies in mm: the measurements shorter than CL (from -1 to -0.5), the measurements exact with CL (0) and the measurements longer than CL (from 0.5 to 1.5). Obtained data were analysed by the Pearson correlation coefficient and *t* test with 5% level of significance.

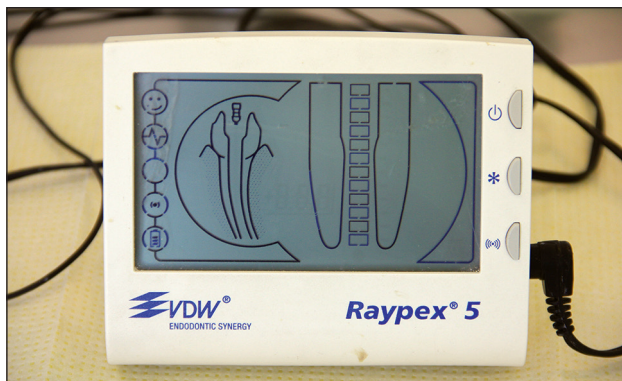


Figure 1. Electronic apex locator Rypex 5 (VDW GmbH, Munich, Germany)

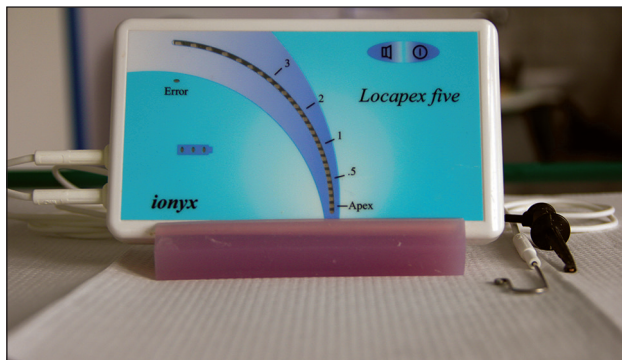


Figure 2. Electronic apex locator Locapex Five (Ionix, Blanquefort, France)



Figure 3. Electronic apex locator Apex D.S.P. (Septodont, France)

Results

Table 1 shows the accuracy of electronic length measurements with three EALs compared to control length measurements. The apical foramen was determined like CL in 70.5% of the specimens for Rypex 5, and in 62.5% and 57.5%, respectively, for Apex D.S.P. and Locapex Five. In 3 cases (7.5%) for Apex D.S.P. and in 5 cases (12.5%) for other two EALs, measurements longer than CL were observed. Taking into consideration clinically acceptable level scores of ± 0.5 mm, incorrect measurements in 5% specimens for Apex A.S.P., in 10% for Rypex 5 and in 17.5% for Locapex Five were presented. An analysis of Pearson's correlation coefficient revealed high levels of agreement between EL obtained by evaluated devices and CL (Tab.2). The *t* test showed no significant differences between CL and Rypex 5 ($p=0.6078$), however, such differences were shown for Apex D.S.P. and Locapex Five ($p=0.006$ and $p=0.0311$, respectively). For both units the mean EL was 0.2 mm shorter than the CL. The data are presented in Table 3.

Table 2. Pearson's correlation coefficient

	Apex D.S.P.	Locapex Five	Rypex 5
r	0.9871	0.9827	0.9719
p	p=0.00	p=0.00	p=0.00

Table 3. Means and standard deviation of measurements obtained with three different electronic apex locators

	Mean $\pm$ SD	p*
Control length	17.0 $\pm$ 1.9	-
Apex D.S.P.	16.9 $\pm$ 1.8	0.006
Locapex Five	16.9 $\pm$ 1.8	0.0311
Rypex 5	17.0 $\pm$ 1.9	0.6078

* *t* test

Discussion

An alginate experimental model for *in vitro* demonstrating and testing electronic apex locators was first introduced by Katz *et al.* (10) in 1992 and is widely used as a reliable and easy to made tool for evaluation of the accuracy of EALs (11, 12). It allows to evaluate the validity of devices by comparing the electronic results with direct visual measurements, as well as by comparing different units. In such researches it is important for the apical part of the root to be blinded for the operator. The other materials used as embedding media were agar, gelatine or saline solution (5, 13-18). According to Baldi *et al.* (13) all of them are characterized by similar effectiveness for *in vitro* assessment of electronic apex locators.

One of the most frequently used devices is the third-generation apex locator Root ZX (J Morita Co, Tustin, USA) - it is widely available and its reliability was proven by numerous studies (4-6,18-21). Two of EALs used for the present study, Rypex 5 and Apex D.S.P., were also positively assessed in *ex vivo* and clinical conditions (6,9,19,21-24). No reports on Locapex Five have been found in the literature at all. Lipski *et al.* (19) found a similar precision of Apex A.S.P. and Root ZX during *in vitro* measurements. The same authors also proved that Apex D.S.P. was a relatively reliable device for determining root canal length in patients (9). However, in the study conducted by Carvalho *et al.* (25), this device was less precise than Root ZX and Elements Diagnostic. Authors who compared Raypex 5 and Root ZX *in vitro* and in clinical conditions did not observe any differences in obtained data (6,21,26). However, data from the literature are difficult to compare due to variations in the development of the study's protocol. Measurements may be provided to minor or major foramen and the

tolerance level may be established at 0 mm, $\pm$ 0.5 mm or $\pm$ 1 mm. Some authors use the observation of the root tip as a control, others, especially during *in vivo* studies, compare electronic measurements with radiographic images.

The accuracy of determining root canal length by Rypex 5, Locapex Five and Apex D.S.P. has not been compared. Data obtained in the present study showed that all three devices demonstrated a high correlation with control measurements. It should be emphasized that the differences between EL and CL obtained in the *t* test for Apex D.S.P. and Locapex Five (0.2 mm $\pm$ 1.8) were clinically insignificant because during endodontic treatment the root canal length is usually measured with 0.5 mm precision. In our study, in case of Apex D.S.P., the percentage of results similar to CL (62.5%) was higher than reported by Lipski *et al.* (9) and Carvalho *et al.* (25), which was 43.1% and 15-20%, respectively. We observed that the number of overestimated measurements was small for every evaluated device (7.5%-12.5%), despite our reference level was not an apical constriction but an apical foramen. The percentage of measurements longer than the visual control reported by other authors varied between 2.6% and 30% (16,20,25). Some authors claim that when the EALs show the file position at "apex" it may have been already placed over the apical foramen (4,9,20). Lipski *et al.* (9) in their *in vitro* evaluation of EAL Apex D.S.P. found that overestimated measurements were more often observed when the end-point of the canal length was at the apex position (the red diode) than at a position 0.25 mm shorter than the apex (the green diode). However, opposite findings were reported by de Vasconcelos *et al.* (20). In their study only Root ZX demonstrated precise measurements in both situations, e.g. the termination of canal measurement at the apical foramen and 1 mm shorter; other devices were more accurate when the file was placed at the apical foramen. Nekoofar *et al.* (1) and Mitelic *et al.* (27) suggested that it was difficult to precisely locate apical constriction even with the currently used EALs. Nekoofar *et al.* (1) recommended to provide canal measurement until the reading of the apical foramen, and then to move the file back by 0.5-1 mm. The described procedure ensures an operator that the canal length is determined properly

and prevents from overinstrumenting and overfilling of root canal, however, it does not mean that the file tip is placed exactly at the apical constriction (1, 20, 21).

Many authors proved that the electronic canal length measurements are independent of the kind of irrigant present in the canal (1,18,25,28). Most frequently canals are irrigated with sodium hypochlorite, saline, chlorhexidine and EDTA. The file number is considered as a factor which may influence the accuracy of root canal measurement, however, data in the literature are ambiguous. According to *Sadeghi & Abolghasemi* (24), in case of Rypex 5, the higher number of correct results was obtained with the file no. 15 compared to files no. 10, 20 and 25 according to ISO. On the other hand, *Cianconi et al.* (4) did not observe any differences when using files no. 06, 08 and 10 (ISO). *Nguyen et al.* (11) came to the same conclusion for the files no. 10 and 60 in the canals which were previously mechanically prepared. Furthermore, the authors observed an interesting pattern: when after canal preparation the instrument was inserted into such canal to a working length determined before the beginning of the treatment, the tip of the instrument was closer to the root apex than before the beginning of the treatment. The cause of shortening of the working length was probably the straightening of the originally curved canal. The phenomenon should be taken into consideration before the final filling of a root canal because it can be one of the causes of canal overfilling.

Other factors influencing the accuracy of EALs are the morphology of apical constriction and the location of apical foramen, particularly if it is located laterally to the root's tip (27,29). *Mitelic et al.* (27) suggest that the reproducibility of different devices depends on anatomical variation, especially at a minor foramen. The influence of the pulp and periapical tissues' condition on the performance of EALs was widely discussed in the literature. Some authors observed that the presence of the periapical lesions reduced the number of proper canal measurements, others did not find any such relationship (6,9,27,28,30). Probably this was a problem when the first and second generations of EALs were used, whereas modern devices are less sensitive to factors connected with the canal morphology or the pulp and periodontal tissues' condition.

Conclusion

Under the condition of this *ex vivo* study, Rypex 5, Locapex Five and Apex D.S.P. EALs were found to be precise in determining the tooth's apical foramen. Differences between direct visual measurements and electronic measurements observed in case of Apex D.S.P. and Locapex Five devices are not clinically significant.

References

1. *Nekoofar MH, Ghandi MM, Hayes SJ, Dummer PMH. The fundamental operating principles of electronic root canal measurement devices. Int Endod J. 2006; 39: 595-609.*
2. *Ricucci D. Apical limit of root canal instrumentation and obturation, part I. Literature review. Int Endod J. 1998; 31: 384-393.*
3. *Cheung GSP, Yang J, Fan B. Morphometric study of the apical anatomy of C-shaped root canal systems in mandibular second molars. Int Endod J 2007; 40: 239-246.*
4. *Cianconi L, Angotii V, Felici R, Conte G, Mnacini M. Accuracy of three electronic apex locators compared with digital radiography: ex vivo study. J Endod 2010; 36: 2003-2007.*
5. *Ravanshad S, Adl A, Anvar J. Effect of working length measurement by electronic apex locator or radiography on the adequacy of final working length: a randomized clinical trial. J Endod 2010; 36: 1753-1756.*
6. *Vieyra JP, Acosta J. Comparison of working length determination with radiographs and four electronic apex locators. Int Endod J 2011; 44, 6: 510-518.*
7. *Real DG, Davidiwick H, Moura-Netto C, Zenkner CLL, Paglairin CML, Barletta FB, de Moura AAM. Accuracy of working length determination using 3 electronic apex locators and direct digital radiography. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011; 111: e44-e49.*
8. *Szczewczenko J, Obersztyn I. Rozwój elektronicznej metody pomiaru długości roboczej kanału na przykładzie najpopularniejszych endometrów – przegląd piśmiennictwa. Twój Przegląd Stomatologiczny 2008; 9: 76-81. [article in Polish].*
9. *Lipski M, Woźniak K, Lichota D, Nowicka A, Jamroszczyk K, Sobolewska E, Tomasik M, Łagocka R, Tomasik E. In vivo root canal length determination using Apex D.S.P. Polish J of Environ. Stud. 2008; 17 (6A Part II): 213-217.*

10. Katz A, Kaufman AY, Szajkis S. *an in vitro model for testing the accuracy of apex locators*. *Revue Francaise D'endodontie*. 1992; 11: 67. [abstract].
11. Nguyen HQ, Kaufman AY, Komorowski RC, Friedman S: *Electronic length measurement using small and large files in enlarged canals*. *Int Endod J* 1996; 29: 359-364.
12. Tinaz AC, Alaçam T, Topuz Ö. *A simple model to demonstrate the electronic apex locator*: *Int Endod J* 2002; 35: 940-945.
13. Baldi JV, Victorino FR, Bernardes RA, de Moraes IG, Bramante CM, Garcia RB, Bernardineli N. *Influence of embedding media on the assessment of electronic apex locators*. *J Endod* 2007; 33:476-9.
14. Aurelio JA, Nahmias Y, Gerstein H. *A model for demonstrating an electronic canal-length measuring device*. *J Endod* 1983; 9: 568-569.
15. Donnelly JC. *A simplified model to demonstrate the operation of electronic root-canal measuring device*. *J Endod*. 1993; 19: 579-580.
16. El Ayouti A, Weiger R, Lost C. *The ability of Root ZX apex locator to reduce the frequency of overestimated radiographic working length*. *J Endod* 2002; 28: 116-118.
17. Goldberg F, De Silvio AC, Manfre S, Nastri N. *In vitro measurement accuracy of an electronic apex locator in teeth with simulated apical resorption*. *J Endod* 2002; 28: 461-463.
18. Jenkins JA, Walker WA 3rd, Schindler WG, Flores CM. *An in vitro evaluation of the accuracy of the Root ZX in the presence of various irrigants*. *J Endod* 2011; 27: 209-211.
19. Lipski M, Woźniak K, Lichota D, Jamroszczyk K, Nowicka A, Góra M, Trabska-Świstelnicka M, Sobolewska E, Tomasik M, Buczkowska-Radlińska J. *[A comparative evaluation of Apex D.S.P. and Root ZX Apex locators. An in vitro study]*. *Ann Acad Med. Stetin* 2008; 54: 33-36. [article in Polish].
20. de Vasconcelos BC, do Vale TM, de Menezes AS, Pinheiro-Junior EC, Vivacqua-Gomes N, Bernardes RA, Hungaro Duarte MA. *An ex vivo comparison of root canal length determination by three electronic apex locators at positions short of the apical foramen*. *Oral Surg Oral Med. Oral Pathol Oral Radiol Endod* 2010; 110: e57-e61.
21. Wrbas KT, Ziegler AA, Altenburger MJ, Schirrmeister JF. *In vivo comparison of working length determination with two electronic apex locators*. *Int Endod J* 2007; 40: 133-8.
22. Lewińska E, Lipski M, Marciniak-Paradowska M, Woźniak K, Lichota D. *[The evaluation of the ability of Apex D.S.P. to determine the length of root canal. In vitro study]*. *Ann Acad Med. Stetin* 2008; 54: 37-40 [article in Polish].
23. Pascon EA, Marrelli M, Congi O, Ciancio R, Miceli F, Versiani MA. *An ex vivo comparison of working length determination by 3 electronic apex locators*. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009; 108 (3): e147-51.
24. Sadeghi S, Abolghasemi M. *The effect of file size on the accuracy of the Rypex 5 apex locator: an in vitro study*. *J Dent Res Dent Clin Dent Prospect* 2008; 2: 24-27.
25. Carvalho ALP, Moura-Netto C, Moura AAM, Marques MM, Davidowicz H. *Accuracy of three apex locators in presence of difference irrigating solutions*. *Braz Oral Res* 2010; 24: 394-398.
26. Somma F, Castagnola R, Lajolo C, Paternò Holzman L, Marigo L. *In vivo accuracy of three electronic root canal length measurement devices: Dentaport ZX, Raypex 5 and Propex II*. *Int Endod J* 2012 Jan 19. doi: 10.1111/j.1365-2591.2011.02010.x. [Epub ahead of print].
27. Mitelic V, Beljic-Ivanovic K, Ivanovic V. *Clinical reproducibility of three electronic apex locators*. *Int Endod J*. 2011; 44: 769-776.
28. Kaufman AY, Keila S, Yoshpe M. *Accuracy of a new apex locator: an in vitro study*. *Int Endod J* 2002; 35: 186-192.
29. Ding J, Gutmann JL, Fan B, Lu Y, Chen H. *Investigation of apex locators and related morphological factors*. *J Endod* 2010; 36: 1399-1403.
30. Pawińska-Magnuszewska M, Waszkiel D, Kierklo A. *Stan okolicy przyszczytowej zębów a wynik elektronicznych pomiarów długości kanałów*. *Mag Stomatol* 1996; 6(7): 41-44. [article in Polish].

Corresponding Author

Joanna Baginska,
Department of Restorative Dentistry,
Medical University of Białystok,
Białystok,
Poland,
E-mail: jbaginska@wp.pl

The effect of caffeic acid phenethyl ester on QT interval in cirrhotic rats

Mahin Dianat¹, Samira Saadat Fard², Mohammad Badavi¹, Akram Ahangarpour¹

¹ Department of Physiology, Physiology Research Center, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran,

² Department of Physiology, Physiology Research Center, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz & Jahrom University of Medical sciences, Iran.

Abstract

Abnormalities in cardiac electrophysiology are established in cirrhotic patients. QT Prolongation is one of the major problems that Increase ventricular arrhythmias risk in cirrhotic patients.

Caffeic acid phenethyl ester (CAPE) is one of the major compounds of propolis that have antiarrhythmic, antioxidant and anti-inflammatory properties.

This study designed to investigate the effect of CAPE on QT interval in rats with biliary cirrhosis.

Thirty male Sprague-Dawley rats (200-250 g) divided into three groups (sham, cirrhotic, cirrhotic treated with CAPE). CAPE administrated (1µg/kg/day, ip) for 5 weeks. In order to induce cirrhosis, bile duct ligation (BDL) was used. In all groups before BDL and five weeks after surgery animals anesthetized and electrocardiogram recorded (lead II). The QT interval was calculated using the Bazzet's formula and QTc was obtained. There was no significant difference in QTc value among groups before BDL. After five weeks of the BDL, in cirrhotic group, QTc significantly increased compared to sham group (198±6.1 vs. 156.5±6.8 msec) (p<0.001). In the CAPE-treated rats, QTc significantly had reduced in compared to cirrhotic group (176.5±4.9 vs. 198±6.1 msec) (p<0.05).

These results reveal that cirrhosis prolonged QT interval, and CAPE has an ameliorating effect on QT prolongation probably via its antiarrhythmic property.

Key words: Cirrhosis, Caffeic Acid Phenethyl Ester, QT Prolongation, bazzet's formula, rat

Introduction

Cirrhosis is known to be associated with numerous cardiovascular abnormalities (1). Destruction of liver function was associated with the

function of the cardiovascular via a hyperdynamic circulation (2).

Hyperdynamic circulation is a common feature in human and experimental portal hypertension, with or without cirrhosis. That is also called hyperdynamic circulatory syndrome, that manifested by increase cardiac output and heart rate with decrease arterial blood flow, arterial blood pressure and total vascular resistance (1, 2). Despite this increase baseline cardiac output cirrhotic, patients show a reduced systolic and diastolic function in the face of physiological pharmacological and surgical stress (1, 3).

Cardiac electrical abnormalities are well documented in patient with liver cirrhosis (4). Prolongation of the QT interval is the most electrophysiological abnormality in cirrhotic patients (5, 6). The QT represents the duration of the ventricular electric systole, and its prolongation predisposes to the development of ventricular arrhythmias. QT interval duration can be determined by ECG recording from the onset of the QRS complex to the end of the T wave (7).

QT interval varies with heart rate, so that its shortness when heart rate increases. The most frequently formula to correct QT for heart rate (QTc) has been proposed by bazzet, who studied the relationship between QT and heart rate under resting and exercise (6, 8).

Bazzet's formula: QTc (QT corrected for HR) = QT/square root RR

Caffeic acid phenethyl ester (CAPE) is the active component of the propolis purified from the hives of honeybees. CAPE is a small lipid-soluble flavonoid-like compound that has antioxidant (9, 10) anti-inflammatory (9, 11, 12), anti-carcinogenic (13, 14), antiviral (9, 15), immunomodulatory (16, 17) and free radical scavenging (18)

properties. It has been found that CAPE has protective effect against carbon tetrachloride-induced liver (19) and kidney (20) injuries in rats and mice. Also CAPE has protective effect on others tissue such as brain, heart (21, 22), and spinal cord (23), and has a potent antiarrhythmic (24) agent.

CAPE prevents the formation of ROS (reactive oxygen species), malondialdehyde (MDA) (23, 25, 26). At a concentration of 10 μ mole, it's completely blocks production of ROS in human neutrophils and suppresses the xanthine/xanthine oxidase system (27).

The aim of this study was to investigate the effect of CAPE on QT interval in billiary cirrhosis, induced by bile duct ligation (BDL) (28).

Material and methods

Animal model: Thirty male Sprague-Dawley rats (prepared by the Research Center for proliferation and maintenance of laboratory animals, Ahvaz JundiShapur University of Medical Sciences) weighing ranges from 200 to 250 g used in study. Animals kept in separate cages under standard laboratory (temperature of 25 ± 2 and 12: 12 h light- dark cycle) with free access to food and water. Protocol implementation was approved by local ethics committee Ahvaz JundiShapur University of Medical Sciences.

Chemical agents: CAPE (C8221) was purchased from Sigma- Aldrich, Germany.

Statistical analysis: For comparison between groups, One-Way ANOVA followed by LSD was used. Data calculated as Mean $\pm$ SEM and $P < 0.05$ was considered significant.

Experimental design: Extrahepatic cholestasis was induced by double ligation. All animals anesthetized with ketamin (50 mg/kg) and xylazine hydrochloride (10 mg/kg) (29). After a mid-line abdominal incision closed to the sternum, the common bile duct was identified; a double ligature was made with 3/0 silk, after that a cut was made between both ligatures (30, 31).

Then animals randomly divided three groups: the first group (n=10) were sham-operated (sham), in the second group animals were bile duct ligation (BDL) and third group animal were BDL treated with CAPE. In the CAPE-treated group, CAPE administrated daily (1 μ g/kg/day, ip) (24)

for 5 weeks (32, 33) and other groups received a similar volume of saline (22, 34).

QT interval assay: In all groups before surgery (BDL) and after five weeks since the BDL, animals were anesthetized (as before said) and lead II electrodes were attached to assess the QT interval (35). Power lab and Bio Amp (making AD-Instrument Co., Australia) used for recorded ECG.

Bilirubin analysis: After opening the chest blood samples collected for measure serum bilirubin in plasma as a markers to show the occurrence cholestasis (36). Then total and conjugated bilirubins tested with kit (pars azmoon, Iran) and were measured by colorimetric method using an autoanalyser (BT3000).

Results

Comparison of bilirubin levels among the groups (Table 1) shows that the amount Conjugated and total bilirubin in cirrhotic and CAPE-treated groups significantly higher than the sham group, but significant difference between the bilirubin levels in cirrhotic and CAPE-treated groups is not observed.

Table 1. Comparison of bilirubin levels in tested groups

animal groups	Bilirubin levels (mg/dl)	
	Conjugated	total
Sham	0.06 ± 0.008	0.17 ± 0.007
Cirrhotic	$4.9\pm 1.02^*$	$7.9\pm 1.3^{**}$
Cirrhotic+ CAPE	$4.9\pm 0.86^*$	$7.9\pm 1.2^{**}$

* Significantly different compared to sham group ($P < 0.01$).

** Significantly different compared to sham group ($P < 0.001$).

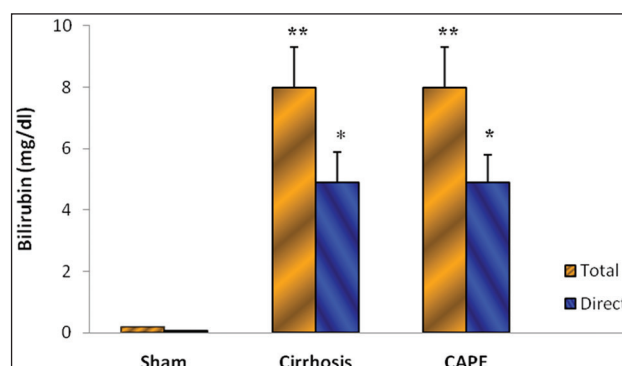


Figure 1. Comparison of bilirubin levels in different groups, 5 weeks after surgery in rat (n=10). Values are expressed as Mean $\pm$ SEM.

*significantly different compared to sham group at $p < 0.01$,

**significantly different compared to sham group at $p < 0.001$.

As is observed in Table 2, QTc in different groups before BDL, does not show a significant difference, but after five weeks of BDL, QTc in cirrhotic group significantly increased compared to sham group ($P<0.001$), also a significant difference between cirrhotic group and CAPE-treated rats was observed ($p<0.05$). So that in the CAPE-treated group observe fewer increased in the QTc ($p<0.05$).

Table 2. Comparison between QTc (in terms of milliseconds) in different groups according to the Bazzet's formula

animal groups	QTc (msec)	
	Before BDL	5 weeks after BDL
Sham	142.33±9	156.5±6.8
Cirrhotic	138.28±8.2	198±6.1 ^a
Cirrhotic+ CAPE	154.5±5.8	176.5±4.9 ^{b,c}

Values are expressed as mean ± SEM.

a: significantly different compared to sham group at $p<0.001$.

b: significantly different compared to cirrhotic group at $p<0.05$.

c: significantly different compared to sham group at $p<0.05$.

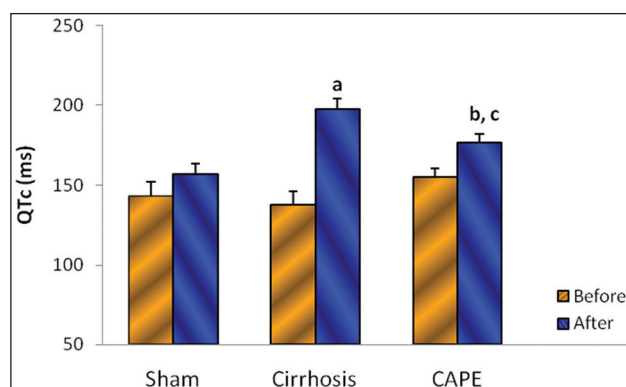


Figure 2. Comparison of QTc interval (according to the Bazzet's formula) in different groups before and 5 weeks after surgery in rat (n=10). Values are expressed as mean ± SEM. a: significantly different compared to sham group at $p<0.001$, b: significantly different compared to cirrhotic group at $p<0.05$, c: significantly different compared to sham group at $p<0.05$.

Discussion

In the present study, the effect of caffeic acid phenethyl ester (CAPE) was determined on QT interval in cirrhotic rats. CAPE has an anti-inflammatory, antioxidant and free radicals scavenging properties, which administrated five weeks to

control cardiovascular complications caused by cirrhosis.

A well-known model to create cirrhosis in animals is bile duct ligation (BDL) (30).

BDL induced cirrhosis in groups, which has reflected by a significant increase in serum bilirubin levels.

A serum bilirubins level has not changed by CAPE treatment. A possible reason for that can be due to dosage of CAPE (1µg/kg/day) which applied in our study.

Cirrhotic groups shown significant increase the QT interval after five weeks of BDL compared to sham group. Also QT interval in CAPE-treated group has been reduced significantly. It seems that CAPE treatment prevented the increases in QT interval and improved prolonged QT interval successfully.

Considering the positive impact of CAPE to avoid further increase in the QT interval in this study seems CAPE has a beneficial effect on cardiac complications followed by cirrhosis (such as QT prolongation) and act as an antiarrhythmic agent.

Mechanism that led to prolongation of QT interval in cirrhotic patients is remains unknown. Several studies have shown that in advanced cirrhosis sympathetic nervous system activity increased and use of beta blockers increased this interval will shorten (6). Summary findings thus suggest that chronic activation of the sympathetic system occurs in cirrhosis may play an important role in the play QT interval prolongation.

It is also likely that ion channels disruption based on QT interval prolongation is occurs in cirrhotic patients. The action potential, in ventricular myocyte from rats with chronic bile duct ligation, was found to be prolonged and whole-cell patch-clamp studies showed an impaired function of K channels responsible for IK (delayed rectifying k channel) and ITO (transient outward) currents, these channels responsible repolarization cells within the Phase 2 and 3 action potential and shorten the period of action potential, (6,7). Stimulation of chronic adrenergic in cirrhosis occurs leading the action potential prolongation and thus QT prolongation (5, 6).

BDL induced cirrhosis elevated liver damage markers. Chronic BDL significantly increases most of plasma and hepatic cytokine levels (36). Several studies have shown that treatment with CAPE remarkable decreases liver damage follow-

ing the closure of the bile duct in rats. Also other results shown that oxidative stress associated with lipid peroxidation is involved in the development of liver damage in cholestatic rats by BDL (37).

KUS and colleagues showed that administration of CAPE to rats on carbon tetrachloride-induced hepatotoxicity, were reduced the amount malonildealdehyde (MDA). MDA is one of the secondary products of oxidative stress is formed during lipid peroxidation and as one of the factors of toxic reactive oxygen species in rats after BDL. CAPE administration reduced the amount of tissue's MDA. Therefore, the findings indicate that CAPE through interfering with the free species decreased oxidative stress in cholestatic rats (38).

Therefore, it seems that protective effects of CAPE are mediated via, antioxidant, free radicals scavenging, blocks channels or inhibition of microsomal enzymes activities and has an antiarrhythmic property.

Acknowledgement

This study is a part of M.Sc. thesis of miss Saadat Fard S. Authors gratefully acknowledges the help and financial support of Physiology Research center of Ahvaz Jundishapur University of Medical Sciences (grant No.PRC-61).

References

1. Lee RF, Glenn TK, Lee SS. Cardiac dysfunction in cirrhosis. *Best Practice & Research Clinical Gastroenterology*. 2007; 21(1): 125-40.
2. Inserte J, Perelló A, Agulló L, Ruiz-Meana M, Schlüter K-D, Escalona N, et al. Left ventricular hypertrophy in rats with biliary cirrhosis. *Hepatology*. 2003; 38(3): 589-98.
3. Møller S, Henriksen JH. Cirrhotic cardiomyopathy: A pathophysiological review of circulatory dysfunction in liver disease. *Heart*. 2002; 87(1): 9-15.
4. Møller S, Henriksen JH. Cardiovascular complications of cirrhosis. *Postgraduate Medical Journal*. 2009; 85(999): 44-54.
5. Wong F. Cirrhotic cardiomyopathy. *Hepatology*. 2009 Mar; 49(3): 294-304.
6. Zambruni A, Trevisani F, Caraceni P, Bernardi M. Cardiac electrophysiological abnormalities in patients with cirrhosis. *Journal of Hepatology*. 2006; 44(5): 994-1002.
7. Møller S, Henriksen JH. Cirrhotic cardiomyopathy. *Journal of Hepatology*. 2010; 53(1): 179-90.
8. Torregrosa M, Aguadé S, Dos L, Segura R, González A, Evangelista A, et al. Cardiac alterations in cirrhosis: reversibility after liver transplantation. *Journal of Hepatology*. 2005; 42(1): 68-74.
9. Okutan H, Özcelik N, Ramazan Yılmaz H, Uz E. Effects of caffeic acid phenethyl ester on lipid peroxidation and antioxidant enzymes in diabetic rat heart. *Clinical Biochemistry*. 2005; 38(2): 191-6.
10. Oktar S, Aydın M, Yonden Z, Alcin E, İlhan S, Nacar A. Effects of caffeic acid phenethyl ester on isoproterenol-induced myocardial infarction in rats. *Anadolu Kardiyol Derg*. 2010; 10(4): 298-302.
11. Michaluart P, Masferrer JL, Carothers AM, Subbaramiah K, Zweifel BS, Koboldt C, et al. Inhibitory effects of caffeic acid phenethyl ester on the activity and expression of cyclooxygenase-2 in human oral epithelial cells and in a rat model of inflammation. *Cancer Res*. 1999 May 15; 59(10): 2347-52.
12. Orban Z, Mitsiades N, Burke Jr TR, Tsokos M, Chrousos GP. Caffeic acid phenethyl ester induces leukocyte apoptosis, modulates nuclear factor-kappa B and suppresses acute inflammation. *NeuroImmunoModulation*. 2000; 7(2): 99-105.
13. Chen YJ, Shiao MS, Wang SY. The antioxidant caffeic acid phenethyl ester induces apoptosis associated with selective scavenging of hydrogen peroxide in human leukemic HL-60 cells. *Anticancer Drugs*. 2001 Feb; 12(2): 143-9.
14. N. Orsolic ST, Z. Mihaljevic, L. Sver and I. Basic. Effects of local administration of propolis and its polyphenolic compounds on tumor formation and growth. *Biological and Pharmaceutical Bulletin*. 2005; 28(10): 1928-33.
15. Fesen MR, Pommier Y, Leteurtre F, Hiroguchi S, Yung J, Kohn KW. Inhibition of HIV-1 integrase by flavones, caffeic acid phenethyl ester (CAPE) and related compounds. *Biochemical Pharmacology*. 1994; 48(3): 595-608.
16. Park EH, Kahng JH. Suppressive effects of propolis in rat adjuvant arthritis. *Archives of Pharmacological Research*. 1999; 22(6): 554-8.
17. Albukhari AA, Gashlan HM, El-Beshbishy HA, Nagy AA, Abdel-Naim AB. Caffeic acid phenethyl ester protects against tamoxifen-induced hepatotoxicity in rats. *Food and Chemical Toxicology*. 2009; 47(7): 1689-95.
18. Wu W-M, Lu L, Long Y, Wang T, Liu L, Chen Q, et al. Free radical scavenging and antioxidative activities of caffeic acid phenethyl ester (CAPE) and its related compounds in solution and membranes: A structure-activity insight. *Food Chemistry*. 2007; 105(1): 107-15.

19. Lee KJ, Choi JH, Khanal T, Hwang YP, Chung YC, Jeong HG. Protective effect of caffeic acid phenethyl ester against carbon tetrachloride-induced hepatotoxicity in mice. *Toxicology*. 2008 Jun 3; 248(1): 18-24.
20. Ogeturk M, Kus I, Colakoglu N, Zararsiz I, Ilhan N, Sarsilmaz M. Caffeic acid phenethyl ester protects kidneys against carbon tetrachloride toxicity in rats. *J Ethnopharmacol*. 2005 Feb 28; 97(2): 273-80.
21. Mollaoglu H, Gokcimen A, Ozguner F, Oktem F, Koyu A, Kocak A, et al. Caffeic acid phenethyl ester prevents cadmium-induced cardiac impairment in rat. *Toxicology*. 2006 Oct 3; 227(1-2): 15-20.
22. Fadillioglu E, Oztas E, Erdogan H, Yagmurca M, Sogut S, Ucar M, et al. Protective effects of caffeic acid phenethyl ester on doxorubicin-induced cardiotoxicity in rats. *J Appl Toxicol*. 2004 Jan-Feb; 24(1): 47-52.
23. Ilhan A, Koltuksuz U, Ozen S, Uz E, Ciralik H, Akyol O. The effects of caffeic acid phenethyl ester (CAPE) on spinal cord ischemia/reperfusion injury in rabbits. *Eur J Cardiothorac Surg*. 1999 Oct; 16(4): 458-63.
24. Huang SS, Liu SM, Lin SM, Liao PH, Lin RH, Chen YC, et al. Antiarrhythmic effect of caffeic acid phenethyl ester (CAPE) on myocardial ischemia/reperfusion injury in rats. *Clin Biochem*. 2005 Oct; 38(10): 943-7.
25. Russo A, Longo R, Vanella A. Antioxidant activity of propolis: Role of caffeic acid phenethyl ester and galangin. *Fitoterapia*. 2002; 73(SUPPL. 1).
26. Altug ME, Serarslan Y, Bal R, Kontas T, Ekici F, Melek IM, et al. Caffeic acid phenethyl ester protects rabbit brains against permanent focal ischemia by antioxidant action: A biochemical and planimetric study. *Brain Research*. 2008; 1201: 135-42.
27. Sud'ina GF, Mirzoeva OK, Pushkareva MA, Korshunova GA, Sumbatyan NV, Varfolomeev SD. Caffeic acid phenethyl ester as a lipoxygenase inhibitor with antioxidant properties. *FEBS Letters*. 1993; 329(1-2): 21-4.
28. Rodriguez-Garay EA. Cholestasis: human disease and experimental animal models. *Ann Hepatol*. 2003 Oct-Dec; 2(4): 150-8.
29. Mitchell GF, Jeron A, Koren G. Measurement of heart rate and Q-T interval in the conscious mouse. *Am J Physiol*. 1998 Mar; 274(3 Pt 2): H747-51.
30. Liu Y, Binz J, Numerick MJ, Dennis S, Luo G, Desai B, et al. Hepatoprotection by the farnesoid X receptor agonist GW4064 in rat models of intra- and extrahepatic cholestasis. *J Clin Invest*. 2003 Dec; 112(11): 1678-87.
31. Rivera-Huizar S, Rincn-Sanchez AR, Covarrubias-Pinedo A, Islas-Carbajal MC, Gabriel-Ortiz G, Pedraza-Chaverri J, et al. Renal dysfunction as a consequence of acute liver damage by bile duct ligation in cirrhotic rats. *Experimental and Toxicologic Pathology*. 2006; 58(2-3): 185-95.
32. Koyu A, Ozguner F, Yilmaz H, Uz E, Cesur G, Ozcelik N. The protective effect of caffeic acid phenethyl ester (CAPE) on oxidative stress in rat liver exposed to the 900 MHz electromagnetic field. *Toxicol Ind Health*. 2009 Jul; 25(6): 429-34.
33. Payabvash S, Kiumehr S, Nezami BG, Zandieh A, Anvari P, Tavangar SM, et al. Endogenous opioids modulate hepatocyte apoptosis in a rat model of chronic cholestasis: the role of oxidative stress. *Liver Int*. 2007 May; 27(4): 538-47.
34. Ebrahimkhani MR, Moezi L, Kiani S, Merat S, Dehpour AR. Opioid receptor blockade improves mesenteric responsiveness in biliary cirrhosis. *Dig Dis Sci*. 2008 Nov; 53(11): 3007-11.
35. Lanjewar P, Pathak V, Lokhandwala Y. Issues in QT interval measurement. *Indian Pacing Electrophysiol J*. 2004; 4(4): 156-61.
36. Fernández-Martínez E, Pérez-Álvarez V, Tsutsumi V, Shibayama M, Muriel P. Chronic bile duct obstruction induces changes in plasma and hepatic levels of cytokines and nitric oxide in the rat. *Experimental and Toxicologic Pathology*. 2006; 58(1): 49-58.
37. Coban S, Yildiz F, Terzi A, Al B, Ozgor D, Ara C, et al. The Effect of Caffeic Acid Phenethyl Ester (CAPE) Against Cholestatic Liver Injury in Rats. *Journal of Surgical Research*. 2008; 159(2): 674-9.
38. Kus I, Colakoglu N, Pekmez H, Seckin D, Ogeturk M, Sarsilmaz M. Protective effects of caffeic acid phenethyl ester (CAPE) on carbon tetrachloride-induced hepatotoxicity in rats. *Acta Histochemica*. 2004; 106(4): 289-97.

Corresponding author

Mahin Dianat,

Department of Physiology,

Physiology Research Center,

Faculty of Medicine,

Ahvaz Jundishapur University of Medical Sciences,

Ahvaz,

Iran,

E-mail: dianat@ajums.ac.ir

Examining the relation between sociotropic and autonomic and problem solving abilities of nursing students

Birsen Altay¹, Huriye Demet Cabar², Bilge Bal Ozkaptan², Kubra Gumus¹

¹ Ondokuz Mayıs University Samsun School of Nursing, Samsun, Turkey,

² Sinop University School of Nursing, Sinop, Turkey.

Abstract

Objective: The objectives of this study is to examine the relation between sociotropic and autonomic personality with problem solving abilities of nursing students

Materials and Methods: This study which is a descriptive cross-sectional type was applied with 283 students studying in the first and fourth classes in nursing schools of Sinop, Samsun and Ordu. As data collection tool student description form guided with literature regarding the topic, sociotropy-otonomy scale developed by Beck et al. (1997) and Heppner and Peterson's problem solving inventory (1982) were implemented.

Result: The mean score was calculated as 68.14 ± 14.34 for sociotrophy and 72.72 ± 12.99 for autonomy of the students. The mean score value obtained from all participants is 95.33 ± 16.64 . It was demonstrated that the female students showed sociotropic (68.86 ± 14.56) and autonomic personality (73.52 ± 12.71) features more than the males and problem solving abilities were stated to be better than the males. The relation between sociotrophy and autonomy mean scores was found out insignificant regarding the classes of the students. Problem solving mean score of first year students was detected higher when compared to fourth classes and the relation between scores was stated statistically significant ($p < 0.05$).

Conclusion: At the end of the study, it was detected that the students showed sociotropic features at medium level and above with insufficient problem solving abilities, the females demonstrated more sociotropic and autonomic personality features and females and fourth classes had more problem solving abilities.

Key words: Nursing students, sociotropy, autonomy, problem solving ability

Introduction

Personality is a compilation of features that separates a person from other individuals and is presented as coherent and unique to individual. Feature of a personality is a collection that the individuals have acquired since birth and that continues by socialization period afterwards. Personality has two dimensions as sociotrophy and autonomy. Sociotrophy (social belonging) is defined as the positive interaction with other people (1, 2, 3). Autonomy is described as decisions independent of conditions and ability to manage oneself. It is the feature to enhance the independence of an individual and to protect the personal rights. The individuals having these personal features become pleased with directing own activities, reaching goals, being successful and controlling things around. The individuals showing sociotrophic features have more inclination to group work while the autonomies tend to work independently and individually (3, 4, 5).

It is significant for the employees to have an autonomic feature to decide and apply decisions (6). Considering professional measures, employees need to have some features of applying the job willingly, not changing the profession in a period of life, having autonomy, self control, personal responsibility and critical thinking (3, 7). These features have a distinctive significance for nursing. Because the features such as critical thinking, autonomy and problem solving abilities increase service quality and cater an identification available to profession (8, 9).

Problem solving is a mental and behavioral period containing effective ways to handle problems encountered in daily life (10). Problem solving ability is one of the important features for the individual to cope with society. Problem solving is a mental period (11). It was detected that the people who per-

ceive themselves sufficient to solve problems have more sociable and positive self perception and present more proper study methods and conditions in terms of academics (12). In the literature, less anxiety and stress, decrease of depression and disparity level were indicated when the individuals had problem solving abilities (11, 13, 14, 15).

When problem solving ability is a necessary skill for everyone living in the society it is pointed out to be more significant for the individuals in some fields of profession and for the health groups providing health service (10, 12). Nurses always encounter problems while working with the patients and the healthy individuals. Therefore problem solving abilities need to be well-performed. Because the ability to solve problems is the significant requirement for the nurse to provide safe, professional and individual centered nursing care (16). The more the nurses feel sufficient to solve the problems, the more their professional abilities, motivations, work satisfactions and performances will improve (5).

Nursing students as being health professionals of future need to have proficiency to handle with clinical problems and daily life stresses since health care quality will be affected directly (16). There are studies examining the relation between problem solving ability and different topics (17-22). However, no study has been encountered assessing the relation among independent decision, autonomy, sociotropy and problem solving to be the expected professional behaviours for nursing. Determination of sociotropic autonomic personality features and problem solving abilities will provide database for the inclusion of graduate and master's curriculum. Regulations associated with improving autonomic and sociotropic personality features, usage in positive ways and advance in problem solving abilities will contribute graduate nurses to gain professional identity. The aim of this study is to examine the relation between sociotropic and autonomic personality features and problem solving abilities of nurses in nursing schools of Samsun, Sinop and Ordu.

Materials and methods

The study population of this descriptive cross sectional type study was formed with nursing students at first and fourth classes in nursing schools of Samsun, Sinop and Ordu between 01.12.2010

- 01.02.2011. The study targeted to include all population and no sample was selected. In these three schools, the total amount of students were 162 individuals for first classes 121 individuals for fourth classes. Total participant amount consisted of 283 students containing 110 students registered to Samsun School of Nursing, 78 students registered to Sinop School of Nursing and 95 students registered to Ordu School of Nursing.

Data Sources

Descriptive form prepared with the guidance of literature associated with the topic, socio tropic -autonomy scale developed by Beck et al and then adapted to Turkish by Şahin et al. (23) in 1997 and problem solving inventory developed by Heppner and Peterson (1982) were implemented (24).

Sociotropy-Autonomy Scale: Sociotropy-Autonomy Scale briefly SAS was developed by Beck et al. The scale was adapted to Turkish by Şahin et al (23). The scale is to measure two different personality features consisting 60 items. 30 items belong to sociotropy subscale and 30 items to autonomy subscale. By commencing from "does not identify me" to " identifies me well" were presented as survey items "in response to "how much does it describe you?" within a five degree Likert type. The best rate to be achieved from a subscale is maximum 120 pts (30 items). While high scores that are gained from sociotropy subscale scores point out high sociotropy personality features, similarly high scores from the autonomy subscale show high level autonomic features. Owing to sociotropy autonomy scale factor analyses results, three factors were found out for each two dimensions.

Disapproval fear (total 10 questions), separation anxiety (total 13 questions) and pleasing others (total 7 questions) formed sociotropy subscale. In autonomy subscale, factors of personal success (total 12 questions) independence (total 12 questions) enjoyment of loneliness (total 6 questions) were carried out. In sociotropy-autonomy, Cronbach's Alpha values were detected as 0.81 in sociotropy and 0.80 in autonomy and in our study the values were presented as 0.80 in sociotropy and 0.76 in autonomy.

The study of Kaya et al. performed with nursing students detected alpha value as 0.84 in sociotropy dimension and 0.82 in autonomy dimension (3). Kokar and Gençöz (2004) in a study with stu-

dents preparing to attend the university found out Alpha value as 0.88 in sociotropy and 0.80 in autonomy (25). These findings show similar results with the ones obtained after the study. Therefore, SAS is a reliable scale tool for this study.

Problem Solving Inventory: Problem Solving Inventory was developed by Heppner and Peterson in 1982 (24). Turkish adaptation was formed by Nail Şahin, Nesrin Hisli Şahin and Paul Heppner in 1993 (23). Inventory, to be a self assessment tool is a self perception one that is applied to adolescents about problem solving abilities of the individual. It is a Likert type scale consisting of 35 items graded between 1-6. In scoring, negative items are reversed. Items of 1, 2, 3, 4, 11, 13, 14, 15, 17, 21, 25, 26, 30 and 34 are the ones to be scored reversely. Some items are kept out of scoring. (items 9,22,29) The lowest score of 32 items is 32 and the highest is 192. The mean score value of inventory is 80. The values above medium show that the individual is insufficient about problem solving and scores below show the contrary. That is, the higher the scores are, the individual percepts himself/herself as insufficient and on the contrary as sufficient.

Cronbach Alpha factor of the scale was found out as 0.88 and reliability factor as $r=0.81$. In this study Cronbach alpha factor was calculated as 0.79. The factors were 0.86 in the study of Taylan (26) 0.75 in the study of Kaya (27), 0.86 in the study of Durmaz et al (28) and 0.88 in the study of Keskin and Yildirim (29). Since these results demonstrate similarity with the findings acquired as a consequence of the study, problem solving inventory becomes a reliable measurement scale. However, correlation among sociotropy-autonomy and total score correlation factor with problem solving inventory mean scores was not found significant.

Statistical Analysis

Data was evaluated by SPSS for Windows 14.00 package programme. In evaluation, descriptive statistics such as percentage, mean, standart deviation and Student t-test, Mann Whitney-U test, One-Way ANOVA, Pearson correlation statistical analysis methods were applied. For the conduct of the study with scientific principles, autonomy, privacy and privacy protection, justice, benefits, informed consent that are proper to universal ethical principles were taken into consideration. The permissions

were obtained from the school of nursing directorates. The goal of the study was expressed to the participating students and oral consent by paying attention to being volunteer and willingness to attend the study was received.

Results

Descriptive features

283 students participated in the study containing 86.2 % female, 13.8% male. 98.6% are between the ages 18-25. 67.1 % of students' mothers are graduates of primary and secondary, 10.6% are literate and 88% do not work. Fathers are graduates of primary and secondary with the rate 49.5%, and 23.7% are graduates of high school and 20.5% are university graduates. 4.2% of fathers do not work, 21.2% are officers, 26.5% are retired. 86.2% have social security and it was evaluated that 74.2% have good, 22.6% have medium and 3.2% have weak family relationship.

Sociotropy-Autonomy Scale Scores

The scores the students received from the Sociotropy-Autonomy Scale is displayed in table 1. Depending on this, sociotropy mean score was detected as 68.14 ± 14.34 . The mean scores of sociotropy subscale dimensions were detected as the highest in terms of "separation concerns" (31.95 ± 7.29), and the lowest (15.17 ± 3.79) over pleasing one another. When these mean scores were examined according to the potential dispersion, students were considered to display sociotropic feature at medium level or above. It was determined that the autonomy mean score was 72.72 ± 12.99 . Autonomy subscale dimensions mean scores were 30.79 ± 6.03 for personal success, 30.92 ± 6.43 for independence, 14.12 ± 4.20 for being pleased with loneliness (table 1). These mean scores acquired point out autonomic personality features over medium level according to potential dispersion.

Problem solving ability

When table 2 was examined it was determined that the highest score was 152 and the lowest was 55. The mean score value that all participants received was 95.33 ± 16.64 . That is, the students were insufficient in solving problems.

Table 1. Sub scale and total score dispersion of sociotropy-autonomy (n: 283) and problem solving scale scores (n: 283)

Sociotropy-Autonomy Scale	Potantial Dispersion	Min.	Max.	Median	X±SS
Sociotropy					
Disapproval Fear	0-40	1.00	36.00	21.00	19.64±8.33
Seperation Anxiety	0-52	11.00	48.00	32.00	31.95±7.29
Pleasing others	0-28	4.00	25.00	15.00	15.17±3.79
Sociotropy General	0-120	27.00	104.00	69.00	68.14±14.34
Autonomy					
Personal Success	0-48	10.00	47.00	32.00	30.79±6.03
Independence	0-48	11.00	46.00	31.00	30.92±6.43
Enjoyment of Loneliness	0-24	3.00	24.00	14.00	14.12± 4.20
Autonomy General	0-120	30.00	106.00	73.00	72.72±12.99
General Total	0-240	65.00	204.00	141.00	140.86±21.82

Table 2. Problem solving inventory sub scales and total score dispersion (n: 283)

Problem Solving Inventory	Range	Min.	Max.	Ortanca	X	Sd
Sub factor						
Impatience approach	33.00	13.00	46.00	30.00	30.09	5.07
Thinking approach	23.00	5.00	28.00	13.00	13.44	4.70
Avoidance approach	15.00	5.00	20.00	13.00	12.62	3.12
Evaluation approach	15.00	3.00	18.00	9.00	8.90	3.40
Confidence approach	27.00	6.00	33.00	18.00	17.31	5.20
Planned approach	18.00	4.00	22.00	11.00	10.71	3.59
Total	97.00	55.00	152.00	97.00	95.33	16.64

The relation between demographic features and scale scores

The scores the students obtained from sociotropy autonomy scale according to personality features is seen on table 3. In this case, it was detected that 86.2% (n=244) of all students were mostly formed with female students and the difference of mean scores within male and female sociotropy-autonomy and problem solving abilities were stated statistically significant ($p<0.05$)(table 3). Sociotropy (68.86±14.56)and autonomy (73.52±12.71) scale scores of female students were found out higher than the male students. (98.56±16.21)

When the distribution of age groups were examined, ages between 26-33 formed the least (1.4%; n=4) and 18-25 made up the most age groups. (98.6%; n=279) While age groups and sociotropy had significant difference statistically, ($p<0.05$), there was no detection of significance between autonomy and problem solving abilities ($p>0.05$) (Table 3).

57.2 % of the students attending the study (n=162) were in their first year of school, 42.8% were in their

fourth year (n=121). When the students' mean scores were examined of sociotropy, autonomy and problem solving inventory, significant relation was not encountered between sociotropy and autonomy mean scores depending on the classes of the students ($p>0.05$). However, problem solving ability mean scores of first year students were noticed as higher when compared to fourth year students and the relation among was found statistically significant ($p<0.05$) (Table 3).

46.3% (n=131) of the students explained that they had spent most of their lives in cities and 32.2% (n=91) in towns. The difference between residence of students and sociotropy-autonomy and problem solving scale mean scores were stated as insignificant ($p>0.05$) (Table 3).

59.4% (n=168) of the students declared that they selected nursing willingly. Willingness to select nursing profession was stated as insignificant on sociotropy and autonomy mean scores. ($p>0.05$) Problem solving mean scores by selecting the profession by coincidence were lower than the ones to select the profession willingly(low score

Table 3. Sociotropy-autonomy personality dimensions and problem solving ability mean scores dispersion considering individual features of students

Personal Features			Sociotropy	Autonomy	Problem Solving Inventory
	n	%	X±Sd	X±Sd	X±Sd
Sex					
Female	244	86.2	68.86±14.56	73.52±12.71	92.22±15.69
Male	39	13.8	63.69±12.13	67.71±13.76	98.56±16.21
Statistic			T=2.102 P=0.036	T=2.615 P=0.009	T=-2.330 P=0.021
Age					
18-25	279	98.6	68.40±14.17	72.80±13.03	95.32±16.68
26-33	4	1.4	44.33±11.23	65.00±6.00	95.50±15.41
Statistic			T=2.930 P=0.004	T=1.034 P=0.302	T=-0.020 P=0.984
Classes					
1 st Class	162	57.2	68.74±14.43	72.79±13.90	98.27±15.52
4 th Class	121	42.8	67.34±14.23	72.61±11.73	91.38±17.32
Statistic			T=0.812 P=0.418	T=0.113 P=0.910	T=3.514 P=0.001
Residence					
City	131	46.3	66.68±15.06	73.63±13.08	95.04±18.03
District	91	32.2	68.20±13.48	73.27±12.72	95.47±15.87
Country	61	21.6	71.19±13.72	69.93±13.02	95.73±14.78
Statistic			T=0.411 P=0.663	T=0.041 P=0.959	F=0.040 P=0.960
Selection of Nursing					
Willing	168	59.4	67.94±14.57	71.76±12.39	95.18±15.92
Unwilling	74	26.1	68.25±14.90	72.12±13.50	98.67±18.85
By coincidence	41	14.5	68.78±12.52	77.70±13.66	89.90±13.90
Total	283		68.14±14.34	72.72±12.99	95.33±16.64
Statistic			T=0.326 P=0.722	T=0.332 P=0.717	F=3.754 P=0.025
School Life					
Pleased	143	50.5	68.06±14.31	72.86±11.70	95.42±16.67
Not pleased	140	49.5	68.23±14.42	72.57±14.23	95.23±16.66
Statistic			T=0.101 P=0.920	T=0.182 P=0.856	t=0.096 P=0.923

showed that the person perceived his/her own as sufficient.) and the difference between the groups was found out as significant ($p<0.05$)(Table 3).

50.5% of the participants declared that they were pleased with school life. Place of residence and state of satisfaction in school life revealed an inefficient result over sociotropy and autonomy personality dimensions and problem solving abilities mean scores. ($p>0.05$) (Table 3)

When the family features of the students were examined, sociotropy-autonomy and scores of problem solving abilities were indicated in table 3. Depending on this, 79.9% ($n=226$) of the students were detected to have a core family type. While no significant difference was defined between family type, sociotropy and problem solving ability, on the other hand, the separate families' scores of autonomy (92.20 ± 6.05) was determined higher compared to

Table 4. Sociotropy-autonomy personality dimensions and problem solving ability mean score dispersion regarding family features of students

Family Features			Sociotropy	Autonomy	Problem Solving Score
	n	%	X±Sd	X±Sd	X±Sd
Family Type					
Core Family	226	79.9	67.55±14.18	72.43±13.06	92.87±15.73
Large Family	52	18.4	70.50±15.27	72.09±11.86	93.73±17.14
Broken Family	5	1.8	70.60±10.66	92.20±6.05	96.80±9.54
Statistic			F= 0.966 P=0.382	F=5.930 P=0.003	f=-0.198 p=0.821
Family General Structure					
Democratic	66	23.3	65.69±12.74	70.53±11.75	92.86±15.89
Authoritarian	22	7.8	66.63±15.82	69.86±15.44	98.45±15.76
Insensitive	9	3.2	64.55±8.44	76.66±17.44	99.33±22.68
Excessive Family Concern	50	17.7	64.84±15.48	72.74±12.49	92.38±18.80
Protective	136	48.1	71.03±14.30	73.97±12.96	96.84±15.75
Statistic			F=2.798 P=0.026	F=1.265 P=0.284	F=1.368 P=0.245
Income State					
High	43	15.2	68.00±16.64	72.81±12.96	88.27±19.00
Medium	208	73.5	68.89±13.76	72.90±12.54	93.18±15.02
Low	32	11.3	63.46±14.32	71.37±16.00	99.06±15.21
Statistic			F=2.004 P=0.137	F=0.193 P=0.824	F=4.336 p=0.014
Number of Siblings					
None	5	1.8	69.20±14.58	69.40±20.23	98.00±21.03
1-2	113	39.9	66.54±14.30	72.92±12.78	92.11±16.84
3-4	118	41.7	68.11±13.74	73.06±12.74	93.68±14.90
5 and over	47	16.6	71.95±15.58	71.72±13.65	93.48±15.70
Total	283		68.14±14.34	72.72±12.99	93.10±15.88
Statistic			F=1.593 P=0.191	F=0.236 P=0.871	F=0.364 P=0.779

core and large scale families, the difference dealing both groups was specified significant ($p<0.05$).

When common structure was grouped as democratic, authoritarian, listless, overconcerned and protective, 48.1% ($n=136$) of the families were indicated as protective and 23.3% ($n=66$) as democratic. The sociotropy mean score (71.03 ± 14.30) of having a protective family feature was identified as higher and this difference was statistically significant ($p<0.05$). There was no significant statistical difference between family structure, autonomy and problem solving mean scores ($p>0.05$) (Table 4).

73.5% of participant students ($n=208$) were in medium level regarding income state. Income rates of the families and sociotropy-autonomy mean

scores pointed out insignificant difference ($p>0.05$). When examined in terms of problem solving, the difference between income rates of the family and problem solving mean scores was found significant statistically ($p<0.05$) (Table 4).

It was detected that 41.7% of the participants ($n=118$) had 3-4 siblings and 39.9% had 1-2 ($n=113$). The sociotropy-autonomy mean scores were not effected statistically in the number of siblings.

According to agreement to a decision and decision making, sociotropic-autonomic personality dimensions and problem solving ability mean scores of the students were indicated in table 5. Depending on this, the students were asked to attendance or non attendance over a necessary de-

Table 5. Sociotropy-autonomy personality dimensions and problem solving ability mean scores related to decision attendance and decision making (n=283)

Decision Attendance and Who to Decide			Sociotropy	Autonomy	Problem Solving Score
	n	%	X±Sd	X±Sd	X±Sd
Decision Attendance State					
Attendance	269	95.1	68.27±14.23	72.91±12.83	92.44±15.88
Non attendance	14	4.9	65.64±16.61	69.00±15.85	105.64±9.72
Total	283	100.0	68.14±14.34	72.72±12.99	93.10±15.88
Statistic			T=0.670 P=0.504	T=1.099 P=0.273	T=3,07 P=0.002
Decision making related to individual					
Me/Myself	80	28.3	65.83±15,65	75.82±13.24	92.83±17.08
Family guidance	28	9.9	76.00±17,57	78,03±12,06	92.92±15.17
Family, Friends and Me	175	61.8	67.94±12,72	70,45±12,54	93.25±15.51
Total	283	100.0	68.14±14.34	72.72±12.99	93.10±15,88
Statistic			F=5.415 P=0.005	F=7.632 p=0.001	F=0,020 P=0.980

cision and 95.1% (n=269) stated to attend. Taking part in family decisions was detected as insignificant in terms of sociotropy-autonomy mean scores. ($p>0.05$) Mean scores of non attendants about problem solving were higher and the difference among was found significant ($p<0.05$) (Table 5).

When the students were asked about who to decide over the subjects related to himself/herself, 61.8 % (n=175) of the majority responded as family, friend and on his/her own. The relation between self decision and sociotropy-autonomy mean scores was detected significant statistically ($p<0.05$). When mutual comparisons were examined (tukey test) making decisions with family guidance were stated as higher in rate when compared to making decisions with family, friends and self support and this difference was detected as significant ($p<0.05$). In terms of problem solving, mean scores were mentioned as insignificant ($p>0.05$) (Table 5).

Discussion

In the literature, various studies to identify sociotropic autonomic personality features in our country showed a change between 68.50 ± 15.60 and 74.0 ± 14.1 in sociotropy mean scores and between 76.49 ± 15.79 and 83.03 ± 14.51 in autonomic mean scores (3,30,31,32). In a study Karagözoğlu conducted with various department students, midwife students' mean scores were higher than dentistry and nursing departments with 83.48 ± 11.98 (33).

In this study, the sociotropy mean scores were indicated as 68.14 ± 14.34 . Sociotropy subscale mean scores were 19.64 ± 8.33 in the dimension of "disapproval anxiety" 31.95 ± 7.29 in "separation anxiety" 15.17 ± 3.79 in "pleasing others". When these mean scores were examined according to potential range, it can be commented as the students displayed sociotropic features as medium and above. The mean autonomy score of the students was detected as 72.72 ± 12.99 and the autonomy subscale mean scores were 30.79 ± 6.03 in "personal success" 30.92 ± 6.43 in independence and 14.12 ± 4.20 in enjoyment of loneliness. These acquired mean scores point out autonomic personality features over medium level considering potential dispersion. Study findings were parallel to Kaya and Özdemir study (3,30) and students' sociotropic-autonomy mean scores with respect to Yildirak et al (2003) study (31) were determined a bit lower. Advanced sociotropic-autonomic personality feature of the students will lead to attitudes of responsibility, questioning, critical thinking and independent decision in professional applications. These features, significant in terms of professionalism, need to be provided to students in nursing profession.

In the literature problem solving abilities were defined in medium level in many studies conducted to detect problem solving abilities of nurses (27,34-36). In a study conducted by Abaan and Altintoprak to evaluate problem solving abilities of nurses, it was defined that nurses that have mana-

gerial responsibility received mean score of 79.45 (± 17.26) from problem solving ability inventory and the nurses without managerial responsibility got a mean score of 77.22 (± 14.43) (35). In the studies with university students medium level of problem solving ability was indicated. (16,29,37-39) In another study by Yurttaş and Yetkin (2003) with nursing school students problem solving ability was identified as 80.25 ± 17 (40). In a study with students in South Africa the mean score in problem solving was found out as 81.20 ± 19.30 (41). In this study, the lowest score to receive from problem solving ability inventory was 55 and highest was 152 and total score of students was 95.33 ± 16.64 . Since the mean score rate was 80 and the rates above mean showed insufficiency and below displayed sufficiency and since problem solving mean score was above average, problem solving ability can be considered as insufficient. This result different from other studies can be identified as the problem solving ability is more insufficient. To play an effective role of nurses having high abilities of problem solving for providing care and health service quality, changes with respect to nursing educational system should be implemented and development of problem solving abilities of students should be assisted.

In a study conducted by Keskin et al. (2008) problem solving, autonomy, multi intelligence conditions were evaluated and when mean scores that the students acquired from problem solving inventory were compared, males (93.1 ± 17.6) were detected to get higher scores than the females (87.3 ± 17.1) and this was evaluated as a significant difference. In this study, sociotropy-autonomy scale mean scores were higher in females and this result was found statistically significant. Problem solving ability mean score was high in males and statistically significant (98.56 ± 16.21). This finding has a parallel side with the study of Keskin et al. (2008) Mean scores that the male students had higher than females from problem solving inventory showed that this ability is less sufficient for male students.

In a study by Uslu et al. (2010) conducted with 890 university students, male students were identified to be more talented compared to females and this was defined as significant statistically (42). In a study by Genç and Kalafat within a context of identifying emphatic and problem solving abilities of stu-

dent teachers, the scores regarding sex were found close to each other and no significance was detected (22). In the study of Olgun et al (2010) with nursing students, problem solving ability and sub dimensional total scores were defined as insignificant statistically (16). In a study in faculty of education by Otacioglu, the males were found out to be more successful in problem solving (43). In this study, like in many other studies females were identified as having more sociotropic autonomic features and problem solving abilities to be better than the males.

In the study of Kaya et al (2006) no significant difference was detected within the sociotropic autonomic features and age (3). Uslu et al. with a population of 890 students the increase of problem solving abilities were detected from the first year through fourth. As the age grows, problem solving ability gets higher (42). Abaan and Altintoprak stated no difference between the ages and scores (35). In the study of Öztürk Can et al. (2009) and Yurttaş et al. (2003) with the growing of age and education problem solving abilities were stated to increase (38-40). As the fourth year students had difference from the first years show parallelism regarding this study. While there is a significant difference between age groups and sociotropy mean scores, significant difference was not identified between autonomy and problem solving abilities mean scores. Average age and sociotropy autonomy mean scores showed no statistical difference as well. When scores were examined of first and fourth classes in sociotropy autonomy and problem solving inventory, no significant relation was detected according to the classes. First class students were defined with higher scores of problem solving when compared with fourth classes and the relation among was defined significant ($p < 0.05$). That is, first class students perceived themselves less sufficient than fourth classes. Getting older and being upper classes provide the students to perceive the issues and find out solutions.

In a study conducted by Özdemir et al. (2009) significant relations were detected between variables such as accommodation in university, restrictions of independence by families, educational grade of fathers and sociotropy autonomy mean scores (30). In the study of Kaya et al. (2006) students' sociotropy autonomy personality features, facilities to attend, willingness to select nursing, family type, number of siblings, economical state, attendance

with decisions also autonomy and general structure of families had no significant difference statistically (3). This study likely with the study of Kaya et al. did not reflect a significant difference with willingness to select nursing, being pleased with school life and sociotropy autonomy and problem solving scale mean scores. When examined in terms of autonomy mean scores, significant difference was not found out between family type and sociotropy of the students and autonomy mean scores of separate families were detected higher compared to core and large scale families. That the children of separate families shoulder the responsibility at small ages might have caused for this feature to develop. Problem solving ability was stated as higher in scores for the students having separate families compared to others and the difference was found statistically insignificant. Regarding problem solving of selecting nursing, the students declaring they selected nursing by coincidence were defined as low in score compared with the ones that selected nursing willingly or unwillingly and this difference was defined as significant statistically. As a consequence the students to choose nursing profession by coincidence was detected better in problem solving abilities. The relation between income state and sociotropy autonomy scores of students were found out as insignificant difference. When examined in problem solving scores, the students having a high income were detected as lower in scores compared to families of students with medium or low income (88.27 ± 19.00). That is, the students have more abilities of problem solving. Income level and problem solving mean scores were detected as significant statistically. No significant difference was identified between number of siblings and sociotropy autonomy and problem solving scores. As advance of sociotropic autonomic personality features can be affected by many factors they are also related with personality features since birth. The problems that the individual and the family encountered in life and experience to cope with these issues can also contribute advance of problem solving abilities.

When sociotropic autonomic personality features were examined according to place of settlement, students staying with a relative or in dormitory were detected as having more sociotropic personality features and students living single were more autonomous than the family residents. Students

having highly sensitive and protective family types had more sociotropic personality features compared to uninterested families and students having extreme concerned families had more sociotropic personality features than democratic families (3). In this study, significant relation was not detected statistically between the place the students spent an important part of their lives and sociotropy autonomy and problem solving scale mean scores. Protective family type of students were higher in score regarding sociotropy and this difference was stated as significant. Students with insensitive family type had the most of the score in autonomy and problem solving. These results indicate a relation between sociotropy and care of family. There was no significant difference detected between autonomy and problem solving scores statistically. The attendance state was indicated to have no effect on scores however the problem solving ability of the students that attend with the decisions were stated in a higher level compared to non attendants.

The students to decide with the support of the family in sociotropy and students to decide on her/his own in autonomy had high scores (3). In this study, autonomy sociotropy scores were higher for the students to decide with family support than the ones to decide individually and with friends, family and etc. and this difference was detected as significant statistically. For the high scored sociotropic individuals to obtain an approval, to be admired and to be seen valuable from others is significant. For this reason, it is not surprising for the individuals to demonstrate sociotropic feature with the guidance and protection of families.

Conclusion

In the study, the students showed sociotropic autonomic personality features medium and over and they were insufficient in problem solving. Females had more sociotropic autonomic personality and were better in problem solving compared to males. It was detected that females and fourth grade students had better problem solving abilities, that is, first classes felt insufficient in problem solving abilities compared to fourth classes. There was no significant difference detected between the place to spend an important part of life and sociotropic autonomic and problem solving scores.

Nursing profession that occupational professionalism, interpersonal interaction and communication were indisputable, necessitates graduates with developed autonomy and problem solving abilities. Adopting profession of a student can be achieved with independent decision taking, producing solutions to the problems fast and effectively and having sociotropic autonomic personality and developing problem solving abilities. A study related to the topic should be accomplished with other nursing students and graduates. As a result of this study by identifying the current status, curriculum of nursing schools and educational schedules of postgraduates can be decided. Interdisciplinary education programmes, seminars and symposium activities can enhance the continuation of education.

References

1. Craven GM. *Sociotropy and autonomy in older adults and the relationships between the personality styles, social support, and affect. A Thesis Presented in Partial Fulfillment of The Requirements for the Degree of Doctor of Philosophy in Psychology at Massey University, Palmerston North 2007.*
2. Kabakçı, E. *Üniversite öğrencilerinde sosyotropik/otonomik kişilik özellikleri, yaşam olayları ve depresif belirtiler (Sociotropic/autonomic personality characteristics, life events and depressive symptoms among university students). Türk Psikiyatri Dergisi 2001; 2(4): 273-82.*
3. Kaya N, Aşti T, Acaroğlu R, Kaya H, Şendir M. *Hemşire öğrencilerin sosyotropik-otonomik kişilik özellikleri ve ilişkili faktörlerin incelenmesi (Determination of sociotropic /autonomic personality characteristics and related factors among nursing students). C.Ü. Hemşirelik Yüksek Okulu Dergisi 2006; 10(3): 1-11.*
4. Beck R, Taylor C, Robins M. *Missing home: sociotropy and autonomy and their relationship to psychological distress and homesickness in college freshmen. Anxiety, Stress, and Coping 2003; 16(2): 155-66.*
5. Çam O, Engin E. *Psikiyatri Kliniğinde çalışan hemşirelerde farkındalık eğitiminin bireysel performans standartlarına etkisi (The effects of self awareness education on the individual performance standards of nurses who work in psychiatry clinic). Anadolu Psikiyatri Dergisi 2006; 7: 82-91.*
6. Babadağ K. *Meslekleşme ve Kadın I. International & VIII. National Nursing Congress, Antalya, 29 Ekim-2 Kasım 2000. Kongre Kitabı: 35-39.*
7. Otacioğlu SG. *Müzik öğretmenlerinin sosyotropik ve otonomik kişilik özellikleri ile depresyon düzeyleri üzerine ilişkisel bir araştırma (A relation analysis on the levels of music teacher's sociotropic and autonomic personality characteristics with depression). Eskişehir Osmangazi Üniversitesi Sosyal Bilimler Dergisi 2008; 9(1): 35-51*
8. Adams D, Miller BK. *Professionalism in nursing behaviors of nurse practitioners. Journal of Professional Nursing 2001; 17(4): 203-10.*
9. Dorothee B, Hampton L. *Professionalism and the nurse midwife practitioner: an exploratory study. J Am Acad Nurs Prac 2000; 12: 19-33.*
10. Hamamcı Z, Esen Çoban A. *Psikodramanın psikolojik danışmanların problem çözme becerilerini algılama düzeyleri üzerine etkisi (The effect of psychodrama on the perceptions of problem solving skills of counselors). Ondokuz Mayıs Üniversitesi Eğitim Fakültesi Dergisi 2009; 28: 63-74.*
11. Dündar S. *Polislerin umutsuzluk düzeyi ile problem çözme becerisi arasındaki ilişkinin incelenmesi (Analyzing the relationship between hopelessness level with problem solving skills of police officers). Polis Bilimleri Dergisi 2008; 10(3): 77-92.*
12. Yalçın B, Tetik S, Açıköz A. *Yükseköğretim öğrencilerinin problem çözme becerisi algıları ile kontrol odağı düzeylerinin belirlenmesine yönelik bir araştırma (A study on the determination of the perceptions of problem solving skills and the levels of locus of control of high school students). Organizasyon ve Yönetim Bilimleri Dergisi 2010; 2(2): 19-27.*
13. Zurilla TJ, Sheedy CF. *Relation between social problem solving ability and subsequent level of psychological stress in college students. Journal of Personnel Social Psychology 1991; 61(5): 841- 46.*
14. Özgüven HD, Soykan Ç, Haran S, Gençöz T. *İntihar girişiminde depresyon ve kaygı belirtileri ile problem çözme becerileri ve algılanan sosyal desteğin önemi (Importance of problem solving skills, perceived social support, and depression and anxiety symptoms on suicide attempts). Türk Psikoloji Dergisi 2003; 18(52): 1-11.*
15. Eskin M, Ertekin K, Harlak H, Dereboy Ç. *Lise öğrencisi ergenlerde depresyonun yaygınlığı ve ilişkili olduğu etmenler (Prevalence of and factors related to depression in high school students). Turkish Journal of Psychiatry 2008; 19(4): 382-89.*
16. Olgun N, Kan Öntürk Z, Karabacak Ü, Eti Aslan F, Serbest Ş. *Hemşirelik öğrencilerinin problem çözme becerileri: bir yıllık izlem sonuçları (Problem solving skills of the nursing students: results of the 1-year*

- observation problem solving skills of the students). *Acibadem Üniversitesi Sağlık Bilimleri Dergisi* 2010; 1(4): 188-94.
17. Jaffee BW, D'Zurilla TJ. Adolescent problem solving, parent problem solving and externalizing behavior in adolescents. *Behaviour Therapy* 2003; 34: 295-311.
 18. Baker RS. A Prospective longitudinal investigation of social problem solving appraisals on adjustment to university, stress, health and academic motivation and performance. *Personality and Individual Differences* 2003; 35: 569-91.
 19. Epstein HL, Paluch RA, Gordy CC, Saelens EB, Ernst MM. Problem solving in the treatment of childhood obesity. *Journal of Consulting and Clinical Psychology* 2000; 68(4): 717-21.
 20. Sukhodolsky GD, Golub A, Stone C, Orban L. Dis-mantling anger control training for children: a randomized pilot study of social problem-solving versus social skills training components. *Behaviour Therapy* 2005; 36(1): 115-24
 21. Zanello A, Perrig L, Huguelet P. Cognitive functions related to interpersonal problem-solving skills in schizophrenic patients compared with healthy subjects. *Psychiatry Research* 2006; 142: 67-78.
 22. Genç SZ, Kalafat T. Öğretmen Adaylarının empatik becerileri ile problem çözme becerileri (Prospective teachers' problem solving skills and emphatic skills). *Kuramsal Eğitim Bilim* 2010; 3(2): 135-47.
 23. Şahin NH, Ulusoy M, Şahin N. Exploring the sociotropy-autonomy dimension in a sample of Turkish psychiatric inpatients. *Journal of Clinical Psychology* 1993; 49(6): 751-763.
 24. Heppner PP, Petersen CH. The development and implications of a personal problem solving inventory. *Journal of Counseling Psychology* 1982; 29(1): 66-75.
 25. Koçkar İA, Gençöz T. Personality, social support, and anxiety among adolescents preparing for university entrance examinations in Turkey. *Current Psychology: Developmental, Learning, Personality, Social* 2004; 23(2): 138-46.
 26. Taylan S. Heppner'in problem çözme envanterinin uyarlama, geçerlik ve güvenirlik çalışmaları (Adaptation, validity and reliability studies of Heppner's problem solving inventory). *Ankara Üniversitesi Sosyal Bilimler Enstitüsü Eğitimde Psikolojik Hizmetler Anabilim Dalı, Yüksek Lisans Tezi*, 1990, Ankara.
 27. Kaya E. Hemşirelerin problem çözme becerilerinin ve etkileyen bazı faktörlerin belirlenmesi (Determination of problem solving skills and effecting factors of nurses). *Cumhuriyet Üniversitesi Sağlık Bilimleri Enstitüsü, Yayınlanmamış Yüksek Lisans Tezi*, 2005, Sivas.
 28. Durmaz Kaçar Z, Can S, Koca R, Yeşilova D, Tortumluoğlu G. Çanakkale Sağlık Yüksekokulu öğrencilerinin problem çözme becerileri (PÇB) ve etkileyen bazı faktörler (Problem solving skills of the students at health high school and the factors affecting them). *Atatürk Üniversitesi Hemşirelik Yüksekokulu Dergisi* 2007; 10(4): 63-71.
 29. Keskin G, Yildirim GÖ. The evaluation of university students in terms of problem solving, autonomy, multiple intelligences based on constructive approach norms. *Inonu University Journal of the Faculty of Education* 2008; 9(16): 67-88.
 30. Özdemir N, Tanrıverdi D. Hemşire öğrencilerin sosyotropik otonomik kişilik özellikleri ve ilişkili faktörlerin araştırılması (Investigation of sociotropic and autonomic personality characteristics and related factors of the nursing students). 45. National Psychiatry Congress, 20-24 October 2009, Ankara, Turkey, Poster Presentation.
 31. Yıldırak Ö, Bulut D. Muğla üniversitesi muğla sağlık yüksekokulu hemşirelik bölümü öğrencilerinin sosyotropi ve otonomi düzeylerinin belirlenmesi (Determination of Sociotropic and autonomic personality characteristics of nursing students in Muğla School of Nursing Department in Muğla University). II. Nursing Students Congress, İzmir, Turkey, 8-9 May 2003; Kongre Özet Kitabı: 101.
 32. Karagözoğlu Ş. Nursing students' level of autonomy: a study from Turkey. *Nurse Education Today* 2009; 29(2): 176-187.
 33. Karagozoglu S. Level of autonomy of turkish students in the final year of university baccalaureate degree in health related fields. *Nursing Outlook* 2008; 56(2): 70-7.
 34. Kelleci M, Gölbaşı Z. Bir üniversite hastanesinde çalışan hemşirelerin problem çözme becerilerinin bazı değişkenler açısından incelenmesi (Determining the problem solving skills and some related factors of nurses who work in a university hospital). *C.U. Hemşirelik Yüksekokulu Dergisi* 2004; 8(2): 1-8.
 35. Abaan S, Altıntoprak A. Hemşirelerde problem çözme becerileri: öz değerlendirme sonuçlarının analizi (Nurses' perceptions of their problem solving ability: analysis of self appraisals). *Hacettepe Hemşirelik Yüksekokulu Dergisi* 2005; 62-76.
 36. Terzioğlu, F. The perceived problem solving ability of nurse managers. *Journal of Nursing Management* 2006; 14(5): 340-47.

37. Yılmaz E, Karaca F, Yılmaz E. Sağlık yüksekokulu öğrencilerinin problem çözme becerilerinin bazı değişkenler açısından incelenmesi (Examining the problem solving skills and some related factors of the health college students). *Atatürk Üniversitesi Hemşirelik Yüksekokulu Dergisi* 2009; 12(1): 38-48.
38. Öztürk Can H, Öner İO, Celebi E. Üniversite öğrencilerinde eğitimin sorun çözme becerisine etkisinin incelenmesi (The assessment effect of problem solving skills of education at university students). *Firat Sağlık Hizmetleri Dergisi* 2009; 4(10): 35-58.
39. Tezel A, Arslan S, Topal M, Aydoğan O, Koç C, Şenlik M. Hemşirelik öğrencilerinin problem çözme becerileri ve depresyon düzeylerinin incelenmesi (The investigation of the problem solving skill and depression level of nursing students). *Atatürk Üniversitesi Hemşirelik Yüksekokulu Dergisi* 2009; 12(4): 1-10.
40. Yurttaş A, Yetkin A. Sağlık yüksekokulu öğrencilerinin empatik becerileri ile problem çözme becerilerinin karşılaştırılması (Comparasion of the problem solving and empathetic skills of the students in a school of health). *Atatürk Üniversitesi Hemşirelik Yüksekokulu Dergisi* 2003; 6(1): 1-13.
41. Heppner PP, Pretorius TB, Wei M, Lee DG, Wang YW. Examining the generalizability of problem solving appraisal in black South Africans. *Journal of Counseling Psychology* 2002; 49 (4): 484-98.
42. Uslu M, Girgin Ç. The effects of residential conditions on the problem solving skils of university students. *Procedia-Social and Behavioral Sciences* 2010; 2(2): 3031-35.
43. Gürşen Otacioğlu S. Prospective teachers' problem solving skills and self-confidence levels. *Educational Sciences:Theory & Practice* 2008; 8(3): 915-23.

Corresponding Author

Birsen Altay,

Ondokuz Mayıs University,

High School of Health,

Samsun,

Turkey,

E-mail: baltay@omu.edu.tr

Children's mental health in northeast Brazil: vulnerability and public policies

Modesto Leite Rolim Neto¹, Alberto Olavo Advincula Reis², Jose Cezario de Almeida³, Marina Lucena de Aguiar Ferreira⁴, Nadia Nara Rolim Lima⁴

¹ Faculty of Medicine, Ceara Federal University - UFC, Barbalha, CE, Brazil,

² Faculty of Public Health, Sao Paulo University - USP, Sao Paulo, SP, Brazil,

³ Faculty of Medicine, Campina Grande University-UFCG, Cajazeiras, PB, Brazil,

⁴ Suicidology Research Group, Ceara Federal University - UFC and Brazilian National Counsel of Technological and Scientific Development - CNPq, Juazeiro do Norte, CE, Brazil.

Abstract

Childhood and adolescence are times of changes and vague stances that make boys and girls to have more risk to develop or show mental health problems. Psychic illnesses frequency at these ages is about 20% and growing. At Brazil's northeast region, social, economic and demographic features make children and teenagers even more vulnerable to mental diseases or disturbs. Brazilian public healthcare system, called SUS, was designed in 1988 to arrange, organize and regulate public health services and actions in every level and is responsible for mental healthcare, accordingly to its basic rules: universality, entirety and equity. Besides SUS' creation, Statute of Children and Adolescents and Brazilian Psychiatric Reform were crucial for achieving the changes in mental healthcare model for children and teenagers and for the reach and effectiveness of this care.

Key words: mental health, public health, SUS.

Background

Worldwide, the attention to mental health of children and adolescents as a public health policy is recent, overwhelmingly in developing countries¹. The Brazilian Psychiatric Reform and the creation of the Statute of Children and Adolescents, a federal law that registers their rights, were key factors for change in how it addresses the psychological and psychiatric issues these individuals.

According to World Health Organization (WHO), at the end of next decade, the incidence of mental disorders in order of population in all age groups will reach 50% and most of them can bring social or economical problems for patients.

In childhood, this percentage ranges between 10% and 20% and the most common are behavior disorders, hyperactivity and attention deficit disorder, anxiety, depression, schizophrenia, anorexia, bulimia, use of alcohol, tobacco and illegal drugs².

In the Northeast region of Brazil, due to social, economic and demographic characteristics, children and adolescents experience a situation of social vulnerability that increases the incidence of mental disorders and makes even more necessary the integral and costless care provided by Brazilian public healthcare system, called Unified Health System (SUS) which maintains all public health services in the country.

Children's and adolescents' mental health

Adolescence is a time of several doubts about sexuality, work and family. Therefore, weaknesses and tendencies are expressed, making this period particularly more conducive to the arising of mental health problems. Some young people are not able to respond positively to stimuli and pressures of this phase, determining psychological distress and the onset of psychopathology³.

Modern society challenges young people to pursue collective definitions and, paradoxically, their own individuality. This task is inherent to modern men, presenting themselves as singular subjects, and begins in youth, when individuals are compelled to take their options against various specific requirements⁴.

Some situations are highlighted as threats to mental health or mental problems, aggravating natural susceptibilities of children and adolescents: chronic diseases that damage their physical or mental health, especially when they lead to

long periods of hospitalization, unplanned teenage pregnancy, parents with severe mental/psychotic disorders and alcohol abuse, living with domestic or communitarian violence, such as abuse or mistreatment; rupture or weakening of family ties; early and abusive use of licit or illicit drugs; disorders produced by praecox work, involvement in violent or harmful situations resulting from their association with criminal groups^{2, 4, 5}.

The establishment of several mental disorders in this age group is earlier than was thought³, making the mental health of this population fits as part of a public health strategy. State should provide to this area attention and investment.

Northeast Brazil

With a population of approximately 50 million inhabitants, 36.3% of them aged between 0 and 19 years, the Northeast region of Brazil presents, in general, low numbers in Human Development Index (HDI) and an intense income⁶ concentration. This situation results of decades of lack of public services. This economic and demographic condition also exposes more children and adolescents who live in this region to a situation of social vulnerability, which is a triggering factor for mental health disorders such as depression and personality disorders.

Traditionally, the region's economy was based on the primary sector (agriculture and vegetal or mineral extraction). In the last two decades, greater public investments, and especially the adoption of welfare policies by Brazilian Federal Government has brought to the region as a whole, and for some cities, in particular, a cycle of economic development intense that, paradoxically, has increased levels of violence and crime, constitutes another indirect threat to the mental health of young people.

SUS: The Brazilian public healthcare system

Created by the National Constitution of 1988, Brazilian public healthcare system, called Unified Health System (SUS) is formed by the set of all actions and health services provided by public federal, state and local administrative bodies and indirect, in a complementary manner, private⁷.

Its legal framework, which had been thought initially from popular initiatives, has been refur-

bished since 1988, incorporating values not provided at the time of conception. Article 198 of the Federal Constitution, later complemented by the Organic Health Law of 1990 established ideological principles or doctrinal and organizational principles for the functioning of SUS⁸, on which lays out guidelines for the operation of the system.

The three doctrinal or ideological principles on which we think the scope of coverage of SUS are universality, integrality and equity. The first concept that summarizes the coverage of the system must be for the whole population, providing health care to all Brazilians, pay attention to what the Constitution states: "Health is everyone's right"⁷. The second relates to the responsibility of the SUS on curative and preventive individual and collective. Finally, the need for coverage that can meet the needs of a mixed population involved in so many economic disparities, social and geographical⁹.

The organization and operation of SUS are based on decentralization, regionalization and hierarchization of health services. This way, resource management is no longer centralized on the Ministry of Health, but closer to the administrative units where the services or procedures are performed⁷. The hierarchy, in turn, provides for distribution of services on a scale of complexity, from basic care, concentrated mainly in the Family Health Strategy, called Programa Saúde da Família (PSF) to tertiary levels of intense technological density⁸.

In the case of mental health care, the main instruments for health care to care for these patients are the Psychosocial Attention Centers (CAPS), in its various forms, such as community mental health services for children and adolescents (CAP-Si)¹⁰. Regionalization allowed the establishment of such a health center in most cities in the Northeast, making possible the access of young people with mental health problems of the region to appropriate treatments.

Mental health inside SUS

According to the principles established by legislation, the role of SUS is to regulate and organize around the country the network of mental health care, on a regional and hierarchical levels of increasing complexity, ensuring the principles of universal access and free actions and health services⁷.

Based on these principles, the network of mental health care consists of Psychosocial Attention Centers (CAPS e CAPSi), Therapeutic Residential Services (STR) and general hospitals¹¹.

CAPS and CAPSi services were proposed by the Ministry of Health in the early 1990s, starting from innovative municipal experiments¹². Although the resonance of the psychiatric reform, went on to propose a model of mental health care based on “psychosocial care”, which defines the set of actions in the field theoretical, ethical, technical, political and social¹³. These establishments are part of community-based care network, which keeps the patient in touch with the community and family, as opposed to institutionalization proposal until shortly before¹⁴.

In the Northeast and Brazil as a whole, the attention for public user, following the principles of the NHS, has secured the necessary scope and some level of resolution for these young people, who mostly would not have otherwise, access to therapy necessary¹⁵.

Conclusion

The high prevalence of mental disorders in children and adolescents and the consequences that these diseases can lead to the development of youth and society to make mental health care for children and youth a topic of extreme importance in the context of public health¹⁶.

In northeastern Brazil, the population of children and adolescents, in general, is in a position of greater social risk, compounded by historical factors such as concentration of income and lack of public investment in the region. Nowadays, with a gradual change in the socioeconomic profile of this part of the country, new threats emerge for mental health of young people, as violence increased.

However, the model of health care in force in the country, through the Unified Health System (SUS), has provided these users a wider attention and affordable, particularly in regard to mental health care. The approach of people with mental health problems children and adolescents in public service is done mainly through the CAPSi services, which represented a major step forward, as they understand these younger patients to need a special care, away the possibility of institutio-

nalization, for example¹⁶. These centers are now accessible to most of the population of children and adolescents in the region.

In the field of care for children and adolescents with psychiatric diseases, respect for the ideological principles of SUS (universality, comprehensiveness, and equity) can produce positive results for the control and treatment of these diseases, with free comprehensive and effective therapy¹⁷. Compliance with the operating principles, especially the hierarchization, provides to the CAPS services (secondary level of attention) greater resolution, being translated as benefits for the users.

Besides the creation and operation of SUS, which dates from 1988, the Child and Adolescent (ECA) and the Brazilian psychiatric reform are fundamental to advances made in addressing the mental health of children and adolescents in the Northeast and Brazil.

Acknowledgements

This study was supported by grants the Ceará Federal University – UFC.

References

1. Bird HR, Duarte CS. *Dados epidemiológicos em psiquiatria infantil: orientando políticas de saúde mental*. Rev Bras Psiquiatr 2002; 24(4): 121-6.
2. Assumpção FB, Kuczinsky E. *Tratado de Psiquiatria da Infância e Adolescência*. 1a. edição. São Paulo: Ed. Atheneu 2003.
3. Menezes TT, Melo VJ. *O pediatra e a percepção dos transtornos mentais na infância e adolescência*. Adolescência e Saúde 2010; 7(3): 36-41.
4. Paula CS, Barros MG, Vedovato MS, D'antino ME, Mercadante MT. *Problemas de saúde mental em adolescentes: como identificá-los?*. Rev Bras Psiquiatr 2006; 28(3): 40-48.
5. Assis SG, Avanci JQ, Pesce RP, Ximenes LF. *Situação de crianças e adolescentes brasileiros em relação a saúde mental e violência*. Ciênc Saúde Coletiva, 2009; 14(2): 12-19.
6. Instituto Brasileiro de Geografia e Estatística. *Censo Populacional 2010*. IBGE: Brasília 2010.
7. Ministério da Saúde do Brasil, Secretaria Executiva. *Sistema Único de Saúde – Princípios e Conquistas*. Editora MS: Brasília 2005.

8. Bertone AA, Viana CMM. *As idéias e as práticas: a construção do SUS*. Instituto de Medicina Social - UERJ: Rio de Janeiro 2002.
9. Ministério da Saúde do Brasil, Secretaria de Atenção à Saúde. *Saúde Mental no SUS: Acesso ao tratamento e mudança no modelo de atenção*. Editora MS: Brasília 2009.
10. Luzio CA, L'abbate AS. *Atenção em Saúde Mental em Municípios de Pequeno e Médio Porte: ressonâncias da reforma psiquiátrica*. *Ciênc Saúde Coletiva* 2009; 14(1): 61-69.
11. Ministério da Saúde do Brasil, Secretaria de Atenção à Saúde. *Saúde Mental no SUS: Os Centros de Atenção Psicossocial*. Editora MS: Brasília 2004.
12. Luzio CA, L'abbate AS. *A reforma psiquiátrica brasileira: aspectos históricos e técnico-assistenciais das experiências de São Paulo, Santos e Campinas*. *Interface* 2006; 10(20): 16-23.
13. Ministério da Saúde do Brasil, Secretaria de Atenção à Saúde. *Caminhos para uma Política de Saúde Mental Infanto- Juvenil. Série B, textos básicos em saúde*. Brasília: Editora MS 2005.
14. Onocko-Campos RT. *Clínica: a palavra negada – sobre as práticas clínicas nos serviços substitutivos de Saúde Mental*. *Saúde em Debate* 2001; 25(58): 20-26.
15. Onocko-Campos RT, Furtado JP. *Entre a saúde coletiva e a saúde mental: um instrumental metodológico para avaliação da rede de Centros de Atenção Psicossocial (CAPS) do Sistema Único de Saúde*. *Cad Saúde Pública* 2006; 22(5): 55-61.
16. Souza RR. *O Sistema Público de Saúde Brasileiro. Seminário Internacional – Tendências e desafios dos sistemas de saúde nas Américas*. Editora MS: Brasília 2002.
17. Tanaka OY, Ribeiro EL. *Ações de saúde mental na atenção básica: caminho para ampliação da integralidade da atenção*. *Ciênc Saúde Coletiva* 2009; 14(4): 74-81.

Corresponding Author
 Modesto Leite Rolim Neto,
 Faculty of Medicine,
 Ceara Federal University - UFC,
 Barbalha,
 Brazil,
 E-mail: modestorolim@yahoo.com.br

Study subclinical hepatitis A infection in ambulatory patients, with nonspecific abdominal complaints in Mofid hospital of Tehran Iran

Fariba Shirvani¹, Naimeh Taslimi², Abodlah Karimi¹, Mohammad Rahbar^{3, 4}

¹ Pediatric Infections Research Center, Mofid Children Hospital, Shaheed Beheshti University of Medical Sciences, Iran,

² Department of Pediatric, Imam Hussein Hospital, Shaheed Beheshti University of Medical Sciences, Iran,

³ Department of Microbiology, Iranian Reference Health Laboratories Research Center, Ministry of Health and Medical Education, Tehran Iran.

⁴ Antimicrobial Resistance Research Center, Tehran University of Medical Sciences, Tehran, Iran.

Abstract

Background and Objectives: Epidemiology of Hepatitis A has changed in recent years, and with increasing age, its subclinical nature in childhood turns to more severe hepatitis. Fever and nonspecific gastrointestinal symptoms are found in common viral infections in children; this study tends to detect Hepatitis A infection in these children in an ambulatory referral children centre in Mofid Children Hospital. Tehran, Iran

Methods: Three hundreds and ten children aged 1-15 years old with nonspecific gastrointestinal symptoms came to emergency room of Mofid Hospital were selected. Each patient who had 4 from 10 defined clinical criteria and laboratory finding was eligible to enter our study. Patients with any hepatic involvement by a confirmed or nonconfirmed infectious and noninfectious cause and hepatic drug reactions were excluded. All data results entered and analyzed in SPSS 18 software (SPSS Inc Chicago)

Results: Three hundred-and-ten patients (184 boys and 126 girls) with mean age of 7.45 ± 4.13 years were investigated. forty (12.9%) were IgM positive and 103 (33.2%) were IgG positive. 90% of hepatitis A IgM positive patients were IgG positive also. 54 patients (17.5%) had SGPT more than 90 IU/ml (more than twice normal), 26 of them (48.1%) were HAV IgM Positive. Logistic Regression Model showed IgM Positive patients had higher Bill ($CI=0.22-0.69$) $P=0.001$, SGPT ($CI=38.3-69.9$) $P=0.000$ and % lymph in CBC ($CI=2.7-11.9$) $P=0.002$, and IgG positive patients had higher SGPT ($CI=9.7-31.5$) $P=0.000$ and total

WBC ($CI=578-2185$) $P=0.001$. There was no significant difference between IgM and IgG Positive and Negative groups in number of their positive clinical criteria.

Conclusion: Children with nonspecific gastrointestinal signs with more than twice normal SGPT are in high probability of Hepatitis A. Epidemiologic investigation of Hepatitis A in our community is in first priority and shows the necessity of Hepatitis A mass vaccination.

Key words: Hepatitis A, Epidemiology of Hepatitis A, Subclinical.

Introduction

Over the last two decades, the epidemiology of Hepatitis A virus (HAV) has changed in many Asian and Middle Eastern countries [1-3]. Hepatic damage caused by hepatitis A virus is neither cytopathic [4-5] nor antibody-mediated [6] but occurs by killer T-lymphocytes activities [7]. These characteristics explain mild symptoms in younger age and possibility of prevention after exposure either by administration of antibody [8-11] or vaccination [12-13]. Lower antibody level at higher age may result in higher proportion of susceptible individuals and ends to more severe mortality and morbidity of Hepatitis A in community. In areas with poor water and sanitary conditions, HAV transmission occurs at earlier age. Improvements in socioeconomic and health status lead to delay acquisition of infection from childhood to adulthood. [14] Increase in SGPT more than twice normal level can be a laboratory sign for subclinical Hepatitis A with higher prevalence in developing

countries [15-17]. In this study we investigated Hepatitis A seropositivity in children with nonspecific gastrointestinal symptoms in a referral Children Hospital Mofid 2009-2010 Tehran, Iran.

Materials and methods

Three hundred and ten children with nonspecific gastrointestinal complaints from Ocher 2009-June 2010) came to emergency department of Mofid Hospital were subject of our study. The sample size was calculated with Epi Info program assuming of 25% prevalence of HAV Seropositivity and 5% error [18] which was 300 cases. Selection criteria were clinical symptoms more commonly found in patients with subclinical Hepatitis A infections. We used ten sign and symptoms which were 1- abdominal pain 2-fever 3-fatigue 4- anorexia 5- nausea 6-vomiting 7- pain and tenderness on Right Upper Quadrant 8- history of hepatitis in one of family members or day care or school 9- dark colored urine and light colored stool 10- hepatomegaly and having 4 criteria was enough to enter the study. CBC, DIFF and PLATELET, Bill Total and Direct, SGPT, Anti HAV IgG and IgM (Panel 1) were performed for all study cases. In children with a history of HIV and/or HCV in mother and other family members. Anti HIV and Anti HCV was performed (Panel 2) for all patients. And in patients with Gianoti Crosti syndrome or serum sickness like syndrome or arthritis and arthralgia or glomerulonephritis in one to two months ago, cases with susceptible history of hepatitis B vaccination and/or blood and blood products transfusion or a history of Needle Stick (Panel 3), HBsAg was performed. In cases with hepato-splenomegaly with FTT and patients with cirrhosis without obvious cause ANA, Anti SMA, Anti KLM (Panel 4) was performed, all patients with panel 4 were also included in panel 1 to 3. Cases with known hepatic disease on any known infectious disease with hepatic involvement and patients with hepatic drug reactions were excluded from study. CBC test was performed with Calibrated Ka21N system, SGPT was performed with Parsazmon Kit, and RA – 1000 SYSTEM, Anti HAV IgG and IgM, HBSAg and AntiHIV and AntiHCV were performed by DIALAB Kit (Enzyme Linked Immunosorbent Assay, Microwell Method, Technischen Produkten und Laborinstrumenten, Geseli-

sschaft M.b.h. office@dialab.at. All data results entered and analyzed in SPSS 18 software (SPSS Inc Chicago) Descriptive analysis was done by bivariate analysis using chi-square with 5% significance level and Multivariate regression analysis used for independent predictors of seropositivity and 95% CI was calculated.

Results

Three hundred-and-ten patients (184 boys and 126 girls) with mean age of 7.45 ± 4.13 years were investigated. Out of 310 patients .40 (12.9%) patients were IgM positive and 103 (33.2%) were IgG positive. 90% of HAV IgM positive patients were IgG Positive. 54 patients (17.5%) had SGPT > 90 IU/L and 26 patients out of them (48.1%) were IgM positive. 130 cases (41.5%) were under 5 years old. (figure 1). There was no significant difference between gender or age and IgM or IgG Positive and Negative results. Logistic Regression Model showed IgM Positive patients had higher Bill (CI=0.22-0.69) $P=0.001$, SGPT (CI=38.3-69.9) $P=0.000$ and %lymph in CBC (CI=2.7-11.9) $P=0.002$, and IgG positive patients had higher SGPT (CI=9.7-31.5) $P=0.000$ and total WBC (CI=578-2185) $P=0.001$. There was no significant difference between IgM and IgG positive and negative groups in number of their positive clinical criteria based on ten signs and symptoms which were selected to be checked in patients with nonspecific Gastrointestinal complaints.

Four cases were IgM+ and IgG-, represents 1% of children with nonspecific gastrointestinal signs and symptoms with acute HAV infection. The results of panel 2 were negative for all 11 cases selected. Seven of 23 cases checked for panel 3 (30.4%) were HBSAg positive. No patient with indication for panel 4 was found. Two age groups with acute (a) and nonacute (b) infection (IgM+IgG+=a) (IgM-IgG+=b) had no significant difference (CI=-1.6-1.7) (data not shown). Table 1 shows, IgM positive children had higher Bill and SGPT and %lymph in CBC, and IgG positive children, had higher SGPT and total WBC and Logistic regression Multivariate analysis confirmed these results.

Table 1. IgM and IgG seropositivity in different clinical and laboratory variables in children with non-specific gastrointestinal symptoms in Mofid Children Hospital(Tehran, Iran)

Variables		Positive	Negative	95%Ci	P value
gender	IgM S.R*	Male 21	163	-	NS
		Female 19	107	-	NS
	IgG S.R	Male 38	68	-	NS
		Female 68	139	-	NS
Clinical criteria**	IgM S.R	4.4±0.9	4.3±0.6	-0.2-3	NS
	IgG S.R	4.3±0.7	4.3±0.6	-0. -2-1	NS
bilirubin	IgM S.R	1.5±0.7	1.1±0.5	0.22-0.69	0.000
	IgG S.R	1.27±0.6	1.15±0.5	0.15-0.2	0.08
SGPT	IgM S.R	91.7±47	37±41	38.3-69.9	0.000
	IgG S.R	58.3±47.1	37.7±43	9.7-31.5	0.000
Total WBC	IgM S.R	8939±4138	7686±2896	-112.2-2618.2	0.07
	IgG S.R	8768±3669	7286±2673	578-2185	0.001
Lymph%	IgM S.R	57±13	49±16	2.7-11.9	0.002
	IgG S.R	52±14	49±16	-0.3-6.8	0.07
Hct	IgM S.R	40±6	38±5	-0.3-3.7	0.09
	IgG S.R	38±5	38±5	01.9-0.6	0.3

*=Serologic Result

** Clinical criteria= FEVER+anorexia+vomiting+nausea+RUQ tenderness+darkUrine+paleStool+hepatomegally+fatigue+AbdominalPain+arthritis

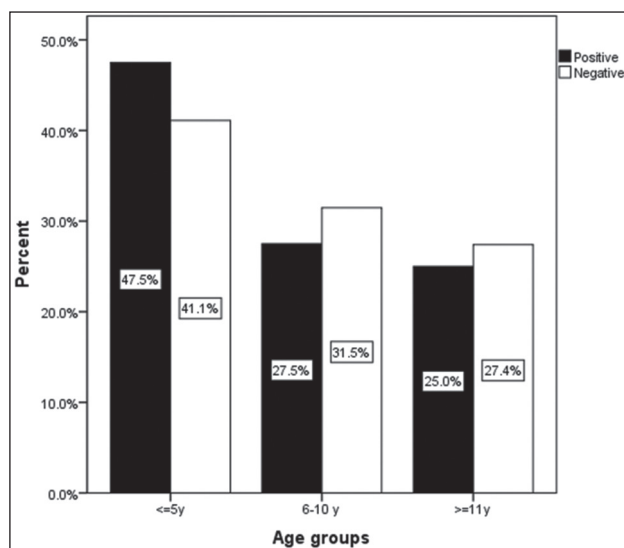


Figure 1. IgM Positive and Negative patients with different age groups in children with nonspecific Gastrointestinal signs and symptoms (Mofid Children Hospital 2009-2010)

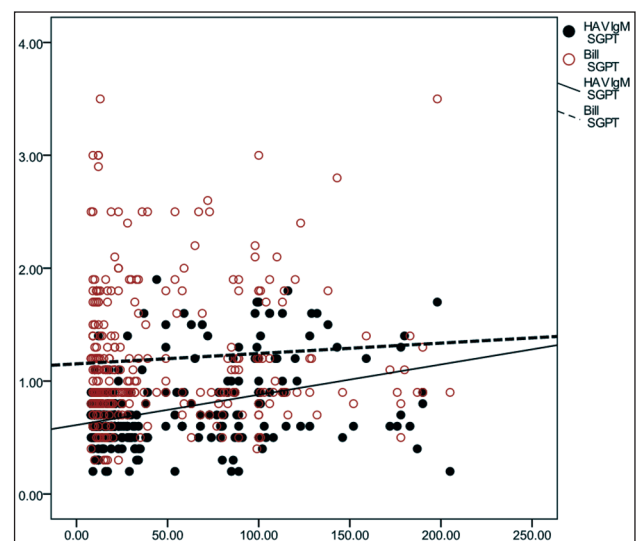


Figure 2. Relation between SGPT value and Bilirubin or HAV IgM in children with nonspecific gastrointestinal signs and symptoms (Mofid Children Hospital 2009-2010)

Discussion

Increase SGPT titer in a child under 5 year with nonspecific GI symptoms can be a laboratory predictor of subclinical hepatitis with the most important etiology of hepatitis A (90% of cases in Pakistan[16] and 50% in USA [19].

In this study 47% of cases with high SGPT had subclinical hepatitis A, means that other viral etiologies are becoming more responsible and hepatitis is shifting towards higher age. Hepatitis A is endemic in developing countries in Asia, Africa and South America. lower socioeconomic status is accompanied by lower age of sickness, in regions with intermediate endemicity, seronegative individuals increase gradually and ends to epidemics with more clinical cases[19]. Approximately 1% of our cases were IgM positive and IgG negative. We assume this phenomena occurs during a three weeks time period, we can calculate the chance of accusing hepatitis A in susceptible children under 15 years old to be approximately 17%, this leaves a high susceptible proportion of children entering adolescence and increases the risk of an epidemics in higher age. As it is seen in figure1, 25% of IgM Positive cases are between 11 and 15 years old. Although we could not found significant statistical difference between age group, but, one fourth of cases with positive results for Hepatitis A in children over 10 years old, is an indication of more susceptible patients at higher age to this infectious disease.

Changing the epidemiologic status of hepatitis A occurs in many countries with higher endemicity history[17-20], In a study in Saudi Arabia, children 1-6 years anti HAV IgG seropositivity was 33.8% overall, increasing age and rural residence and non availability of safe water were the most important independent predictors [21]. Tandon B.N. 1984 Showed 28% IgM positive cases from 90 healthy children, and 3 out of 16 IgM positive children had transaminase level more than two times above normal value . He reported, almost 30% of children below the age of 10 had subclinical acute hepatitis A in north India [22]

Any combination of four or more clinical finding such as fever, anorexia, nausea, vomiting, RUQ tenderness, dark urine, pale stool, hepatomegaly, fatigue, abdominal pain couldn't help us to distinguish hepatitis A in our cases, but IgM seropositivity was accompanied with higher Billirubin and SGPT Titer and lymphocyte predominance in CBC, Higher number of total WBC is accompanied with IgG seropositivity (Table 1), figure 2 shows the positive relationship between SGPT titer and HAV IgM .higher angle for SGPT, HAV IgM line confirms the positive relationship

between these laboratory findings in children with hepatitis A infection.

In this study we selected children with a number of clinical findings, accordingly, seroprevalance can be lower in healthy children, the last study in Iran reported the prevalence of total anti-HAV to be 61.6%. HAV prevalence rates according to age groups were 61.5% between 6 months and 1.9 years, 51.7% between 2 and 5.9 years, 52.9% between 6 and 10.9 years, 65.2% between 11 and 15.9 years and 85% between 16 and 20 years.[23]. Our data shows that after approximately five years 50% of children between 6- 15 years with nonspecific gastrointestinal complaint are seronegative for hepatitis A infection, thus more precise investigation of hepatitis A is mandatory to show the changing epidemiology of this disease.

The WHO position paper on hepatitis A vaccines [24] declares that in countries of intermediate endemicity, considering childhood vaccination can be considered as a supplement to health education and improved sanitation.

Acknowledgement

We are appreciated to thank Dr Masomeh Navidinia, Mr Mohammad Ali malekan, Mrs Zari Golinejad for their technical supports. We also thanks personnel of Mofid hospital for their kindly cooperation.

References

1. Steffen R, *Changing travel-related global epidemiology of Hepatitis A. Am J Med*, 2005. 118((10A)): p. 46S-9S.
2. Kalaajieh W, et al., *Seroprevalence of Hepatitis A antibodies in Lebanese children. Med Mal Infect*, 2000. 30: p. 757-61.
3. Kunasol P, et al., *Hepatitis A virus: declining seroprevalence in children and adolescents in Southeast Asia. Southeast Asian J Trop Med Public Health*, 1998. 29(2): p. 255-62.
4. Provost P.J and Hilleman M.R, *Propagation of human hepatitis A virus in cell culture in vitro. Proc. Soc. Exp. Biol. Med.*, 1981. 160: p. 213-21.
5. Vallbracht A, et al., *Persistent infection of human fibroblasts by hepatitis A virus. J. Gen.Virol.*, 1984. 65: p. 609-15.

6. Gabriel P, Vallbracht A, and Flehming B, Lack of complement-dependent cytolytic antibodies in hepatitis A virus infection. *J. Med. Virol.*, 1986. 20: p. 23-31.
7. Vallbracht A., et al., Cell-mediated cytotoxicity in hepatitis A virus infection. *Hepatology*, 1986. 6: p. 1308-41.
8. Banatvala J.E, *Epidemiology of Hepatitis A (HAV) in Europe and its relationship to immunisation, in Enterically Transmitted Hepatitis Viruses.* 1996, La Simmarre, Joue-le-Tours. p. 72-7.
9. Sundkvist T, et al., Outbreak of hepatitis A spread by contaminated drinking glasses in a public house. *Commun. Dis. Public Health*, 2000. 3: p. 60-2.
10. Gustafson T.L, et al., An outbreak of foodborne hepatitis A: the value of serologic testing and matched case-control analysis. *Am. J. Public Health*, 1983. 73: p. 1199-201.
11. Locarnini S, A virological perspective on the need for vaccination. *J. Viral Hepatitis*, 2000. 7: p. 5-6.
12. Pramoolsinsap C, et al., Susceptibility to hepatitis A virus infection among chronic liver disease patients and healthy blood donors in Thailand. *Southeast Asian J. Trop. Med. Public Health*, 1999. 30: p. 91-5.
13. Pramoolsinsap C, Acute hepatitis A and acquired immunity to hepatitis A virus in hepatitis B virus (HBV) carriers and in HBV or hepatitis C virus-related chronic liver diseases in Thailand. *J. Viral Hepatitis*, 2000. 7: p. 11-12.
14. Jacobsen KH and K. JS., Declining hepatitis A seroprevalence: a global review and analysis. *Epidemiol Infect*, 2004. 132: p. 1005—22.
15. Yong-de S, et al., Clinical/subclinical case ratio in Hepatitis A. *The Lancet*, nov 1988.
16. Malik R, et al., Hepatitis A frequency in children with nonspecific abdominal symptoms. *J Coll Physicians Surg Pak*, 2004. 14(6): p. 348-50.
17. Pohlet Odon, et al., Retrospective detection of a subclinical hepatitis A virus (HAV) epidemic affecting juvenile cohorts of the Hungarian population. *FEMS Immunology and Medical Microbiology*, 2003 38: p. 85-91.
18. Malik R, et al., Hepatitis A frequency in children with nonspecific abdominal symptoms. *J Coll Physicians Surg Pak*, jun 2004. 14(6): p. 348-50.
19. Kleigman R, et al., *Nelson Textbook of Pediatrics*, ed. 18. Vol. 1. 2008: Saunders-elsevier
20. Dautovic-Krkic S, Hadzic A, Mesic A Contribution to the epidemiology prolonged forms hepatitis "A" *HealthMED Journal*, 2011, 6:1829- 34
21. Gilany, A.-H., et al., Seroprevalence of hepatitis A antibodies among children in a Saudi community. *Asian Pacific Journal of Tropical Medicine*, 2010: p. 278-282.
22. Tandon B, et al., Subclinical hepatitis in north Indian children. *The Lancet* 1984. feb.11.
23. Sofian, M., et al., Seroepidemiology of hepatitis A virus in children of different age groups in Tehran, Iran: Implications for health policy. *Travel Medicine and Infectious Disease*, 2005. 8(3): p. 176-179.
24. WHO., Hepatitis A vaccines, in WHO position paper, *Wkly Epidemiol Rec.* 2000. p. 38-44.

Corresponding Author

Mohammad Rahbar,
Department of Microbiology,
Iranian Reference Health laboratory,
Ministry of Health and Medical Education,
Tehran,
Iran,
E-mail: rahbar_reflab@yahoo.com

Body image dissatisfaction and risk factors among female adolescents: A sample from Turkey

Perim Turker, Murat Bas, Mendane Saka, Sinem Metin

Baskent University, Health Sciences Faculty, Department of Nutrition and Dietetics, Ankara, Turkey

Abstract

The aim of the present study was to find the predictors and prevalence of body image dissatisfaction (BID) among adolescent girls in Ankara, the capital city of Turkey. A sample of 945 adolescent girls aged 12-16 years old was recruited from public and private schools in Ankara. The participants completed measures regarding their self-esteem, depressive symptoms, attitudes to eating and weight teasing, as well as body shape questionnaires. Approximately 20.2% of the participants displayed BID in which abnormal eating behaviours, BMI and weight teasing were positive predictors of BID. In addition, the negative effects of media pressure and the perceived pressure to be thin from parents, peers and dating partners predicted an increase in body dissatisfaction. However, in contrast to other research, this study indicated that age, depression and self-esteem do not predict an increase in body dissatisfaction.

Key words: body image dissatisfaction, adolescents, eating behaviours

Introduction

A large proportion of adolescent girls have reported significant body dissatisfaction (1). This body dissatisfaction is associated with marked emotional distress, rumination on one's appearance and unnecessary cosmetic surgery (2). Body dissatisfaction also increases the risk of the subsequent onset of an eating disorder (3) and depression among adolescent girls (4). Many factors have been investigated in relation to their effects on body image. Parental or peer teasing, social comparison and the media have been the most widely explored in recent years with regard to their negative influence on body image (5,6). Studies have investigated the ways in which these variables interact to influence negative body image or body dissatisfaction and, in turn, eating disorders (7,8).

The characteristics and perceptions of a person's physical self affect their self-concept, interpersonal relations and even professional choices. One's interest in appearances increases during adolescence, a period marked by significant physical changes (9). During adolescence, many people experience an increase in their dissatisfaction with their physical appearance, partly because normative physical changes such as weight gain which occur during puberty are at odds with the socially-prescribed and internalised ideals of physical attractiveness (10). In recent years, there has been an increasing level of awareness of the prevalence of body image problems among children and adolescents in developed societies (11). Peer and family influences have also been posited to play an important role while sociocultural frameworks (12) and media influences have been explored alongside peer and family influences in integrative models (13). In addition, research has indicated that individual attributes, such as low self-esteem and depressive moods, as well as a higher body mass index (BMI) are risk factors for an increase in body dissatisfaction (14,15). In addition, sociocultural pressures, such as exposure to idealised media figures, family and peer dieting, the pressure to be thin and weight teasing, have been shown to be risk factors for an increase in body dissatisfaction (16).

In the few studies which have compared body image among obese binge eaters and non-binge eaters, obese binge eaters reported greater body dissatisfaction than non-binge eaters, with general body dissatisfaction being shown to be positively related to the severity of bingeing (17). Obese binge eaters are more likely to evaluate themselves based on their body weight and concerns about their shape (18), as evidenced by greater levels of distress on attitudinal measures of body image (i. e. drive for thinness, feelings about certain body parts, fear of weight gain), even after controlling for the level of negative affect (19). Additionally,

obese binge eaters are more likely to report larger discrepancies between their current and ideal body shapes than obese non-binge eaters, regardless of their obesity level (20).

Despite epidemiological research which has shown concerns with weight and body image to be prevalent among adolescents from the United States (21), these issues are no longer limited to Westerners. In Western society, concerns with body image are so prevalent among young women that they have been called normative, with body dissatisfaction appearing in girls as young as five years old (22). The proportion of adolescent girls who are dissatisfied with their body shape has been reported to range between 37 and 54% (23). A recent study has indicated that body image dissatisfaction (BID) has been observed in approximately 60% of adolescent girls and 30% of adolescent boys in the United States (24). In the United Arab Emirates, 66% of adolescent girls (aged 13–18 years) have the desire to be thin (25). Moreover, the prevalence of BID among adolescent girls in Pakistan was reported as 11.4% (26) and 13% in Palestine (27).

Some evidence has provided support for the different propositions for the relationship between BID and risk factors in samples from Western cultures. However, there has been no attempt to test these propositions in Eastern cultures. Accordingly, the primary aim of this study is to test the hypothesis that BMI, abnormal eating behaviours, binge eating behaviours, weight-related teasing, depression, self-esteem, media pressure, post-menarcheal status and other indicators would predict a subsequent increase in body dissatisfaction over time in adolescent girls. A secondary aim was to determine the prevalence of BID in Turkish girls.

Methods

Participants

The participants were 945 females aged between 12 and 16 years old from both public and private schools in Ankara, the capital city of Turkey. Of the 1123 surveys which were distributed, 178 had missing information, and therefore we used 945 surveys for the present analyses (a response rate of 84.2%). Measurement and data collection were conducted during an eight month period between September 2009 and April 2010. The ques-

tionnaires were administered under the supervision of 23 dietetic students at the universities and a researcher. Questions could be addressed to the researcher, to ensure that the adolescents understood the meaning of each item. After completing the questionnaire, each adolescent was taken out of the class to a private place where her body weight and height were measured. BMI was calculated as weight (kg) divided by height squared (m^2). World Health Organization (WHO) Growth Reference Data for 5–19 year old children were used to evaluate the adolescents. They were grouped into two categories: normal-weight and overweight/obese, in accordance with the cut-off points of the 5th to 85th and >85th percentiles. A BMI between the 5th and 85th percentile was defined as normal weight, and a BMI at or above the 85th percentile was defined as overweight or obese (28). The mean age was 14.7 ± 1.2 years old. Approximately 41.8% of the participants were post-menarcheal, with a mean menarcheal age of 12.2 ± 1.5 years.

Measures

Demographic data and other characteristics of the participants were obtained through a constructed questionnaire which gathered information regarding age, BMI, menarcheal status, media influence, parents' and peers' dieting status, alcohol consumption and smoking.

The Body Shape Questionnaire (BSQ) (29) was developed in 1987 to measure individuals' concerns about their body shape, and especially their concerns regarding "feeling fat." It is a self-report questionnaire that consists of 34 questions that refer to the subject's feelings about their appearance over the previous four weeks. The questions are answered using a six-point Likert scale ranging from "never" to "always". Each answer is assigned a value from 1 to 6, resulting in total scores that can range from 34 to 204. Those who are considered to be probable or definite cases of bulimia score around 130 or above on the BSQ. Body dissatisfaction is considered to be present in cases with a score of 110 or above. The reliability and validity of the instrument for Turkish adolescents were determined in a recent study carried out by Bozan, Bas and Asci (30).

Self-esteem was measured via the Rosenberg Self-Esteem Scale (31). This scale is the most widely used measure of global self-esteem and has been

shown to be valid and reliable among students in grades 7 to 12 (32). Responses to the 10 items were rated on a four-point scale (“strongly disagree” to “strongly agree”), yielding scores between 10 and 40, with higher scores indicating higher levels of self-esteem. The reliability and validity of the instrument for use with Turkish adolescents were determined in a recent study carried out by Çuhadaroglu (33).

Depression was measured with the 21-item Beck Depression Inventory (BDI) (34). The BDI measures the severity of depressive symptoms. Items are scored on a four-point scale. One item concerning weight loss was excluded from the analysis, and the total from the remaining 20 items was calculated. A higher score indicates more severe depression. A recommended cut-off of 17 is used to define depression. The BDI is an internally consistent and valid measurement. A valid and reliable Turkish translation of the scale was used (35). Cronbach’s alpha coefficients for the sample of adolescents were 0.88 in the present study.

The Eating Attitudes Test (EAT-26) is a screening tool for negative eating attitudes in nonclinical settings. It was developed by Garner and Garfinkel (36) to measure symptoms of anorexia nervosa. The EAT-26 is based on an original Eating Attitudes Test (EAT-40). Total scores on the EAT-26 are derived as a sum of the composite items, ranging from 0 to 53, with a score of 20 on the EAT-26 used as the cut-off (37). The reliability of the EAT-26 was also determined by a pilot study using 50 university students. The internal consistency (Cronbach’s alpha) of the EAT-26 was 0.70, and its interclass correlation coefficient was 0.98 in the pilot study. Participants who scored 20 or above were placed in the “abnormal eating behaviour” category, and those scoring below 20 were placed in the “normal eating behaviour” category.

Weight teasing was assessed with a three-item scale on which participants were asked to rate how

often teasing occurred, including: “How often are you teased about your weight?” Ratings were given on a five-point scale ranging from never (1) to at least once a week (5). Individual scores were taken to be the average of the three items. Similar single items assessing the frequency of teasing have been found in previous research to correlate with body image (38). Cronbach’s alpha was 0.82.

Statistical analysis

Descriptive statistics for the variables (means and standard deviations) and Pearson’s correlation coefficient for all of the predictor variables were examined. Linear regression models were performed to examine the association between BID (BSQ-34 scale) and other indicators. BID was analysed as the dependent variable, whereas age, BMI, depression, self-esteem, weight teasing and abnormal eating attitudes (measured using the EAT-26 scale) were used as the predictors. In order to examine the odds ratios (OR) of BID and other indicators, 2 x 2 tables and Chi-squared tests were used. ORs were reported with a 95% confidence interval. All statistical analyses were performed using SPSS (version 15; SPSS Inc, Chicago, IL) and in all analyses, a 5% significance level was used.

Results

The mean BSQ-34, self esteem, BDI and weight teasing scores were 73.1 ± 32.1 , 18.0 ± 4.1 , 17.7 ± 11.8 and 1.3 ± 0.8 , respectively. According to the BSQ-34, 20.2% of the participants scored at or above the cut-off point for BID. The proportion of participants who had >17 points according to the BDI was 32.7%. Participants had a mean EAT-26 score of 15.9 ± 9.6 , and disturbed eating behaviour ($EAT \geq 20$) was found in 31.7% of the total sample. In addition, the mean BMI was 22.3 ± 3.5 kg/m², and 21.5% of the participants were overweight or obese.

Table 1. Correlation among predictors for participants

	(1)	(2)	(3)	(4)	(5)	(6)
(1) Body image dissatisfaction	1	0,27**	0,13**	0,24**	-0,12**	0,33**
(2) BMI		1	0,12**	0,09**	-0,09**	0,11**
(3) Depression			1	0,12**	-0,36**	0,13**
(4) Abnormal Eating Behaviour				1	-0,05	0,24**
(5) Self-Esteem					1	0,01
(6) Weight Teasing						1

*Pearson’s correlation coefficient is significant at the 0.01 level

From the analysis of the correlations among the variables, there was a significant positive correlation between BID and BMI ($r=0.27$; $p<.01$), depression ($r=0.13$; $p<.01$), abnormal eating behaviours ($r=0.24$; $p<.01$) and weight teasing ($r=0.33$; $p<.01$). In addition, the results revealed a significant negative correlation between BID and self-esteem ($r=-0.12$; $p<.01$) (Table 1).

Table 2 shows the odd ratios (OR) for BID and selected risk factors. The results indicate that participants who were overweight or obese [OR: 5.1 (3.5–7.5), $p<.01$] had abnormal attitudes to eating [OR: 2.1 (1.5–2.9), $p<.01$], engaged in binge eating behaviours [OR: 3.4 (2.3–4.9), $p<.01$] or engaged in self-induced vomiting [OR: 4.2 (2.3–7.5), $p<.01$] were at a significantly higher risk of BID. Receiving

negative comments regarding their weight from a boyfriend [OR: 2.1 (1.4–3.2), $p<.01$], peers [OR: 1.9 (1.3–2.9), $p<.01$] or parents [OR: 1.8 (1.2–2.6), $p<.01$] was associated with BID in the participants.

Age, BMI, weight teasing, depression, self-esteem and abnormal eating behaviours accounted for 21% of the variance in BID ($F = 41.550$, $p < .01$). Associations between BID and BMI, weight teasing and abnormal eating behaviour were found to be significant ($p < .01$), while associations between BID and age, depression and self-esteem were not found to be statistically significant ($p > .01$). Abnormal eating behaviour, BMI and weight teasing were positive predictors of BID. Therefore, depression, self-esteem and age did not serve as predictors of BID (Table 3).

Table 2. Association between BID and selected risk factors for the sample

Indicator	Body Image Dissatisfaction			
	Odd ratios	95% Confidence interval	χ^2	p value
Being post-menarcheal	1.833	1.305-2.576	12.407	0.000
BMI status (being overweight and obese)	5.140	3.544-7.456	84.350	0.000
Media body comparison	1.816	1.222-2.699	8.896	0.003
Go on a diet to lose weight or exercise because of media pressure	1.744	1.151-2.643	6.998	0.007
Parents dieting environment	1.638	1.182-2.270	8.801	0.002
Peers dieting environment	1.773	1.270-2.477	11.455	0.001
Boyfriend dieting	2.663	1.898-3.735	33.508	0.000
Depressive mood	1.699	1.226-2.354	10.256	0.001
Weight teasing	3.027	2.113-4.336	38.689	0.000
Negative comments from weight				
From parents	1.762	1.181-2.629	7.838	0.005
From peers	1.916	1.253-2.930	9.248	0.002
From boyfriend	2.123	1.406-3.205	13.258	0.000
Abnormal eating behaviour (EAT $\geq$ 20)	2.117	1.525-2.938	20.599	0.000
Smoking status	1.520	0.994-2.322	3.780	0.036
Alcohol use	1.197	0.822-1.741	0.881	0.199
Self-induced vomiting	4.191	2.335-7.521	26.521	0.000
Binge eating behaviour	3.383	2.316-4.942	42.853	0.000

Table 3. Linear regression analysis according to BID

	β	SEM	t	p
Age	0.303	0.861	0.352	0.725
BMI	1.306	0.268	4.866	0.000
Abnormal eating behaviour	0.953	0.101	9.464	0.000
Depression	0.059	0.086	0.692	0.489
Self esteem	-0.576	0.244	-2.358	0.019
Weight teasing	8.947	1.224	7.307	0.000

Discussion

The proportion of adolescent girls who are dissatisfied with their body shape has been reported to range between 37 and 54% (23,39). The current study has investigated the occurrence of BID in adolescent schoolgirls aged 12–16 years old in Turkey. Our findings demonstrate that 20.2% of the sample was dissatisfied with their body image. According to our findings, the occurrence of BID in this sample was higher than the prevalence rates observed among adolescent girls in Saudi Arabia (16%) (40) and Pakistan (11.4%) (26). The estimate of BID for this sample was lower than the estimates for Canada (47%) (41), Jordan (21.2%) (42) and Iran (84%) (43). Turkey is located between Europe and Asia. Turkish people are influenced by the values of both European and Asian society. In addition, Turkey is a fast-developing country that has been exposed for more than a decade to Western culture in the form of the Western media. With an increase in the rate of the globalisation of the Turkish economy and a greater emphasis on meeting international standards in every sphere, girls and women in Turkey are increasingly exposed to images from the Western media (44).

BMI is a commonly used measure of body size that is based on height as well as weight. BMI also correlates with body dissatisfaction and the risk of eating disorders in females in the majority of the cultures and ethnic groups which have been studied (45). Research has suggested that having a higher BMI than one's perceived ideal is associated with greater levels of BID (46,47). Studies have found that having a higher BMI than one's perceived ideal is associated with greater levels of BID, and thus dieting behaviours and maladaptive eating practices are likely to be initiated as a means of weight loss and in an attempt to attain the thin ideal (3,47). Similarly, in the current study, BMI has been shown to be strongly and positively correlated with BID. BMI was a significant predictor of body dissatisfaction. In previous research, an elevated BMI has been found to be highly correlated with body image and self-dissatisfaction in female college students (48). A similar study was conducted in a more representative sample of female college students, and found that a higher BMI was associated with a more negative body image (49). In contrast, one

study examining adolescent body dissatisfaction found that BMI did not predict body dissatisfaction for adolescent girls. The strength of this study was its use of an ethnically diverse sample (50).

There was a significant relationship between BID and abnormal eating behaviours in our study. Abnormal attitudes to eating were found to be strong predictors of BID in this study. Previous studies support these findings regarding body image and eating behaviours among girls. For example, one longitudinal study showed that over a two-year time period, baseline body dissatisfaction was a significant predictor of eating disturbances during the follow-up (3). Finally, data from three-year studies were consistent with the structural equation models positing BID as a precursor of the development of eating disorders (51).

Mussell et al. (19) examined body image in women seeking treatment for obesity by comparing non-binge eaters to those who were binge eaters, and found that, after controlling for depression, differences in body dissatisfaction were no longer significant. On the contrary, the girls who reported binge eating behaviours were at a higher risk of BID than girls who did not have binge eating behaviours in the current study. A review of the literature points to a strong relationship between binge eating and BID (52,53). In addition, obese individuals with binge eating disorder (BED) (19) and non-overweight individuals with BED (54) have reported higher levels of concerns about their body image compared to their counterparts without BED. Clearly, body dissatisfaction, BED and obesity appear to be highly interrelated (55) but the nature of and conditions under which these relationships operate merit further study.

Body dissatisfaction has been linked to the development of depression in adolescent girls. Rierdan and Koff (56) found that dissatisfaction with weight and concerns about body image were associated with a greater number of depressive symptoms. Similarly, Stice et al. (4) reported that in adolescent girls, initial body dissatisfaction, dietary restraints and bulimic symptoms predicted the onset of depression. Similarly, girls with high levels of depression were at a higher risk of BID than girls with low levels of depression in our study.

In the present study, body dissatisfaction was associated with weight teasing in girls. Teasing in

relation to weight and appearance has been one of the most empirically well-supported links to body dissatisfaction (1), with one report finding that 72% of females at college age were teased about their appearance during childhood and adolescence over an average period of five years (57). In addition to body dissatisfaction, previous studies have reported significant associations between teasing and restrictive eating, bulimic behaviours, self-esteem, internalisation of the thin ideal and depression (58,59,60,61). A recent study has indicated that the association between body dissatisfaction and weight-related teasing is stronger for children and adolescents than for adults. The same pattern was true for the relationship between weight-related teasing and dietary restraint for children and adolescents and for adults (62).

Body dissatisfaction was associated with low self-esteem and high levels of depression in our study. Friedman, Reichmann, Costanzo and Musante (63) reported that body image satisfaction partially mediated the relationship between BMI, depression and self-esteem. Pesa, Syre and Jones (64) also stated that body image might explain the low self-esteem of overweight female adolescents. Receiving negative comments regarding weight from parents, friends and boyfriends doubled the likelihood that the school-age girls in our study would experience BID. Presnell et al. (65) opposed this finding, reporting that the perceived pressure to be thin from family members was not associated with BID. On the contrary, Mousa et al. (42) reported that negative comments from peers and parents regarding the physical appearance of adolescent girls influence BID.

The aim of the present study was to investigate the relationship between the media and body dissatisfaction in school-age girls. Research investigating the effects of media exposure on body image has found that exposure to images of thin people in the media resulted in heightened levels of body dissatisfaction and distorted body image in school-age girls, adolescents and young adults (59,65,66,67). Van den Berg et al (16) reported that comparing one's body with those shown in the media partially or fully mediated the relationships between self-esteem, depressive moods, friends' dieting habits, exposure to messages from magazines, BMI and body dissatisfaction in females.

The study showed that maternal dieting and having other relatives who are dieting were more consistently associated with eating disorders in girls than paternal variables. For example, having a mother who was dieting was associated with a greater use of unhealthy and extreme weight control behaviours in the girls, whereas associations with fathers who were dieting were not statistically significant (68). In our study, having dieting relatives increased the risk of displaying BID. Similarly, Byely et al. (12) and Mousa et al. (42) reported that adolescent girls who lived in environment where dieting was normal were more likely to experience BID. Another study showed that the prevalence of misperceived overweight and obesity in population aged 20 years and over was 63.2%. Misperceived overweight was greater in men, persons living in rural area and in poorest people. It was found that women, higher educated people and richest people more objective assess their body weight (69).

One limitation of this study is that the sample is only representative of a female population. Therefore, the results may only be generalised to adolescent girls. A second limitation of this study is that participants self-reported the degree to which they were dissatisfied with their bodies. Some individuals may not have acknowledged their level of dissatisfaction with their own bodies and/or others may have amplified their actual levels of body satisfaction. When relying on self-report measures to determine categorical qualities within samples, there is always a concern that the data will be inaccurate due to under-reporting or over-reporting by participants (70).

In conclusion, the findings of the current study support the statement made by recent studies that adolescent girls in Turkey experience concerns regarding their shape which are similar to those found in Western populations. The findings of this study show that elevations in BMI, disturbed eating behaviours, negative affect, media pressure and the perceived pressure to be thin from parents, peers and dating partners predicted an increase in body dissatisfaction. However, in contrast to other research, this study indicated that age, depression and self-esteem do not predict an increase in body dissatisfaction.

References

1. Thompson JK, Heinberg LJ, Altabe M, & Tantleff-Dunn S. *Exacting beauty: Theory, assessment, and treatment of body image disturbance*. Washington, DC: American Psychological Association. pp. 1999; 151–174.
2. Ohring R, Graber JA, & Brooks-Gunn J. Girls' recurrent and concurrent body dissatisfaction: Correlates and consequences over 8 years. *International Journal of Eating Disorders* 2002; 31: 404–415.
3. Attie I, & Brooks-Gunn J. Development of eating problems in adolescent girls: A longitudinal study. *Developmental Psychology* 1989; 25: 70–79.
4. Stice E, Hayward C, Cameron R, Killen JD, & Taylor CB. Body image and eating disturbances predict onset of depression in female adolescents: A longitudinal study. *Journal of Abnormal Psychology* 2000; 109(3): 438–444.
5. Dunkley TL, Wertheim EH, & Paxton SJ. Examination of a model of multiple sociocultural influences on adolescent girls' body dissatisfaction and dietary restraint. *Adolescence* 2001; 36: 265–280.
6. Field AE. Media influence on self-image: the real fashion emergency. *Healthy Weight Journal* 2000; 14: 88–91.
7. McCabe MP, & Ricciardelli LA. Parent, peer, and media influences on body image and strategies to both increase and decrease body size among adolescent boys and girls. *Adolescence* 2001; 36: 225–240.
8. Rieves L, & Cash TF. Social developmental factors and women's body image attitudes. *Journal of Social Behavior & Personality* 1996; 11: 63–79.
9. Cok F. Body image satisfaction in Turkish adolescents. *Adolescence* 1990; 25: 409–12.
10. Striegel-Moore RH, & Cachelin FM. Etiology of eating disorders in women. *The Counseling Psychologist* 2001; 29: 635–661.
11. Thompson JK, van den Berg P, Roehrig M, Guarda AS & Heinberg LJ. The sociocultural attitudes towards appearance scale-3 (SATAQ-3): Development and validation. *International Journal of Eating Disorders* 2004; 35(3): 293–304.
12. Byely L, Archibald AB, Graber J, & Brooks-Gunn J. A prospective study of familial and social influences on girls' body image and dieting. *International Journal of Eating Disorders* 2000; 28: 155–164.
13. Keery H, van den Berg P, & Thompson JK. An evaluation of the Tripartite Influence Model of body dissatisfaction and eating disturbance with adolescent girls. *Body Image* 2004; 1: 237–251.
14. Field AF, Carmago CA, Taylor CB, Berkey CS, Roberts SB, & Colditz GA. Peer, parent and media influences on the development of weight concerns and frequent dieting among preadolescent and adolescent girls. *Pediatrics* 2001; 107: 54–60.
15. Paxton SJ, Eisenberg ME, & Neumark-Sztainer D. Prospective predictors of body dissatisfaction in adolescent girls and boys: A five year longitudinal study. *Developmental Psychology* 2006; 42: 888–899.
16. Van den Berg P, Paxton SJ, Keery H, Wall M, Guo J, & Neumark-Sztainer D. Body dissatisfaction and body comparison with media images in males and females. *Body Image* 2007; 4: 257–268.
17. De Zwaan M, Nutzinger DO, & Schoenbeck G. Binge eating in overweight women. *Comprehensive Psychiatry* 1992; 33: 256–261.
18. Cash TF. Binge-eating and body image among the obese: a further evaluation. *Journal of Social Behavior and Personality* 1991; 6: 367–376.
19. Mussell MP, Peterson CB, Weller CL, Crosby RD, de Zwaan M, & Mitchell JE. Differences in body image and depression among obese women with and without binge eating disorder. *Obesity Research* 1996; 4(5): 431–439.
20. Antony MM, Johnson WG, Carr-Nangle RE, & Abel JL. Psychopathology correlates of binge eating and binge eating disorder. *Comprehensive Psychiatry* 1994; 35: 386–392.
21. Neumark-Sztainer D, Story M, Hannan PJ, Perry CL, & Irving LM. Weight-related concerns and behaviors among overweight and nonoverweight adolescents: Implications for prevention weight-related disorders. *Archives of Pediatrics and Adolescent Medicine* 2002; 156: 171–178.
22. Davison KK, Markey CN, & Birch LL. A longitudinal examination of patterns in girls' weight concerns and body dissatisfaction from ages 5 to 9 years. *International Journal of Eating Disorders* 2003; 33: 320–332.
23. Børresen R, Rosenvinge JH. Body dissatisfaction and dieting in 4,952 Norwegian children aged 11 to 15 years: less evidence for gender and age differences. *Eating and Weight Disorders* 2003; 8: 238–241.
24. Presnell K, Bearman S, & Stice E. Risk factors for body dissatisfaction in adolescent boys and girls: A prospective study. *International Journal of Eating Disorders* 2004; 36: 389–401.
25. Eapen V, Mabrouk AA, & Bin-Othman S. Disordered eating attitudes and symptomatology among adolescent girls in the United Arab Emirates. *Eating Behaviors* 2006; 7: 53–60.

26. Mumford DB, Whitehouse AM, & Choudry IY. Survey of eating disorders in English-medium schools in Lahore, Pakistan. *International Journal of Eating Disorders* 1992; 11: 173–184.
27. Latzer Y, Tzischinsky O, & Asaiza F. Disordered eating related behaviors among Arab schoolgirls in Israel: An epidemiological study. *International Journal of Eating Disorders* 2007; 40: 263–270.
28. De Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, & Siekmann J. Development of a WHO growth reference for school-aged children and adolescents. *Bulletin of the World Health Organization* 2007; 85(9): 649–732.
29. Cooper PJ, Taylor MJ, Cooper Z, & Fairburn CG. The development and validation of the Body Shape Questionnaire. *International Journal of Eating Disorders* 1987; 6: 485–494.
30. Bozan N, Bas M, & Asci FH. To Determine of the DEBQ's and BSQ Reliability and Validity on Turkish University Students, Unpublished Master Thesis, Baskent University, Turkey 2009.
31. Rosenberg, M. *Society and the Adolescent Self-Image*, Revised edition. Middletown, CT: Wesleyan University Press 1989.
32. McCarthy JD, & Hoge DR. Analysis of age effects in longitudinal studies of adolescent self-esteem. *American Journal Sociology* 1982; 18: 372–79.
33. Çuhadaroglu, F. Self-esteem in adolescents. Unpublished doctoral dissertation, Hacettepe University, Turkey 1986.
34. Beck AT, Ward CH, Mendelson M, Mock J, & Erbaugh J. An inventory for measuring depression. *Archives of General Psychiatry* 1961; 4: 561–571.
35. Hisli N. The validity of Beck Depression Inventory (Turkish). *Psikoloji Dergisi* 1988; 6(22): 118–26.
36. Garner D, & Garfinkel P. The EAT: An index of the symptoms of anorexia. *Psychological Medicine* 1979; 9: 273–279.
37. Garner DM, Olmsted MP, Bohr Y, & Garfinkel PE. The eating attitudes test: Psychometric features and clinical correlates. *Psychological Medicine* 1982; 12: 871–878.
38. Fabian LJ, & Thompson JK. Body image and eating disturbance in young females. *International Journal of Eating Disorders* 1989; 8: 64–74.
39. Moore DC. Body image and eating behavior in adolescent girls. *American Journal of Diseases of Children* 1988; 142: 1114–1118.
40. Al-Subaie A. Some correlates of dieting behavior in Saudi schoolgirls. *International Journal of Eating Disorders* 2000; 28: 242–246.
41. Jones JM, Bennett S, Olmsted MP, Lawson ML, & Rodin G. Disordered eating attitudes and behaviors in teenaged girls: A school-based study. *Canadian Medical Association Journal* 2001; 165: 547–552.
42. Mousa TY, Mashal RH, Al-Domi HA, & Jibril MA. Body image dissatisfaction among adolescent schoolgirls in Jordan. *Body Image* 2010; 7: 46–50.
43. Nobakht M, & Dezhkam M. An epidemiological study of eating disorders in Iran. *International Journal of Eating Disorders* 2000; 28: 265–271.
44. Uzun Ö, Güleç N, Özşahin A, Doruk A, Özdemir B, Çalışkan U. Screening disordered eating attitudes and eating disorders in a sample of Turkish female college students. *Comprehensive Psychiatry* 2006; 47: 123–126.
45. Shisslak CM, Crago M, McKnight KM, Estes LS, Gray N, & Parnaby OG. Potential risk factors associated with weight control behaviors in elementary and middle school girls. *Journal of Psychosomatic Research* 1998; 44: 301–313.
46. Taylor CB, & Altman T. Priorities in prevention research for eating disorders. *Psychopharmacology Bulletin* 1997; 33: 413–417.
47. Vincent MA, & McCabe MP. Gender differences among adolescents in family, and peer influences on body dissatisfaction, weight loss, and binge eating behaviours. *Journal of Youth and Adolescence* 2000; 29: 205–221.
48. Yates A, Edman J, Crago M, Crowell D, & Zimmerman R. Measurement of exercise orientation in normal subjects: Gender and age differences. *Personality and Individual Differences* 1999; 27: 199–209.
49. Burger M, & Doiny D. The relationship among Body Mass Index, body image, exercise habits and stage of change in college-aged females. *Women in Sport and Physical Activity Journal* 2002; 11(2): 1–11.
50. Bearman SK, Presnell K, Martinez E, & Stice E. The skinny on body dissatisfaction: A longitudinal study on adolescent girls and boys. *Journal of Youth and Adolescence* 2006; 35: 229–241.
51. Cattarin JA, & Thompson JK. A three-year longitudinal study of body image, eating disturbance, and general psychological functioning in adolescent females. *Eating Disorders, The Journal of Treatment and Prevention* 1994; 2(2): 114–125.
52. Grilo CM, & Masheb RM. Correlates of body image dissatisfaction in treatment-seeking men and women

- with binge eating disorder. *International Journal of Eating Disorders* 2005; 38: 162–166.
53. Sorbara M, & Geliebter A. Body image disturbance in obese outpatients before and after weight loss in relation to race, gender, binge eating, and age of onset of obesity. *International Journal of Eating Disorders* 2002; 31: 416–423.
 54. Barry DT, Grilo CM, & Masheb RM. Comparison of patients with bulimia nervosa, obese patients with binge eating disorder, and non-obese patients with binge eating disorder. *Journal of Nervous and Mental Disease* 2003; 191: 589–594
 55. Devlin MJ, Goldfein JA, & Dobrow I. What is the thing called BED? Current status of binge eating disorder nosology. *International Journal of Eating Disorders* 2003; 34: S2–S18.
 56. Rierdan J, & Koff E. Weight, weight-related aspects of body image, and depression in early adolescent girls. *Adolescence* 1997; 32: 615–624.
 57. Cash TF. Developmental teasing about physical appearance: retrospective descriptions and relationships with body image. *Journal of Social Behavior and Personality* 1995; 23: 123–129.
 58. Brown TA, Cash TF, & Lewis RJ. Body-image disturbances in adolescent female binge-purgers: A brief report of the results of a national survey in the U. S. A. *Journal of Child Psychology and Psychiatry* 1989; 30: 605–613.
 59. Lieberman M, Gauvin L, Bukowski WM, & White DR. Interpersonal influence and disordered eating behaviors in adolescent girls: The role of peer modeling, social reinforcement, and body-related teasing. *Eating Behaviors* 2001; 2(3): 215–236.
 60. Shroff H, & Thompson JK. The tripartite influence model of body image and eating disturbance: A replication with adolescent girls. *Body Image*, 2006; 3: 17–23.
 61. Thompson JK, Cattarin J, Fowler H, & Fisher E. The Perception of Teasing Scale (POTS): A revision and extension of the Physical Appearance Related Teasing Scale (PARTS). *Journal of Personality Assessment* 1995; 65: 146–157.
 62. Menzel JE, Schaefer LM, Burke NL, Mayhew LL, Brannick MT, & Thompson JK. Appearance-related teasing, body dissatisfaction, and disordered eating: A meta-analysis. *Body Image* 2010; 7: 261–270.
 63. Friedman KE, Reichmann SK, Costanzo PR, & Musante GJ. Body image partially mediates the relationship between obesity and psychological distress. *Obesity Research* 2002; 10: 33–41.
 64. Pesa JA, Syre TR, & Jones E. Psychosocial differences associated with body weight among female adolescents: the importance of body image. *Journal of Adolescence Health* 2000; 26: 330–337.
 65. Gowers SG, & Shore A. Development of weight and shape concerns in the aetiology of eating disorders. *British Journal of Psychiatry* 2001; 179: 236–242.
 66. McVey GL, Pepler D, Davis R, Flett GL, & Abdolell M. Risk and protective factors associated with disordered eating during early adolescence. *Journal of Early Adolescence* 2002; 22: 76–96.
 67. Rubin LS, Nemeroff CJ, & Russo NF. Exploring feminist women's body consciousness. *Psychology of Women Quarterly* 2004; 28: 27–37.
 68. Neumark-Sztainer D, Bauer KW, Friend S, Hannan PJ, Story M, & Berge JM. Family Weight Talk and Dieting: How Much Do They Matter for Body Dissatisfaction and Disordered Eating Behaviors in Adolescent Girls?. *Journal of Adolescent Health* 2010; 47: 270–276.
 69. Grujic V, Dragnic N, Ukropina S, Niciforovic Surkovic O, Cankovic D. *Health Med* 2011; 5(2): 372–383.
 70. Schwarz N. Self-reports: How the questions shape the answers. *American Psychologist* 1999; 54: 93–105.

Corresponding Author

Perim Turker,
Baskent University,
Health Sciences Faculty,
Department of Nutrition and Dietetics,
Ankara,
Turkey,
E-mail: pfturker@baskent.edu.tr

Mothers' knowledge, attitude, and practice: The performance of the nationwide integrated maternal health care project

Forouzan Akrami¹, Gohar Mohammadi², Mohammad Esmail Motlagh³, Ali Ramezankhani², Shahrzad Valafar⁴

¹ Department of Neonatal Health, Deputy of Public Health, Ministry of Health and Medical Education, Tehran, Iran,

² School of Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran,

³ Department of Pediatrics, Ahvaz Jundishapur University of medical sciences, Ahvaz, Iran,

⁴ Department of Maternal Health, Deputy of Public Health, Ministry of Health and Medical Education, Tehran, Iran.

Abstract

Aim: to examine the impact of the nationwide implementation of the Integrated Maternal Health Care Project on the attitude, cognition, and behavior of the women who were given the maternity health care by health facilities.

Methods and materials: this quasi-experimental clinical trial was conducted on 824 women who referred to health facilities of Ray (402 controls) or Islamshahr (422 cases) during their 2-month post-partum period. As a part of the Integrated Maternal Health, health care providers working in health facilities were required to provide clients contemplating to be pregnant with predetermined face-to-face interview. During interview, clients were provided with information required for safe maternity. Women were also provided with a booklet containing health messages.

Results: When we considered the potential confounding effects of age, income, education levels, and urbanization, mean score for knowledge of intervention group was 7.4 percent point higher than knowledge of control group (P value <0.001), mean score for attitude of intervention group was 1.9 percent point lower than those of control group (P value $=0.041$), and mean score for practice of intervention groups was 6.1 percent point higher than, that of control group (P value <0.001).

Conclusion: We observed that the Integrated Maternal Health Care program effectively improved the knowledge and practice of the participant. Opposite findings were observed for attitude; that is attitude of the control group was more positive towards maternal care than was the attitude of the intervention group. The improvements observed were not substantial and there are many rooms for improving instruction methods.

Key words: Maternal care, health facility, pregnancy, attitude, knowledge, practice

Introduction

In 2007, the Safe Motherhood Initiative celebrated its 20th anniversary (1, 2). Many countries, including Iran, have been able to improve the health and well-being of mothers and newborns over the last 20 years (3). However, countries with the highest burdens of mortality and illness have made the least progress, and inequalities between countries are increasing. In many places, inequalities within countries are increasing too, between those who live in better conditions and have access to care, and those who for a variety of reasons are excluded.

Several papers focus on important technical areas, particularly the management of post-partum complications, and saving pregnant women and newborns' lives by providing evidence and recommendations for policy changes and program implementation. Other papers provide evidence that simple but effective monitoring of programs in developing countries is possible (4).

However, the challenges to be met are not new technologies or new knowledge about effective interventions, because we mostly know what needs to be done to save the lives of mothers and newborns. The real challenges are how to deliver services and scale up interventions, particularly to those who are vulnerable, hard to reach, marginalized and excluded. Effective health interventions exist for mothers and babies, and several proven means of distribution can be used to put these in place. However, none will work if policies are absent where it matters most: at national and district levels (4).

Despite the importance of pre-, intra-, and post-pregnancy counseling, no compiled program had ever existed in this regard in the health care system of Iran until 2003. It was then that the issue was discussed as a part of necessary care services for women when designing and implementing the integrated maternal health Care pilot project. As a part of Integrated Maternal Health Care Project all women seeking maternity care from health facilities are to be educated, consulted, and instructed about different aspects of the maternal and neonatal care.

In the current study we examined the impact of the nationwide Integrated Maternal Health Care Project on the attitude, cognition, and behavior of the women who were given the maternity health care by health facilities.

Methods and materials

Study population

The current study was a quasi-experimental clinical trial, designed to examine the impact of implementing the Integrated Maternal Health Pilot Project (2003-2007) on the cognition and behavior of mothers. The study sample consisted of 824 women who referred to health facilities of Ray or Islamshahr during their 2-month post-partum period. Ray and Islamshahr are two small cities located in the south of the Tehran, capital of Iran. Integrated Maternal Health Pilot Project has been implemented in Islamshahr. The intervention arm of the study consisted of 422 women referring to the health centers of the Islamshahr. The control arm of the study consisted of 402 women referring to the health centers of Ray. Apparently healthy women with their first or second pregnancy (primigravid or bigravid) were eligible for the current study if they were of Persian ancestry, married, permanent resident of the city they were living in during their recruitment, and able to read and write (were not illiterate).

Measurements

Data were secured using a predetermined questionnaire consisted of 4 main components. A trained interviewer collected data on clients' demographic characteristics, knowledge, attitude and practice. Participants were classified based their levels of education into 4 groups of primary education, less than diploma, diploma, and academic

education. Monthly income of participants' family was discretized into less than 1000, 1000-1500, and more than 1500 U.S. dollars.

Outcomes

The knowledge of participants was quantified by using scores assigned to correct answers. The overall knowledge variable was then calculated as the fraction achieved of the maximum point-total that participants were expected to achieve. The practice was quantified by using scores assigned to correct healthy behaviors. The practice variable was then calculated as the fraction achieved of the maximum point-total that participants were expected to achieve. For attitude participants were asked to complete phrases on a 5-point response scale in which 0 represents the strong disagreement and 4 represents the strong agreement. Scores of each dimensions of attitude were then multiplied by 100/5. Our method can be visualized by imagining an elastic rule with five equidistant numerals is stretched evenly to fit alongside a longer ruler with 100 numerals or one with 100 numerals compressed to fit alongside a ruler with five (5). As such, we were able to quantify attitude on similar scale as knowledge and practice. Furthermore, results from other studies on an n-point scale could be comparable if multiplied by 100/n.

Interventions

The pilot study of the Integrated Maternal Health was conducted from 2003 to 2007. We implemented our survey during 2006, before the study conducted a nationwide taskforce. As a part of the pilot study of the Integrated Maternal Health, health care providers working in health centers were required to provide clients who were contemplating to be pregnant with predetermined face-to-face interview. During interview, clients were provided with information required for safe maternity. Women were also provided with a booklet containing health messages. The medical (including obstetric-gynecologic) history of women as well as results obtained from physical (including obstetric-gynecologic) examination were also recorded in the booklet. Clients were asked to bring the booklet along while referring to their midwife, physician, health facility, or hospital. The booklet included data on:

1. Risk factors during pregnancy
 - a. Vaginal Spotting or bleeding
 - b. Reduced or absent fetal movement
 - c. Leaking of amniotic fluid
 - d. Unilateral pain or swelling on a leg or thigh
 - e. Heart burn
 - f. Flank pain
 - g. Dysuria
 - h. Sever relentless vomiting (including hematemesis or without it)
 - i. Fever
 - j. Dyspnea and palpitation
 - k. Palpitation
 - l. Edema on upper extremity or face
 - m. Headache and Blurred vision
 - n. Weight gain (more than a one-kg/week)
 - o. Dental infection or abscess
2. Risk factors during postpartum period
 - a. Heavy vaginal bleeding during first week
 - b. Pain on or purulent discharge from wounds (including episiotomy)
 - c. Abdominal or flank pain
 - d. Postpartum depression (or psychosis)
 - e. Dysuria
 - f. Purulent vaginal discharge
 - g. Pain on or swelling of breast
 - h. Fever
 - i. Unilateral pain or swelling on a leg or thigh
3. Risk factors during Neonatal period
 - a. Jaundice during first 24 hours of life
 - b. Intercoastal retraction
 - c. Grunting
 - d. Pallor or ecchymosis
 - e. Relentless vomiting
 - f. Periorbital erythema
 - g. Flappy baby
 - h. Irritability
 - i. Purulent discharge from umbilicus
 - j. Poor feeding
 - k. No voiding or defecation (including meconium excretion) for first 24- 48 hours of life
 - l. Diffuse purulent skin rash
 - m. Fever or hypothermia
 - n. Conjunctivitis
4. Maternal health including prenatal instructions on
 - a. How to deal with nausea and vomiting
 - b. How to deal with constipation
 - c. How to deal with leg swelling
 - d. How to achieve personal and sexual hygiene
 - e. How and what to eat
 - f. Supplements consumption
 - g. Safe delivery
 - h. Immediate Breast feeding
5. Maternal health including postnatal instructions on
 - a. Vaginal and breast hygiene
 - b. Copping with pain and discomfort on perineum
 - c. Intercourse
 - d. Contraception and birth spacing
6. Neonatal care including instructions on
 - a. Umbilical hygiene
 - b. Sleep position
 - c. Avoiding eye-make up
 - d. Preventing trauma
 - e. Exclusive breast feeding
 - f. How to carry the baby

Statistics

Data are presented as mean (SD) and frequencies (%) for continuous and categorically distributed variables, respectively. To release the assumption of normality, we used Mann-Whitney U test to examine if the differences in the median of each dimension knowledge, attitude, or practice were statistically significant. We developed a series of general linear models for implementing analysis of covariance to examine if the implementation of the Integrated Maternal Health Care Program has a linear effect on the value of the knowledge, attitude, or behavior. We estimated marginal mean differences between knowledge, attitude and behavior of intervention and control group, after taking into account the potential confounding effects of age, income, education levels, and urbanization. We also hypothesized that living place (urban vs. rural) might have modified the effects of the implementation of the Integrated Maternal Health Care Program on knowledge, attitude, or practice of the participant. As such, we developed an interaction term for residence $\times$ intervention and introduced it into the multivariate models. The significance of interactions was examined by likelihood ratio test which compares two nested models, one with and the other without the interaction term of interest.

We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during

this research. Informed written consent was obtained from all participants and the research deputy of the ministry of health approved the design of this study. We set the statistical significance level at a two-tailed type I error of 0.05. All statistical analyses were performed using STATA version 12 (STATA, College Station, Texas USA).

Results

Mean age of the participants was 25.2 (4.6) years. The majority of participants (94%) were living in urban areas at the time of the investigation. Baseline characteristics of the participants are presented in table 1.

Table 1. The distribution of demographic characteristics across control and intervention group

	Control	Intervention
Characteristics	N (%)	N (%)
Education		
Illiterate	87 (58.4)	62 (41.6)
Less than diploma	121 (46.0)	142 (54.0)
Diploma	166 (46.5)	191 (53.5)
Academic	26 (53.1)	23 (46.9)
Residence		
Urban	51 (12.7)	351 (87.3)
Rural	6 (1.4)	416 (98.6)
salary		
< 1000 dollars	97 (53.6)	84 (46.4)
1000- 1500 dollars	224 (47.4)	249 (52.6)
>1500 dollars	76 (47.8)	83 (52.2)

Table 2 compared knowledge scores of the cases with controls. Cases generally scored above than controls. Knowledge of the both groups about drugs, alcohol, and smoking during pregnancy, safe delivery, and contraception after delivery were alike.

As shown in Table 3, the attitude of the cases was generally different from controls. Few exceptions observed were about effect of breast feeding on breast size and shape and postpartum care where controls presumed more positive attitude and safe delivery where participants in the intervention group presumed more positive attitude.

Practically cases and controls remained generally alike (Table 4). Intervention group achieved higher score for some behaviors including using supplements after delivery, postpartum visits, and neonatal care.

When we considered the potential confounding effects of age, income, education levels, and urbanization, mean score for knowledge of intervention group was 7.4 percent point higher than knowledge of control group (P value <0.001), mean score for attitude of intervention group was 1.9 percent point lower than those of control group (P value=0.041), and mean score for practice of intervention groups was 6.1 percent point higher than, that of control group (P value<0.001).

An effect of intervention measures of the attitudes of participants was significantly modified by their residence. That is in rural areas control group presumed more positive attitude than intervention group (P for interaction <0.001).

Table 2. Differences in the knowledge of control and intervention group

	Control	Intervention	P value
High risk pregnancy	62.2 (23.4)	71.8 (25.5)	<0.001
Symptoms of concern during pregnancy	73.9 (27.0)	84.4 (23.2)	<0.001
Sexual hygiene	66.7 (20.5)	72.4 (19.8)	<0.001
Mouth and teeth hygiene	62.3 (22.6)	67.7 (26.3)	0.002
Using drugs, alcohol, and smoking	87.8 (22.3)	89.9 (22.3)	0.163
Prevalent complaints among pregnancy	66.0 (21.7)	73.6 (22.6)	<0.001
Using supplements during pregnancy	74.5(11.0)	77.5 (13.4)	0.001
Safe delivery	86.3 (23.6)	86.3 (22.4)	0.604
After delivery care	76.9 (21.5)	78.5 (20.3)	0.275
Symptoms of concern after delivery	72.4 (28.5)	83.0 (26.0)	<0.001
Using supplements after pregnancy	58 (29.9)	73.6 (29.0)	<0.001
Contraception after delivery	73.4 (43.9)	76.0 (42.0)	0.370
Neonatal care	71.2 (21.9)	85.3 (19.25)	<0.001
Breast feeding	77.3 (17.8)	83.0 (18.5)	<0.001

Table 3. Difference in the attitude of cases vs. controls

	Control	Intervention	P value
Mouth and teeth health	19.1 (24.1)	18.5 (24.1)	0.722
Supplement consumption during pregnancy	43.6 (26.2)	42.4 (24.3)	0.483
Fast foods	51.6 (31.2)	54.6 (28.7)	0.095
Care of umbilical cord	70.7 (27.1)	71.7 (25.4)	0.154
Importance of colostrum	77.9 (31.5)	81.6 (27.0)	0.605
Exclusive breast feeding	92.2 (14.5)	87.1 (21.4)	0.070
Effects of breasts size of breast-feeding	78.1 (25.8)	75.5 (25.3)	<0.001
Effects breast-feeding on shape of breasts	56.9 (34.2)	63.1 (30.5)	0.144
Safe delivery	69.4 (33.8)	73.0 (28.3)	0.007
Puerperal care	85.4 (24.8)	68.2 (32.6)	<0.001

For attitude participants were asked to complete phrases on a 5-point response scale in which 0 represents the absence of the theoretical construct and 4 represents the theorized maximum amount of the construct being measured. Scores of each dimensions of attitude were then multiplied by 5/100. Our method can be visualized by imagining an elastic rule with five equidistant numerals is stretched evenly to fit alongside a longer ruler with 100 numerals or one with 100 numerals compressed to fit alongside a ruler with five [5]. As such, we were able to quantify attitude on similar scale as knowledge and practice. Furthermore, results from other studies on an n-point scale could be comparable if multiplied by n/100.

Table 4. Differences in the practice of control and intervention group

	Control	Intervention	P value
Exposure to smoking	88.0 (30.4)	86.7 (32.7)	0.775
Prevalent complaint in pregnancy	63.2 (14.8)	66.2 (17.3)	0.768
Using supplements	76.0 (29.7)	83.3 (28.0)	0.054
How often to be visited during pregnancy	89.0 (21.8)	87.8 (23.9)	0.658
Safe delivery	99.5 (7.0)	99.5 (6.9)	0.997
Using supplements after delivery	61.0 (32.6)	74.8 (30.0)	<0.001
Contraception after delivery	90.3 (12.8)	90.7 (14.4)	0.753
Visits after delivery	32.0 (24.0)	47.9 (21.7)	0.005
Neonatal care	24.7 (18.9)	33.9 (20.5)	0.004
Breast-feeding	89.3 (11.0)	89.0 (11.2)	0.574

Table 5. Effects* of the implementation of the Integrated Maternal Health Program on knowledge, attitude, or practice of the participants by residence

	Rural residence		Urban residence		P for interaction**
	Mean difference (%)	P value	Mean difference (%)	P value	
Knowledge	14.6 (3.9-25.3)	0.007	6.7 (4.8-8.5)	0.000	0.154
Attitude	-17.7 (-27.6- -7.7)	0.000	-1.2 (-3.0-0.6)	0.199	0.001
Practice	10.1 (2.5-17.6)	0.000	5.1 (3.8-6.4)	0.000	0.206

* We estimated marginal mean differences between knowledge, attitude and behavior of intervention and control group, after taking into account the potential confounding effects of age, income, education levels, and urbanization.

**We hypothesized that living place (urban vs. rural) might have modified the effects of the implementation of the Integrated Maternal Health Program on knowledge, attitude, or practice of the participants. As such, we developed an interaction term for residence×intervention and introduced it into the multivariate models. The significance of interactions was examined by likelihood ratio test which compares two nested models, one with and the other without the interaction term of interest.

Discussion

In this study we demonstrated the effectiveness of implementation of a nationwide integrated health care program. We observed that the Integrated Maternal Health Care program effectively

improved the knowledge and practice of the participant and that residence did not modified these associations. Opposite findings were observed for attitude; that is attitude of the control group was more positive towards maternal care than was the

attitude of the intervention group. The effect of interventions on the attitude was modified by residence with difference in scores for attitude being higher for residents living in rural areas as compared to those living in the urban areas.

Few studies have examined the effectiveness of the nationwide Integrated Maternal Health Care programs. It has been shown that such programs can effectively increase the knowledge of mothers. Whether increase in knowledge can be translated to improvement in behaviors, however, remained to be elucidated. In the current study we observed that the Integrated Maternal Health Care program effectively improved the behaviors of mothers.

Our finding of interest was that the Integrated Maternal Health Care program failed to improve the attitude of the participant mothers. It has been previously shown that attitude of people could not easily be changed (6). Motivational interviewing in the scientific setting have been demonstrated to be effective in changing attitude and behaviors (7, 8). The Integrated Maternal Health Care program has mostly been focused on delivering due information in due time to the mothers. The way the information is transferred could have possibly affected the efficacy of instructions. The Integrated Maternal Health Care program has mostly been focused on delivering due information in due time to the women before, during, and after their pregnancy (9). The way the information is transferred could have possibly affected the efficacy of instructions. The Integrated Maternal Health Care will best be promoted in the future by incorporating effective introductions and motivational interviewing methods. As such the program will become a real challenge to the policy makers who are expected to run the program on nation-wide scale (10). It is not easy to resolve major public health problem that do not require technological breakthroughs. In this case, the challenge is to put our knowledge to work. We need to challenge our policy-makers and program managers to refocus program content and to shift focus from development of new technologies towards development of viable organizational strategies that ensure a continuum of care and account for every birth and death (10).

“A deep, dark, continuous stream of mortality! How long is this sacrifice to go on?” William Farr, asked this question about maternal mortality in En-

gland in 1838; two century later, we still have not answered it (11-13). Nearly, all of these deaths take place in developing countries (14). In 1985, Rosenfield et al. asked “Where’s the M in MCH?(15).” In that paper, they asserted that the problem of pregnancy-related deaths among women in developing countries had been neglected by the medical, obstetric and public health communities. They pointed out that conventional maternal health programs focused primarily on the health of infants not on the health of women, and that consequently these programs would not improve maternal health. The Safe Motherhood Initiative was launched at an international conference in Nairobi in 1987 (16). A series of national and regional Safe Motherhood meetings, to raise awareness among policy makers, followed the conference. The obstetric community has also become more involved-at the 1998 meeting of the International Federation of Obstetrics and Gynecology, there was plenary sessions on maternal mortality in developing countries, and a program of collaboration between obstetrics societies in developed and developing countries was begun. Despite such advances, however, relatively few large programs focus directly on pregnancy-related deaths in developing countries, and maternal mortality has apparently not decreased (16). The causes of maternal deaths are well known and are remarkably similar in developed and developing countries (17-19). An important reason for the lack of progress in reducing maternal mortality has been shown to be the absence of a clear strategic focus in the Safe Motherhood Initiative (20). The Integrated Maternal Health Care Program was specifically aimed at meeting this need. We observed, however, that simply increasing knowledge of the mothers might have not been enough for modifying their behavior.

Limitations and strengths

The strength of the current study lies in examining a nationwide implementation of the Integrated Maternal Health program. The findings the study, however, should be interpreted in the context of its limitations. Few fraction of the participants were living in rural areas, the generalizability of our findings to people living in rural areas, therefore, might have been affected by this limitation. The program has been introduced by mass Medias. Control group, thus, might have been exposed to education in this

way. This limitations, however, is unlikely to affect difference we found to be significant. Since such misclassification tend to bias the estimates towards null. The limitation, however, could have possibly contributed to our findings regarding attitude.

Conclusion

We observed that the Integrated Maternal Health Care program effectively improved the knowledge and practice of the participant. Opposite findings were observed for attitude; that is attitude of the control group was more positive towards maternal care than was the attitude of the intervention group. The improvements observed were not substantial and there are many rooms for improving instruction methods.

Acknowledgement

The authors would like to express their gratitude to health care providers of the health facilities of Islamshahr and Ray. We are also grateful to participants for their patients and time.

References

1. Lynn PF, Wendy JG, Ellen B, et al. Practical lessons from global safe motherhood initiatives: time for a new focus on implementation. *The Lancet* 2007; 370(9595): 1383-91.
2. Herz B, Measham A, Bank W. *The safe motherhood initiative: Proposals for action: World Bank Washington DC* 1987.
3. Heidari G, Heidari R. Iran Millennium Development Goal's in a Glance. *Iranian Journal of Public Health* 2009; 38(Suppl 1).
4. Islam M. The safe motherhood initiative and beyond. *Bulletin of the World Health Organization* 2007; 85: 735-.
5. Preston CC. Comparing rating scales of different lengths: equivalence of scores from 5-point and 7-point scales 1.2.
6. Verma M, Chhatwal J, Varughese PV. Antenatal period: an educational opportunity. *Indian pediatrics* 1995; 32(2): 171-7.
7. Burke BL, Arkowitz H, Menchola M. The efficacy of motivational interviewing: A meta-analysis of controlled clinical trials. *Journal of consulting and clinical psychology* 2003; 71(5): 843.
8. Rubak S, Sandbæk A, Lauritzen T, et al. Motivational interviewing: a systematic review and meta-analysis. *The British journal of general practice* 2005; 55(513): 305.
9. Beigi M, Javanmardi Z, Khani B, et al. *The effect of using maternal care log book on pregnancy outcome in clients referred to private gynecologists and midwives offices* 2011.
10. Freedman L, Graham W, Brazier E, et al. Practical lessons from global safe motherhood initiatives: time for a new focus on implementation. *The Lancet* 2007; 370(9595): 1383-91.
11. Hill K, Thomas K, AbouZahr C, et al. Estimates of maternal mortality worldwide between 1990 and 2005: an assessment of available data. *The Lancet* 2007; 370(9595): 1311-9.
12. AbouZahr C, Wardlaw T. Maternal mortality at the end of a decade: signs of progress? *Bulletin of the World Health Organization* 2001; 79: 561-73.
13. Hill K, AbouZahr C, Wardlaw T. Estimates of maternal mortality for 1995. *Bulletin of the World Health Organization* 2001; 79: 182-93.
14. Zahr C, Wardlaw T, Hill K, et al. Maternal mortality in 2000: estimates developed by WHO, UNICEF and UNFPA: *World Health Organization* 2004.
15. Rosenfield A, Figdor E. Where is the M in MTCT? The broader issues in mother-to-child transmission of HIV. *American Journal of Public Health* 2001; 91(5): 703.
16. Rosenfield A. The history of the Safe Motherhood Initiative Introductory remarks. *International Journal of Gynecology and Obstetrics* 1997; 59: 7-9.
17. Berg C, Atrash H, Koonin L, et al. Pregnancy-related mortality in the United States, 1987-1990. *Obstetrics & Gynecology* 1996; 88(2): 161-7.
18. Deneux-Tharaux C, Berg C, Bouvier-Colle M, et al. Underreporting of pregnancy-related mortality in the United States and Europe. *Obstetrics & Gynecology* 2005; 106(4): 684.
19. Chang J, Elam-Evans L, Berg C, et al. Pregnancy-related mortality surveillance—United States, 1991–1999. *MMWR Surveill Summ* 2003; 52(2): 1-8.
20. Maine D, Rosenfield A. The Safe Motherhood Initiative: why has it stalled? *American Journal of Public Health* 1999; 89(4): 480.

Corresponding Author
Gohar Mohammadi,
School of Health,
Shahid Beheshti University of Medical Sciences,
Tehran,
Iran,
E-mail: go_mohamadi@yahoo.com

Clopidogrel resistance in patients with type 2 Diabetes Mellitus: A comparison between oral antidiabetic agents and insulin

Zuhal Ariturk¹, Habib Cil¹, Ercan Gunduz², Celal Yavuz³, Hasan Kaya¹, Faruk Ertas¹, Mustafa Oylumlu¹, Serdar Soydinc¹

¹ Dicle University, Medicine Faculty, Department of Cardiology, Turkey,

² Dicle University, Medicine Faculty, Department of Internal Medicine, Turkey,

³ Dicle University, Medicine Faculty, Department of Cardiovascular surgery, Turkey.

Abstract

Background: Clopidogrel resistance has been found in certain patient populations, including patients with acute coronary syndrome, ischemic stroke, patients undergoing percutaneous coronary intervention with a drug-eluting stent, diabetes mellitus, ischemic stroke and stent restenosis. The aim of this study was to assess clopidogrel resistance in diabetic patients taking oral antidiabetic drugs and insulin.

Methods and Results: Platelet aggregation was measured after clopidogrel treatment in 101 diabetic patients undergoing percutaneous coronary intervention. Two diabetic patient subpopulations were compared: patients who used insulin (group 1) and patients who used oral antidiabetic agents (group 2). Clopidogrel nonresponders and responders were defined by a relative inhibition of adenosine diphosphate (20 mol/L) induced platelet aggregation of < 10% and ≥30%, respectively. Among group 1 patients, 12.5% were clopidogrel nonresponders and Among group 2 patients, 9.4% were clopidogrel nonresponders. There were no statistical differences found between the two groups (P=0.618).

Conclusions: This study demonstrates that there was no significant difference in the clopidogrel resistance between type 2 diabetes mellitus patients taking insulin or oral antidiabetes medication. The clinical implications of this finding are unknown and need to be evaluated in large-scale clinical trials.

Key words: Clopidogrel, Diabetes Mellitus, Platelets

diabetic patients with acute myocardial infarction (AMI) remains high (2). Many factors, such as severe coronary artery disease, diabetic cardiomyopathy, autonomic imbalance, and decreased fibrinolytic function may contribute to morbidity and mortality (3). Data suggest that DM patients with high residual platelet reactivity despite clopidogrel therapy are at greater risk for thrombotic events after percutaneous coronary intervention (PCI) (4).

Patients with type 2 diabetes mellitus have enhanced platelet reactivity and reduced *in vitro* responsiveness to antiplatelet agents (5). The past decade has seen a surge of interest in identifying the biochemical etiology of antiplatelet resistance. The cause of such resistance is likely multifactorial; Clinical, cellular, and genetic (6.) Resistance to antiplatelet medication has mainly been studied in patients with coronary artery disease, but a few studies have explored this phenomenon in diabetes mellitus.

One of the normal physiological roles of insulin is to inhibit platelet function, and thus insulin may help prevent thrombus formation, the release of vasoactive mediators and chemotactic mitogenic substances, thus helping to reduce the incidence of thrombosis, hypertension and atherosclerosis (7). Furthermore, if platelets were able to develop insulin resistance, this could lead to an increased risk of cardiovascular problems. The aim of this study was to determine the incidence of clopidogrel resistance in patients with diabetes and to compare this incidence in patients using oral antidiabetic drugs (OAD) and insulin.

Introduction

Diabetes mellitus (DM) is a well known risk factor for the development of atherosclerotic coronary artery disease (CAD) (1). Mortality among

Methods

Patients and study protocols

The institutional review board approved the protocol, and a written informed consent was

obtained from each subject before enrollment. The study protocol was approved by the Ethics Committee of the Medical University of Dicle in accordance with the Declaration of Helsinki.

The medical record of each patient was reviewed, and demographic, laboratory, and platelet aggregation data were recorded.

We enrolled 101 consecutive DM patients who were admitted in order to undergo elective coronary artery intervention and who received an oral loading dose of 600 mg of clopidogrel which was recommended to be given 2 hours prior to catheterization followed by a daily dose of 75 mg. All patients were enrolled and studied prospectively between June 2010 and March 2011. Patients were stratified according to the presence of type 2 diabetes, which was defined according to World Health Organization criteria. Patients were on insulin or oral hypoglycemic medication, and were between the ages of 29 and 86 years. Group 1 was composed of 48 patients who used insulin. Group 2 was composed of 53 patients who used oral antidiabetic agents. Patients in both groups 1 and 2 underwent elective percutaneous coronary intervention performed according to the current standard guidelines and received clopidogrel in the doses described above. **Exclusion criteria:** diabetic subjects who controlled blood sugar levels through their diet, previous treatment with clopidogrel or aspirin, liver disease, gastrointestinal ulcer, pregnancy, a history of bleeding diathesis, patients with a cerebrovascular event within the last 3 months, major surgical procedure within one week prior to enrollment in the study, malignant paraproteinemias, platelet count $< 100,000 / \text{mm}^3$, hemoglobin $< 8 \text{ g/dl}$, or a history of heparin-induced thrombocytopenia and a prothrombin time > 1.5 times control. **Inclusion criteria:** All patients were on hypoglycemic treatment (oral antidiabetic agents or insulin) for at least 1 year, had symptomatic, stable coronary artery disease and had elected to have a coronary intervention. The 600-mg clopidogrel loading dose was recommended to be given at least 2 h before catheterization and the follow-up clopidogrel dose was 75 mg/day. The blood sample for the aggregation test was obtained from an antecubital vein, using a 21-gauge needle, 2-5 h after oral administration of the 600 mg tablet of clopidogrel which was swallowed

with some water. Blood samples were collected in tubes containing 3.2% citrate.

Platelet aggregation was measured by a Multiplate analyzer.

The clopidogrel-induced platelet inhibition is dose- and time-dependent. Maximal inhibition following a single dose of 600-mg clopidogrel is achieved after 2-5 h (R).

Platelet Aggregation

Platelet aggregation was determined using a multichannel Multiplate analyzer (MEA, Dynabyte) using arachidonic acid (ASPItest, 0.5 mM), collagen (COLtest, 3.2 $\mu\text{g/ml}$), ADP (ADPtest, 6.4 μM), and TRAP-6 (TRAPtest, 32 μM) as activators (4). ADP-induced platelet aggregation in whole blood was assessed using multiple electrode platelet aggregometry (MEA). MEA analyses platelet function in whole blood at 37°C by the attachment of platelets onto metal electrodes, leading to a change in the electrical conductivity (or impedance), which is continuously recorded. The Multiplate instrument helps improve impedance aggregometry measurements by using a computer-controlled 5-channel device and disposable test cells with a dual sensor unit allowing duplicate analyses with each test. Aggregation is recorded for 6 minutes. The instrument design allows testing of samples with any platelet agonist.

The results were expressed as arbitrary areas under the curve (AUC). The AUC can be considered to be the integral of platelet function, dependent on both the aggregation (maximal aggregation) and velocity (steepness of the curve).

Statistical analysis

In patients with DM, paired 2-sample t-tests and chi-square tests were used to compare platelet aggregation in patients taking oral antidiabetic agents and insulin. Statistical analysis was performed using the statistical software SPSS v15.0 (SPSS Inc; Chicago, IL, USA). All values were expressed as mean $\pm$ SD. $P < 0.05$ was considered statistically significant.

Results

Of the 101 patients enrolled, 53 (52.5%) were male and the mean age was 66 ± 7 years. Patient demographics are shown in Table 1. Patients within

the upper quartile of the ADP area under the curve (AUC) 0-400 normal range (the upper quartile scores ranged from 401-900) were considered to have drug resistance. The mean AUC found when using ADP and collagen was 179.9 ± 147.9 in patients who used insulin whereas it was 196.6 ± 185.1 in patients who used OAD. Patients who fell within the upper quartile of the ADP area under the curve (AUC) were categorized as clopidogrel non-responders and the mean AUC of the non-responders was 556 ± 10 for group 1 and 525 ± 10 for group 2. In patients who used insulin, 48 (12.5%) had clopidogrel resistance and in patients who used OAD, 53 (9.4%) had clopidogrel resistance (Table 2). However, no statistical difference was found between the groups ($P=0.618$) (Figure 1).

There were no significant differences in the baseline demographic and clinical characteristics. Additionally, there were no significant differences between clopidogrel resistance and blood parameters such as platelet counts, hematocrit, hemoglobin, mean platelet volume, sedimentation, C-reactive protein levels, urea, creatine, sodium, potassium, ALT, AST, blood glucose, albumin, lipid

parameters and thyroid hormones. Similarly, there were no significant differences in the medications given to the patients during hospitalization.

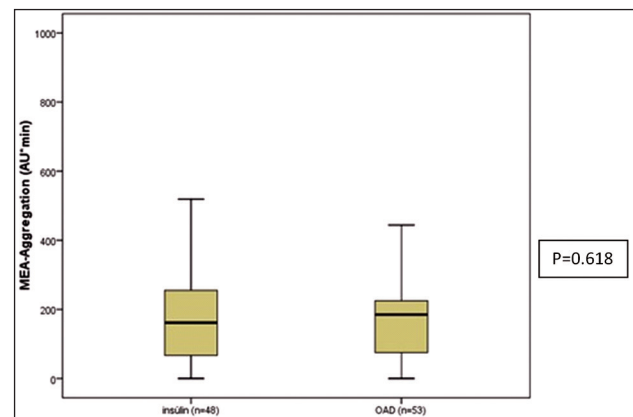


Figure 1.

Discussion

Diabetes is commonly associated with accelerated atherosclerosis, which can cause premature coronary artery disease, increased risk of cerebrovascular disease, and severe peripheral vascular disease (1). Platelet dysfunction contributes to the

Table 1. Patient characteristics at time of randomization

Parameters	Group 1 (n=48)	Group 2 (n=53)	P
Age, years	65±8	66±7	0.65
Sex, n (%)			
Male	24 (50%)	27 (50.9%)	0.84
Female	24 (50%)	26 (49.1%)	0.12
Body mass index (kg/m ²)	27±4	27±4	0.63
Hypertension	33(69.5%)	37(70%)	0.09
LVEF (%)			
35% ≤	8 (16.7%)	11 (20%)	0.07
35% ≥	40 (83.3%)	42 (80%)	0.62
Smoker	23 (49.1%)	25 (49.2%)	0.083
DM duration, years	8.51±6.43	8.42±7.52	0.54
HbA1c (%)	6.7± 6 2.5	7.46±2.6	0.08
High-density lipoprotein, mg/dl	39.2 ± 16.3	41.7± 15.3	0.56
Low-density lipoprotein, mg/dL	125.9 ± 35.7	133.4 ± 23.6	0.66
Triglycerides, mg/dl	165.7 ± 65.5	186.9 ± 86.5	0.09

LVEF; Left ventricular ejection fraction

Table 2.

Clopidogrel	Group 1	MeanAUC Induced by ADP	Group 2	MeanAUC- induced by ADP
Responder	42 (87.5%)	179.9±147.9	48 (90.6%)	196.6±185.1
Nonresponder	6 (12.5%)	556±10	5 (9.4%)	525±10.
Total	48(100.0%)		53 (100.0%)	

increased risk of atherothrombotic complications in the diabetic population (2). Evidence for altered platelet function is supported by a hypersensitivity to aggregants observed in *in vitro* studies (8). Although clopidogrel is an effective anti-thrombotic drug, to the best of our knowledge, this is the first study to report its antiplatelet effect in diabetic patients and to demonstrate an association between clopidogrel resistance and the use of hypoglycemic drugs.

Importantly, reduced sensitivity or “poor response” to clopidogrel has been associated with an increased risk of ischemic events (9). In the present study, ADP-induced platelet aggregation was studied following clopidogrel administration in diabetic patients undergoing elective PCI. It was found that of the patients using insulin, 48 (12.5%) were clopidogrel resistant and in patients using OAD, 53 (9.4%) were clopidogrel resistant. However this difference was not statistically significant. Additionally, there were no significant associations between clopidogrel resistance and blood parameters.

Several mechanisms of clopidogrel resistance are possible. Extrinsic mechanisms include inappropriate dosing or underdosing of clopidogrel and drug interactions, including a possible interaction between clopidogrel and atorvastatin (10).

There is a positive correlation between clopidogrel response and CYP3A4 activity (measured using an erythromycin breath test), suggesting that one important explanation for resistance may be variable conversion to the active metabolite. Other potential extrinsic mechanisms could include variable absorption of the prodrug or clearance of the active metabolite. Intrinsic mechanisms could include P2Y₁₂ receptor variability, an increase in the number of receptors, an increased release of ADP or upregulation of other platelet activation pathways.

Lau *et al.* reported that platelet inhibition following clopidogrel administration displays inter-individual variability, which correlates with CYP3A4 metabolic activity (11). Measurement of antiplatelet drug efficacy with a point-of-care device and alternative antithrombotic strategies for clopidogrel non-responders and low responders could reduce the incidence of thrombotic events that continue to occur despite oral antiplatelet therapy.

In a study by Gurbel *et al.*, 96 patients who were undergoing elective coronary stenting were monitored before and at multiple time points after

standard clopidogrel therapy (300-mg loading dose followed by 75 mg daily). Clopidogrel resistance, empirically defined as <10% reduction in aggregation following the administration of 5 μ mol/L ADP compared with pretreatment values, was seen in 63% of patients at 2 hours, 31% at 24 hours, 31% at 5 days, and 15% at 30 days. The patients with the highest pretreatment values had the least antithrombotic protection over the first 5 days (12). In another report by Muller *et al.*, non-responders were defined as patients with <10% reduction in platelet aggregation to ADP and semi-responders as those with 10% to 29% reduction 4 hours after a 600-mg clopidogrel loading dose, and no additional effect was seen with this treatment regimen at 24 hours. This study found that 5% were nonresponders and 9% were semiresponders when 5 μ mol/L ADP was used as a platelet aggregation agonist, and that when 20 μ mol/L ADP was used, 11% were nonresponders and 26% were semiresponders (13).

Platelets from individuals with type 2 diabetes mellitus have been shown to have a reduced response to clopidogrel (14).

The body mass index of the patient may be another contributing factor to the variability in platelet response to clopidogrel. Overweight patients (body mass index > 25 kg/m²), due in part to their higher incidence of insulin resistance, demonstrated a reduced antiplatelet effect with clopidogrel (15). The term *resistance* encompasses patients for whom clopidogrel does not achieve its pharmacological effect and *failure of therapy* reflects patients who have recurrent events while on therapy.

In the present study, 48 patients (12.5%) who were using insulin had clopidogrel resistance compared to 53 patients (9.4%) who were using OAD. In a previous report, the incidence of clopidogrel nonresponders was 10% and the incidence of low responders was 20%. This finding is in accordance with the studies by Gum *et al.* (16) and Chen *et al.* (17) The prevalence of clopidogrel non-response in patients is estimated to be between 4% and 30% 24 h after administration (6,13,18,19). The reported rates vary between studies because of the technique used to measure the extent of platelet aggregation and the presence of factors contributing to greater baseline platelet reactivity. Furthermore, the definition of non-responders is not standardized. Matetzky and colleagues add a

new and important piece to the emerging clopidogrel resistance picture: correlation of laboratory measurements of clopidogrel nonresponse with clinical outcomes. Patients who underwent primary PCI (n=60) with stenting and patients who underwent primary angioplasty for STEMI (n=10) received 300 mg aspirin on admission and eptifibatide and heparin during PCI. Those who received stents were treated with clopidogrel (300 mg immediately after PCI and 75 mg daily for 3 months). Platelet function tests were performed with turbidometric analysis after stimulation with ADP (5 μ mol/L) and epinephrine (10 mol/L) (19). Muller *et al* used ADP to stimulate platelet aggregation and defined non-responders as those with a 10% reduction in platelet aggregation and semi-responders as those with 10% to 29% reduction 4 hours after the 600 mg clopidogrel loading dose (20). Lepantalo *et al.* reported that a low response to clopidogrel was associated with high levels of glycosylated hemoglobin and C-peptide (21). The question of whether increased doses of clopidogrel might overcome this resistance in non-responsive patients warrants further investigation.

The GRAVITAS trial had a third observational arm. In this study, 5429 patients underwent platelet-function testing following a regular clopidogrel dose after PCI and were divided into those with high residual platelet reactivity and those without high residual activity. All patients were then continued on daily 75-mg clopidogrel and followed for six months. There was no benefit seen with regards to cardiovascular outcomes or stent thrombosis when patients with drug-eluting stents with high residual platelet activity following a regular clopidogrel dose were given a double dose of clopidogrel in the GRAVITAS trial (22).

Future investigations are needed to determine whether these patients are aspirin resistant, clopidogrel resistant, or both. Additionally, the possibility that drug interactions between clopidogrel and OAD contribute to these events needs to be evaluated. Consistent definitions for clopidogrel resistance are needed that can be created using reliable laboratory testing and associated with increased risk for thrombotic complications. In the future, measurement of antiplatelet drug efficacy with a point-of-care device and alternative antithrombotic strategies for poor responders could re-

duce the resistance incidence. The current available data show that between 4% to 30% of patients treated with the conventional dose of clopidogrel do not display an adequate antiplatelet response (6,13,18,19,23).

Study limitations

There are some inherent limitations in our study. First of all, the present study is observational and has a relatively small sample size, thus definitive conclusions cannot be made. The finding should be confirmed in a larger-scale study.

These measurements in the study reflect the extent of platelet inhibition 2-5 hours after PCI and one measure of platelet function may not be sufficient to diagnose clopidogrel resistance when optimal inhibition is required. It can be argued that platelet aggregation measurements are instrument-dependent and laboratory-dependent. Platelet function is measured *in vitro* in most instances by light transmission aggregometry and this method is still considered the gold standard. MEA is not the gold standard test, although it is a reliable test. Our definition of clopidogrel resistance is arbitrary because there have been no extensive reports or consistent standards in the past literature.

Conclusion

In conclusion, this study demonstrates that there was no significant difference in the clopidogrel resistance between type 2 diabetes mellitus patients who were taking insulin or OAD. Clopidogrel resistance is a term widely used but not clearly defined. Usually it is used to reflect failure of clopidogrel to achieve a platelet inhibition effect. Large clinical trials relating clinical efficacy to biological effects are needed in the future.

References

1. Kannel WB, McGee DL. Diabetes and cardiovascular disease. The Framingham study. *JAMA*. 1979; 241: 2035–8.
2. Stamler J, Vaccaro O, Neaton JD, et al. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care*. 1993; 16: 434–44.
3. Detre KM, Guo MP, Holubkov R, et al. Influence of diabetes on 5-year mortality and morbidity in a randomized trial comparing CABG and PTCA in patients with multivessel disease: the Bypass Angioplasty Revascularization Investigation (BARI). *Circulation*. 1997; 96: 1761–9.
4. Elezi S, Kastrati A, Pache J, et al. Diabetes Mellitus and the Clinical and Angiographic Outcome After Coronary Stent Placement. *JACC*. 1998; 32: 1866–73.
5. Prasad A, Stone GW, Stuckey TD, et al. Impact of Diabetes Mellitus on Myocardial Perfusion After Primary Angioplasty in Patients With Acute Myocardial Infarction. *JACC*. 2005; 45: 508–511.
6. Angiolillo DJ, Ortiz AF, Bernardo E, et al. Platelet Function Profiles in Patients With Type 2 Diabetes and Coronary Artery Disease on Combined Aspirin and Clopidogrel Treatment. *Diabetes*. 2005; 54: 2430–2435.
7. M.Trovati, G.Anfossi. Insulin, insulin resistance and platelet function: similarities with insulin effects on cultured vascular smooth muscle cells. *Diabetologia*. 1998; 41: 609–622.
8. Glauser J, Emerman CL, Bhatt DL, et al. Platelet aspirin resistance in ED patients with suspected acute coronary syndrome. *American Journal of Emergency Medicine*. 2010; 28: 440–444.
9. Bonvini RF, Reny JL, Mach F, et al. Acute Coronary Syndrome and its Antithrombotic Treatment: Focus on Aspirin and Clopidogrel Resistance. *Current Vascular Pharmacology*. 2009; 7:198–208.
10. Lau WC, Waskell LA, Watkins PB, et al. Atorvastatin reduces the ability of clopidogrel to inhibit platelet aggregation: a new drug-drug interaction. *Circulation*. 2003; 107: 32–7.
11. Lau WC, Waskell LA, Watkins PB, et al. Atorvastatin Reduces the Ability of Clopidogrel to Inhibit Platelet Aggregation A New Drug–Drug Interaction. *Circulation*. 2003; 107: 32–37.
12. Gurbel PA, Bliden KP, Hiatt BL, et al. Clopidogrel for Coronary Stenting Response Variability, Drug Resistance, and the Effect of Pretreatment Platelet Reactivity. *Circulation*. 2003; 107: 2908–2913.
13. Muller I, Besta F, Schulz C, et al. Effects of statins on platelet inhibition by a high loading dose of clopidogrel. *Circulation*. 2003; 108: 2195–7.
14. Angiolillo DJ, Ortiz AF, Bernardo E, et al. Clopidogrel Withdrawal Is Associated With Proinflammatory and Prothrombotic Effects in Patients With Diabetes and Coronary Artery Disease. *Diabetes* 2006; 55: 780–784.
15. Tamminen M, Lassila R, Westerbacka J, et al. Obesity is associated with impaired platelet-inhibitory effect of acetylsalicylic acid in nondiabetic subjects. *International Journal of Obesity*. 2003; 27: 907–911.
16. Gum PA, Marchant KK, Welsh PA, et al. A Prospective, Blinded Determination of the Natural History of Aspirin Resistance Among Stable Patients With Cardiovascular Disease. *JACC*. 2003; 41: 961–5.
17. Chen WH, Lee PY, Ng W, et al. Aspirin Resistance Is Associated With a High Incidence of Myonecrosis After Non-Urgent Percutaneous Coronary Intervention Despite Clopidogrel Pretreatment. *JACC*. 2004; 43: 1122–6.
18. Wiviott SD, Antman EM. Clopidogrel Resistance. *Circulation* 2004; 109: 3064–3067.
19. Matetzky S, Shenkman B, Guetta V, et al. Clopidogrel resistance is associated with increased risk of recurrent atherothrombotic events in patients with acute myocardial infarction. *Circulation*. 2004; 109: 3171–3175.
20. Muller I, Besta F, Schulz C, et al. Prevalence of clopidogrel nonresponders among patients with stable angina pectoris scheduled for elective coronary stent placement. *Thromb Haemost*. 2003; 89: 783–787.
21. Lepantalo A, Virtanen KS, Heikkila J, et al. Limited early antiplatelet effect of 300 mg clopidogrel in patients with aspirin therapy undergoing percutaneous coronary interventions. *Eur Heart J*. 2004; 25: 476–83.
22. Price MJ, Berger PB, Angiolillo DJ, et al. Evaluation of individualized clopidogrel therapy after drug-eluting stent implantation in patients with high residual platelet reactivity: design and rationale of the GRAVITAS trial. *Am Heart J*. 2009; 157: 818–24.
23. Wiviott SD, Antman EM. Clopidogrel Resistance. *Circulation*. 2004; 109: 3064–3067.

Corresponding Author
Zuhal Ariturk,
Dicle University,
Medicine Faculty,
Department of Cardiology,
Diyarbakir,
Turkey,
E-mail: zariturk@yahoo.com

Circulating levels of Homocysteine, Zinc, Iron and Copper in pregnant women with pre-eclampsia

Zoleikha Atarod¹, Hamed Roohanizadeh², Marzieh Saberi¹, Seyyed Abbas Hashemi³, Mehran Fazli³

¹ Departments of Obstetrics and Gynecology, Mazandaran university of medical sciences, Sari, Iran,

² Department of Pediatrics, Mazandaran University of medical sciences, Sari, Iran,

³ Faculty of medicine, Student research committee, Mazandaran University of medical sciences, Sari, Iran.

Abstract

Backgrounds: Hypertensive diseases like pre-eclampsia during pregnancy are one of the main causes of maternal death worldwide.

Objective: To evaluate the serum levels of zinc, iron, copper and homocystein in preeclamptic women and compare them to healthy matched pregnant women to reveal the role of these factors in progression and severity of preeclampsia.

Methods and Material: A case-control study, performed by a single center, included 30 pregnant women with mild preeclampsia, 10 pregnant women with severe pre-eclampsia and 40 healthy pregnant women. Serum levels of zinc, iron and copper were evaluated by spectrophotometry and serum homocysteine was examined by HPLC (high performance liquid chromatography). For statistical analysis, SPSS software was used applying t test and ANOVA. ROC curve was used to examine the homocysteine cut off point. $P < 0.05$ was defined as significant.

Results: Serum levels of zinc, iron, copper and homocysteine were significantly higher in patients' suffered from mild and severe preeclampsia in comparison with healthy matched pregnant women. Based on ROC curve, the cut off point for serum homocystein level was 7.08 with sensitivity of 94% and specificity of 88%.

Conclusion: Maternal serum homocysteine, zinc, iron and copper levels were found to be significantly higher in patients with preeclampsia compared to control group. This evidence showed that elevated serum levels of homocysteine, zinc, iron and copper could be correlated with progression of preeclampsia.

Key Words: Preeclampsia, Zinc, Iron, Copper, Homocystein

Introduction

Hypertensive disorders during pregnancy remain a leading reason of maternal death globally (1,2,3). The definition of Preeclampsia is hypertension complicated with proteinuria (4), which is a multiorgan disorder imposes the liver, kidneys, brain and blood clotting system. Severe pre-eclampsia causes life threatening disorders including eclampsia (fitting) and the HELLP syndrome (haemolysis, elevated liver enzymes and low platelets). Preeclampsia causes different disorders in baby. Preeclampsia is noted in 12% of subjects of intrauterine growth restriction (5). Small babies are predisposed to health disorders like poor growth in childhood (6) and elevated risk of hypertension and diabetes in adulthood (7).

Antioxidants serve proteins and enzymes from oxidation and destruction by free radicals. Antioxidants can be divided as either free radical scavengers which trap existing free radicals, or cellular and extracellular enzymes that prevent peroxidase reactions included in the manufacture of free radicals (8,9).

Activation of antioxidant enzymes depends on the co-factors like selenium, zinc and iron. A woman's risk of, and responses to, oxidative stress rely on different factors. These involve the propensity for small dense low density lipoproteins, hyperhomocysteinaemia, and a genetically defined poor resistance to oxidative stress, and a lack of dietary antioxidants (10). Deficiencies of antioxidant activities cause poor pregnancy outcomes, including fetal growth restriction and preeclampsia (11, 12).

Therefore in this trial, we examined the serum level of zinc, iron, copper and homocystein in preeclamptic women and compared them with healthy matched pregnant women to elucidate the role of these factors in progression and severity of preeclampsia.

Methods and material

The ethics committee of Mazandaran University of medical sciences approved this study. The study population included 40 patients with preeclampsia (30 patients with mild preeclampsia and 10 subjects with severe preeclampsia) and 40 healthy matched pregnant women. All subjects provided written informed consent to participate in the study. This sample size was considered suitable for measurement of serum level of zinc, iron, copper and homocystein and to supply statistical power appropriate for exploratory statistical data analysis.

Inclusion and exclusion criteria

Our inclusion criteria (for cases) included gestational age more than 20 weeks, blood pressure > 140/90 mmHg and urine protein level of 24 hr more than 300 mg or urine analysis of 1+. Our exclusion criteria involved chronic hypertension, diabetes, dislipidemia, renal and cardiac disorders and minus history of folic acid after 12 weeks of pregnancy.

Case matching

40 pregnant women with gestational age more than 20 weeks without history of hypertension and matched body mass index (BMI), age and parity served as control group.

Sampling

Heparinized tubes were used for zinc, iron, and copper and for homocysteine, tubes with EDTA were applied. Serum homocysteine was measured by HPLC (high performance liquid chromatography, ClinRep, HPLC, Germany). Serum zinc, iron, and copper were evaluated by spectrophotometry.

Statistical analysis

Data were presented as Mean $\pm$ SD. For statistical analysis, SPSS software (Version 16, Chicago, IL, USA) was used applying t test and ANOVA. ROC curve was used to examine the homocysteine cut off point. $P < 0.05$ was defined as significant.

Results

Demographic data of the study population are summarized in table 1. There were no significant changes in age, BMI, parity and gestational age between two groups (table 1).

Table 1. Demographic features of study population

Objective	Case	Control	P value
Age	27.8 $\pm$ 4.9	27.9 $\pm$ 5	not significant
BMI	25.9 $\pm$ 1.5	25.9 $\pm$ 1.3	not significant
Parity	1.2 $\pm$ 0.7	1.1 $\pm$ 0.5	not significant
Gestational age	33.6 $\pm$ 2.57	33.6 $\pm$ 2.57	not significant

Mean $\pm$ SD of serum homocystein level in patients with severe preeclampsia was 11.8 $\pm$ 2.6, in patients with mild preeclampsia was 8.9 $\pm$ 4.7 and in control group was 5.5 $\pm$ 1.3. There was statistically significant alteration among these groups (table 2). According to ROC curve, the cut off point for serum homocystein level was 7.08 with sensitivity of 94% and specificity of 88%.

Mean $\pm$ SD of serum iron level in patients with severe preeclampsia was 105 $\pm$ 4.5, in patients with mild preeclampsia became 87.3 $\pm$ 12 and showed significant changes in comparison with control group (table 2). In this regard, there were significant changes in serum levels of copper and zinc versus control group (table 2).

Discussion

This study was conducted to evaluate the serum levels of zinc, iron, copper and homocystein in patients suffered from pre-eclampsia to examine the role of these agents and antioxidant system in progression of pre-eclampsia in such patients. Our study revealed that the serum level of zinc, iron, copper and homocystein were significantly

Table 2. Serum levels of Homocystein, Iron, Copper and Zinc in this series

Objective	Severe Preeclampsia n; 10	Mild Preeclampsia n; 30	Control N; 40	P value
Homocystein	11.8 $\pm$ 2.6	8.9 $\pm$ 4.7	5.5 $\pm$ 1.3	$P < 0.05$
Iron	105 $\pm$ 4.5	87.3 $\pm$ 12	78.3 $\pm$ 10.9	$P < 0.05$
Copper	150 $\pm$ 5.5	126.4 $\pm$ 7.8	95.1 $\pm$ 8.6	$P < 0.05$
Zinc	118 $\pm$ 2.6	102 $\pm$ 8.2	90.8 $\pm$ 10.2	$P < 0.05$

higher in subjects with pre-eclampsia in comparison with healthy control group.

There are different reports about the level of homocystein in preeclampsia. In this relation, Middel-drop et al (13) noted that the serum level of homocystein was not predisposal factor for pre-eclampsia but in consistent with their study, Makedosl et al (14) reported higher amount of homocystein in pre-eclamptic patients. In their investigation the mean level of homocystein in patients was 11.11 $\mu\text{mol/l}$ versus 6.4 $\mu\text{mol/l}$ in control group ($p < 0.001$). But both of these studies did not consider the effect of severity of preeclampsia on homocystein level.

Khosrowbeygi A et al (15) and Acilmis YG et al (16) reported that maternal serum levels of homocysteine were found to be significantly higher in pre-eclamptic women than in normal pregnant women. They showed hyperhomocysteinemia was associated with severity of pre-eclampsia. In the current research we revealed higher level of homocystein closely connected with the severity of preeclampsia. The level of homocystein almost was twice more than control group (9.7 against 5.5 $\mu\text{mol/l}$). This was the first study which evaluated a cut off for serum level of homocystein. The cut off for this study was 7.08 with sensitivity of 94% and specificity of 88%.

Sedar et al (17) examined the serum level of copper and iron in mild and severe preeclampsia and indicated an increase in the serum level of these substances. In this regard, the current research provided the same evidences to support this idea. Bashher et al (18) evaluated the serum iron level in pre-eclamptic patients and control group. Likewise with our study, they revealed higher amount of serum iron in pre-eclamptic patients.

Conclusion

Considerable hyperhomocysteinaemia in pre-eclamptic patients showed endothelial cell damage could be result of activation of oxidant pathway and by reducing the serum level of oxidants we can decrease the severity of disease. Further investigations are required to accurately quantify levels of micronutrients in pregnant women and how these levels differ over the course of pregnancy.

Acknowledgments

This research was supported by a grant of the Mazandaran University of Medical Sciences, Sari, Iran.

References

1. HMSO. *Report on confidential enquiries into maternal deaths in the United Kingdom 1994-1996*. London: HMSO, 1998.
2. NHMRC. *Report on Maternal Deaths in Australia 1991-1993*. NHMRC, 1998.
3. Aghamohammadi A. *Maternal obesity and preeclampsia*. *healthmed journal* 2011; 5(6): 1484-87
4. Gifford RWJr, August PA, Cunningham G, Green LA, Lindhemier MD, McNellis D, et al. *Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy*. *American Journal of Obstetrics and Gynecology* 2000; 183: 1-22.
5. Kramer MS, Seguin L, Lydon J, Goulet L. *Socio-economic disparities in pregnancy outcome: why do the poor fare so poorly?*. *Paediatric and Perinatal Epidemiology* 2000; 14: 194-210.
6. McCowan L, Harding J, Barker S, Ford C. *Perinatal predictors of growth at six months in small for gestational age babies*. *Early Human Development* 1999; 56(2-3): 205-16.
7. Barker DJP, Gluckman PD, Godfrey KM, Harding JE, Owens JA, Robinson JS. *Fetal nutrition and cardiovascular disease in adult life*. *Lancet* 1993; 341: 938-41.
8. Diplock AT, Charleux, JL, Crozier-Wili G, Kok FJ, Rice-Evans C, Roberfroid M, et al. *Functional food science and defence against reactive oxidative species*. *British Journal of Nutrition* 1998; 80: 77- 112.
9. Ozcetin M, Katar M, Yilmaz R, Karaaslan E, Ozugurlu F. *Free Oxygen Radicals Associated with Growth in Coeliac Disease*. *Healthmed journal* 2011; 5(5): 1008-14
10. Roberts JM, Cooper DW. *Pathogenesis and genetics of pre-eclampsia*. *Lancet* 2001; 357: 53-56.
11. Fall CH, Yajnik CS, Rao S, Davies AA, Brown N, Farrant HJ. *Micronutrients and fetal growth*. *Journal of Nutrition*. 2003; 133(5, supplement 2): 1747S-1756.
12. Rumbold A, Duley L, Crowther CA, Haslam RR. *Antioxidants for preventing pre-eclampsia*. *Cochrane Database of Systematic Reviews*. 2008; (1) Article ID CD004227.

13. Middeldorp S, van de Poel MH, Bank I, Hamulyák K, Libourel EJ, Koopman MM, et al. Unselected women with elevated levels of factor VIII: C or homocysteine are not at increased risk for obstetric complications. *Thromb Haemost.* 2004 Oct; 92(4): 787-790.
14. Makedosl G, Papanicolaoul A, Hitoglou A, Kalo-
giannidlis I, Makedosl A, Vazioti V, et al. *Journal of
archive of gynecology and obstetrics*; 2006, 95(3);
125-134
15. Khosrowbeygi A, Ahmadvand H. Circulating levels
of homocysteine in preeclamptic women. *Banglade-
sh Med Res Counc Bull.* 2011; 37(3): 106-9.
16. Acilmis YG, Dikensoy E, Kutlar AI, Balat O, Cebe-
soy FB, Ozturk E, et al. Homocysteine, folic acid and
vitamin B12 levels in maternal and umbilical cord
plasma and homocysteine levels in placenta in pre-
gnant women with pre-eclampsia. *J Obstet Gynae-
col Res.* 2011; 37(1): 45-50.
17. Sedar Z, Gur E, Develioglu O. Serum iron and copper
status and oxidative stress in severe and mild preec-
lampsia. *Call biochem funct*; 2006, 24(3), 209-215
18. Bashher K, Dab K. alteration in iron status in preec-
lampsia. *Mymensigh Med*; 2006, 15(1); 22-24

Corresponding Author

Seyyed Abbas Hashemi,

Faculty of medicine,

Student research committee,

Mazandaran University of medical sciences,

Sari,

Iran,

E-mail: abbas.hashemi30@gmail.com

Risk of depression and anxiety in high school students and factors affecting it

Zehra Tezvaran¹, Hulya Akan², Oguzhan Zahmacioglu³

¹ Family Medicine Department, Maltepe University Faculty of Medicine, Turkey,

² Family Medicine Department, Yeditepe University faculty of medicine, Turkey,

³ Child Psychiatry Department, Yeditepe University Faculty of medicine, Turkey.

Abstract

Objective: The risk of depression and anxiety in adolescent age group, the identification and investigation of factors affecting

Methods: All high school students as a sample taken from the borough of Korkut. 12-item sociodemographic questionnaire administered to students prepared by the researchers. Hospital Anxiety and Depression Scale (HADS) was applied to students to determine the risk of depression and anxiety in students.

Results: Research was made 338 students. The students' ages ranged from 13 to 19. Cases with HADS Anxiety scores ranged between 0 and 2.71 average 1.26 ± 0.50 cent. 39.1% of the students' anxiety risk is the observed. Cases with HADS depression scores ranged between 0 and 2.57 average 0.95 ± 0.44 'roll. 48.8% of students' risk of depression is observed. Girl students' average anxiety scores were significantly higher than male students. Male students' average depression scores were significantly higher than female students. Family relations affect the risk of anxiety and depression.

Conclusion: Based on the results of this study, adolescents characteristics of this period by mental health professionals providing information and sources of information about changes in adolescents teaching should be recommended

Key words: Depression, anxiety, adolescents health

Introduction

The adolescent period is a transition period in which the person has physical, psychological and social changes during the development and growing process going to adulthood from the childhood. In this period, as there are developmental conflicts, there can be difficulties in the separation

of the normal and pathology. According to many researchers, the extension of this period, gaining the social and biological maturation together, the surplus of the adult roles, erosion in the familial and social support networks and activities threatening the life become the important effects in the formation of the emotional problems. (1, 2, 3)

Among the mental health problems arising in the youth period, the most encountered one is depression. It has been showed that the adolescents getting the diagnosis of the depression are exposed to much more stressful life events when compared to the healthy adolescents in the pre-illness period and there is a significant relationship between the type of the indications they have showed and the stressful life events. (1, 4)

Depression is a syndrome characterized with the collapse, deep sadness, sometimes together with both anxiety and sad feeling situation with the feelings and thoughts, slowness in speaking, motion and physiological operations, slowdown and in addition to these, the feelings and thoughts of unworthiness, smallness, weakness, reluctance, pessimism. (5, 6)

Anxiety is a situation related to the somatic complaints accompanying to the extensive fear feeling. The somatic complaints such as tachycardia and sweating indicate the hyperactivity of the autonomic nerve system. The anxiety affects cognition and tends to form distortion in perception. It is different from fear as a response appropriate to a known danger; anxiety is a response given to the unknown or contradictory threat. (7)

In our research, the determination of the risk of the depression and anxiety encountered in the high school student, namely adolescent age group has been realized and the factors affecting this have been researched.

Method

Sample

All students of Çok Programlı Lise (Multi-Programmed High School) and Kız Teknik Lisesi (Girls Technical High school) located in Muş Korkut have been taken as a sample. As there are two high schools in the district, both have been included to the study.

Data collection tools

12-item questionnaire prepared by the researchers composed of questions unveiling socio-demographic features and related to the depression and anxiety was administered to students.

Hospital Anxiety and Depression Scale (HADS) was applied to students to determine the risk of depression and anxiety in students. This scale is composed of 14 questions. HAD is a scale which is filled by the patients themselves on whom the indications of the anxiety and depression are scanned. (8). The validity of its Turkish translation has been realized by Aydemir and friends. (9)

Operation

From students, it has been requested to answer the questionnaire and scale without writing their names. It has been said that only the students getting help write their names. From Kız Lisesi (Girls High School), 73 persons have said that they want to get help. From Çok Programlı Lise (Multi-Programmed High School), 43 persons have wanted to get help. The face-to-face interviews have been made with these students, their HAD scales have been evaluated and it has been ensured that the ones deemed required have been directed to the Child Psychiatry available in Muş city.

Statistical Analysis

For statistical analyses, NCSS (Number Cruncher Statistical System) 2007&PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA) program has been used. While evaluating the study data, the definitive statistical methods (Mean, standard deviation, median, frequency) and additionally in the inter-group comparisons of the para-

meters having normal distribution, One-way Anova test and in the determination of the group causing the difference Tukey HSD test and in the evaluations according to two groups Student t test has been used. In the inter-group comparisons of the parameters not having normal distribution due to the case numbers Kruskal Wallis test and in the determination of the group causing the difference and in two group evaluations Mann Whitney U test has been used. In the evaluation of the relationship of the scale points with the parameters, Pearson and Spearman's correlation analysis has been used. The results have been evaluated in the confidence interval of % 95 and the significance is evaluated at the level of $p < 0.05$.

Findings

The research has been made to 338 students. The students' ages have ranged from 13 to 19, its average has been $15,63 \pm 1,30$ years. As the 41,7% ($n=141$) of the students is composed of females, its 58,3% ($n=197$) is composed of males. While 5,9% ($n=20$) of the students smoke, its 94,1% ($n=318$) does not smoke.

The number of the students' brothers and sisters have ranged from 1 to 26, its average has been $6,91 \pm 3,03$. 40,2% ($n=136$) of the students have been at the 9th grade, its 24,6% ($n=83$) at the 10th grade, 25,4% ($n=86$) at the 11th grade and 9,8% ($n=33$) at the 12th grade. 17,5% ($n=59$) of the students regard themselves very successful in their courses, 78,1% ($n=264$) as successful at medium levels and 4,4% ($n=15$) of them as unsuccessful. While 48,8% ($n=165$) of the students make physical exercises, 51,2% ($n=173$) of them does not do physical exercise. (Table-1)

13,3% ($n=45$) of the students have families having more income than expenditures, 43,8% ($n=148$) have families having equal income and expenditures and 42,9% ($n=145$) of them have families with more expenditures than incomes. The mothers of 63,9% ($n=216$) of the students are not literate, 12,7% ($n=43$) of them are literate, 21,0% ($n=71$) of them is a graduate of primary-secondary school, 2,1% ($n=7$) of them is a graduate of high school and 0,3% ($n=1$) of them is a university graduate. The fathers of 12,1% ($n=41$) of the students are not literate, 23,1% ($n=78$) of them is literate, 52,1% ($n=176$) of them is a graduate of primary-secondary school, 10,6% ($n=36$) of

Table 1. Distribution of Social Features

Number of brothers and sisters		Min-Max	Ave±SS
		1 – 26	6,91±3,03
		n	%
Which Grade	9. Grade	136	40,2
	10. Grade	83	24,6
	11. Grade	86	25,4
	12. Grade	33	9,8
Finding themselves successful in courses	Very successful	59	17,5
	Medium successful	264	78,1
	Unsuccessful	15	4,4
Physical exercise	Yes	165	48,8
	No	173	51,2
Sport Types (n=165)	Basketball	5	3,0
	Box	2	1,2
	Football	81	49,2
	Wrestling	1	0,6
	Running	62	37,6
	Tennis	7	4,2
	Volleyball	7	4,2

Table 2. Distribution of the features related to the family

		n	%
Income of the family	More income than expenditure	45	13,3
	Equal income and expenditure	148	43,8
	More expenditure than income	145	42,9
Education status of the mother	Not literate	216	63,9
	Literate	43	12,7
	Primary school – secondary school	71	21,0
	High school	7	2,1
	University	1	0,3
Education status of the father	Not literate	41	12,1
	Literate	78	23,1
	Primary school – secondary school	176	52,1
	High school	36	10,6
	University	7	2,1
Evaluation of the families by the cases	Perfect in all respects	207	61,2
	Perfect in some respects	115	34,0
	Not too much perfect	16	4,8
Relations with the family	Very bad	1	0,3
	Bad	11	3,2
	Average	30	8,9
	Good	107	31,7
	Very good	189	55,9

them is a graduate of high school and 2,1% (n=7) of them is a university graduate. (Table-2)

In our cases HADS Anxiety scores ranged between 0 and 2.71 and its average is 1.26 ± 0.50 . In 39.1%

of the students' anxiety risk is observed. In our cases with HADS depression scores ranged between 0 and 2.57 and its average is 0.95 ± 0.44 . In 48.8% of students, risk of depression is observed. (Table-3)

Table 3. Distribution of Hospital Anxiety and Depression Scale (HAD)

HAD	HAD			
	Minimum	Maximum	Average	St. Deviation
Anxiety	0,00	19,00	8,81	3,53
Depression	0,00	18,00	6,69	3,10
		n	%	
Anxiety	available (≥ 10)	132	39,1	
	unavailable (< 10)	206	60,9	
Depression	available (≥ 7)	165	48,8	
	unavailable (< 7)	173	51,2	

Table 4. Relation of various parameters with HAD Scale Scores

	Anxiety	<i>p</i>	Depression	<i>p</i>
	Ave±SS		Ave±SS	
Gender				
<i>Female</i>	9,42±3,67	<i>0,007**</i>	6,28±2,96	<i>0,044*</i>
<i>Male</i>	8,38±3,37		6,97±3,18	
Grade				
<i>9. grade</i>	8,71±3,41	<i>0,607</i>	7,02±2,89	<i>0,045*</i>
<i>10. grade</i>	8,96±3,86		5,85±2,98	
<i>11. grade</i>	8,58±3,43		6,91±3,29	
<i>12. grade</i>	9,48±3,45		6,82±3,50	
Monthly income				
<i>Less income than expenditure</i>	8,15±3,63	<i>0,007**</i>	6,35±2,71	<i>0,109</i>
<i>Equal income and expenditure</i>	8,34±3,56		6,38±2,97	
<i>More income than expenditure</i>	9,50±3,36		7,10±3,32	
Family relation status				
<i>Bad</i>	10,58±3,85 (11,00)	<i>0,002**</i>	11,92±2,90 (11,50)	<i>0,001**</i>
<i>Average</i>	9,80±3,20 (9,00)		7,27±2,98 (7,00)	
<i>Good</i>	9,43±3,09 (9,00)		6,58±2,65 (7,00)	
<i>Very good</i>	8,19±3,68 (8,00)		6,32±3,08 (6,00)	
Family evaluation				
<i>Perfect in all terms</i>	8,32±3,57 (8,00)	<i>0,012*</i>	6,53±3,18 (6,00)	<i>0,134</i>
<i>Perfect in some terms</i>	9,61±3,29 (9,00)		6,76±2,81 (6,00)	
<i>Not too much perfect</i>	9,44±3,76 (9,00)		8,18±3,89 (8,00)	

There is a significant difference between the average of the anxiety scores of the cases according to the gender ($p < 0,01$). Girl students' average anxiety scores were significantly higher than male students. There is a significant difference between the average of the depression scores of the cases according to the gender ($p < 0,05$). Male students' average depression scores were significantly higher than female students. There is a significant difference between the average of the anxiety scores of the cases according to the families' monthly incomes ($p < 0,01$). The average of the anxiety scores of the cases having

families with more expenditures than incomes is significantly high according to the cases having equal incomes and expenditures ($p: 0,012$). There are not statistical difference between the other income groups ($p > 0,05$).

There is not statistical difference between the anxiety and depression scores of the cases according to the mother's education status ($p > 0,05$). There is not statistical difference between the anxiety and depression scores of the cases according to the father's education status ($p > 0,05$). There is statistical difference between the average of the anxiety scores

according to the way that the students evaluate their families ($p < 0,05$). The average of the anxiety scores of the cases finding their families perfect in some respects is statistically significantly higher than the average of the anxiety scores of the cases finding their families perfect in all respects ($p: 0,003$). Among the other evaluations, there is not statistically significant difference ($p > 0,05$). There is statistical difference between the average of the anxiety scores according to the status of their relations with their families ($p < 0,05$). The average of the anxiety scores of the cases finding their relations with their families very well is statistically significantly lower than the scores of the ones finding their relations with their families bad, medium and good ($p: 0,007$; $p: 0,021$; $p: 0,002$). Among the other relation statuses, there is not statistically significant difference ($p > 0,05$). There is statistical difference between the average of the depression scores according to the status of their relations with their families ($p < 0,05$). The average of the depression scores of the cases finding their relations with their families very bad is statistically significantly higher than the scores of the ones finding their relations with their families good and very good ($p: 0,019$; $p: 0,011$). The average of the depression scores of the cases finding their relations with their families bad is statistically significantly higher than the scores of the ones finding their relations with their families medium, good and very good ($p: 0,001$; $p: 0,001$; $p: 0,001$). Among the other relation statuses, there is not statistically significant difference ($p > 0,05$). (Table-4)

There are not statistically significant differences between the averages of the anxiety and depression scores according to the their own success statuses in the courses ($p > 0,05$).

Discussion

According to our research, the anxiety risk is observed in %39,1 of the students. The depression risk is observed in %48,8 of the students. While in %46.8 of the female students, the anxiety risk is observed, in the 33.1% of the male students, the anxiety risk is observed. Again, in %46.8 of the female students, the depression risk is observed, in %50.1 of the male students the depression risk is observed.

Without making gender discrimination, in the literature as being the nearest to these rates, in a re-

search made in the total 444 students of the last grade of 6 high schools in Mardin centrum, the depressive deficiency has been obtained as %37 according to the Beck Depression Scale. (10) In the research made with Beck Depression Scale, in 334 high school students in İzmit 3.5 years after Marmara earthquake, the depression frequency has been found as %30.8 in all students. In 39% of the female, in 21.7% of the male students, depression has been determined. (11) In another research made to 504 students in Pamukkale University in 1999-2000 by using Beck Depression Scale, the depression frequency has appeared to be %26.2. (12)

In our research, the average of the female students' anxiety scores is significantly higher than the male students. There is statistically significant difference between the students' depression scores according to gender ($p < 0,05$). The average of the depression scores of the male students is statistically significantly higher than the female students. In some studies made with Beck Depression scale in USA in 1990 in 14-17 aged 5596 high school students, via the same scale in 1996 in Finland in 1656 university students and with Diagnostic Interview for Children and Adolescents diagnosis scale in Columbia in 14-16 aged 150 students, as compliant with this study, it has been determined that the depression frequency is at higher rates in the female students. (13) In the study made with Beck Depression scale to totally 936 students composed of İnönü University medicine faculty and health academy students in 2003, in 27.2% of the students, the depression indication has been determined. In 21.5% of the male students and in 31.4% of the female students, the depression indication has been observed. (13) In a research made with the high school students in a region of İstanbul having low social-economic levels, the frequency of encountering depression has been found as %30.3. (14) In a research made to 4143 students selected from 18 schools in Mersin centrum in 2002, the depression frequency has been found to be %12.5. %47.1 of the students having depressive deficiency is male and %52.8 of them are female students. (15) We can interpret the higher depression risk in the male students in our results as the regional characteristics and the difference of the used scale.

In our research, there is statistically significant difference between the average of the anxiety sco-

res of the cases according to the monthly incomes of the families. ($p < 0,01$). The average of the anxiety scores of the cases having families with more expenditures than incomes is statistically significant higher than the cases whose incomes are equal to the expenditures ($p: 0,012$). It can be said that the research of the relations of the anxiety scores with the family income cause anxiety score highness arising from its realization in a district with low socio-economic situation.

It has been observed in our research that the education status of the father and mother do not have effects to the anxiety and depression risk. In the region, the level of mother and father education level is generally low. These problems and features of the adolescents in liking or disliking and evaluation of their families have been found to be related with the creation of anxiety in them. When it is considered that one of the most important features of the adolescent period is his/her relation with his/her family, the results have appeared to be compliant with the literature. In our research, in addition to anxiety, the depression risk also has been found to be high in the ones having bad-very bad relations with their families according to the others.

As in our research it has been found that finding themselves successful or not does not have significant relationship with the depression and anxiety risk, indeed it has revealed the ineffectiveness of an important stress factor for that age period. In a study made between the high school students in Malatya centrum, there has been a significant difference between the success situations of the students and the encountering of the depressive deficiency. In %36.8 of the successful ones, in %46.7 of the medium level successful ones and in 64.2% of the unsuccessful ones, the indication of depressive deficiency has been observed.

In unsuccessful students, the depressive deficiency indication is at more higher rates. (16)

Based on the results of this research, providing information by the health professionals to the adolescents regarding the mental changes specific to this period and teaching the information sources to the adolescents can be recommended. The students should be supported with effective guidance given by the guide teachers on the opportunity of getting know and developing themselves and techniques of overcoming the stress for students.

With the scanning, the students having liminal and serious levels of mental problems should be determined by the guide teacher and the early treatment should be applied.

References

1. Demir T, Demir D, Kayaalp ML, et.al. Penetration of the Depressive deficiency in adolescents and features of the adolescents having depressive deficiency. *Child and Youth Mental Health Journal*. 1999; 6: 3-11.
2. Hankin BL. *Adolescent Depression; Description. Causes and Interventions*. *Epilepsy- Behavior* 2008; 1: 102-14.
3. Berk EL. *Infant. Children and Adolescent*. Illinois State University. 1993
4. Çuhadaroğlu F. Encountering depression and anxiety in adolescents. *Turkish Psychiatry Journal* 1993; 4: 189-94.
5. Öztürk O. *Mental Health and deficiencies*. 8. Edition. Ankara. 2001.
6. Doğan O, Gülmez H, Ketenoglu C, et al. *Epidemiology of Mental deficiencies*. Dilek Printing House. Sivas. 1999.
7. Sadock B.J, Sadock V.A. *Clinic Psychiatry Manual*. 4. Edition. Ankara. 2009
8. Zigmund AS, Snaith RP. *The Hospital Anxiety and Depression Scale*. *Acta Psychiatr Scand* 1983; 67: 361-370.
9. Aydemir Ö, Güvenir T, Küey L. *Validity and reliability of Turkish version of Hospital Anxiety and Depression Scale*. *Turkish Journal of Psychiatry* 1997; 8: 280-287.
10. Ceylan A, Özen Ş, Palanci Y, and et al. *Anxiety-Depression Levels and Harmful Habits in High School Last Grades: Mardin Study*. *Journal of Anatolia Psychiatry*; (2003; 4(3): 144-50.
11. Karakaya I, Ağaoğlu B, Coşkun A, et al. *TSSB in adolescents after three and half years from Marmara Earthquake . Depression and Anxiety Indications*. *Turkish Journal of Psychiatry* 2004; 15(4) ; 257-63.
12. Özdel L. *Comparison of depression frequency and socio-demographic features and depressive indications according to Beck Depression Scale in Pamukkale University*. Unpublished Master's Thesis. Denizli. 2001.
13. Kaya M, Genç MF, Kaya B, Pehlivan E. "Depressive indication penetration, styles of overcoming the stress and factors affecting them in the medicine faculty and health academy students". *İnönü University Medicine Fac. Community Health AD Published Expertise Thesis*. 2006; 18(2): 137-46

14. Görker I, Korkmazlar Ü. Durukan M, Aydoğdu A. *Indication and Diagnosis Distribution in Adolescents applying to the Child and Adolescent Psychiatry Clinics Clinic Psychiatry* 2004; 7; 103-10.
15. Toros F, Bilgin NG, Buğdayci R. et al. *Prevalence of Depression as Measurement by the C.B.D.I in a Predominantly Adolescent School Population in Turkey. European Psychiatry* 2004; 19(5) 264-71
16. Özfirat Ö. Et al. *Depression prevalence and factors affecting it in the high school last grade students in Malatya centrum. İnönü University Journal of Medicine Faculty* 16(4) 247-259.2009

Corresponding Author

Zehra Tezvaran,
Family Medicine Department,
Maltepe University Faculty of Medicine,
Turkey,
E-mail: ztezvaran@yahoo.com

Effects of intraoperative skin surface warming on postanesthetic recovery and shivering: A prospective, randomized, clinical trial

Salih Yildirim¹, Canan Baran Unal¹, Isa Dongel², Cevdet Duger³, Ali Feyzullah Sahin⁴, Idris Ersan¹

¹ Numune Public Hospital, Department of Anesthesiology, Sivas, Turkey,

² Numune Public Hospital, Department of Thoracic Surgery, Sivas, Turkey,

³ Cumhuriyet University, School of Medicine, Department of Anesthesiology, Sivas, Turkey,

⁴ Numune Public Hospital, Department of Urology, Sivas, Turkey.

Abstract

Objective: In this study, we aimed to evaluate the effects of skin surface warming during operation on postoperative recovery and shivering.

Materials and Methods: Eighty seven patients with the risk classification of American Society of Anesthesiologists (ASA) class I-II who were scheduled for elective open cholecystectomy were enrolled in this study. Peripheral body temperatures and tympanic temperatures were measured in all patients before the operation. Patients randomized into two groups. The patients in the first group were heated to 37°C peripheral temperature with a warming pad (KanMed heater device) placed under the patient during surgery. Heating process is not implemented in the other group. heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAB), peripheral oxygen saturation (SpO₂), tympanic membrane temperature, peripheral temperature and room temperature were recorded at induction and pre-induction with 5-minute intervals. In 5-10-15 minutes after extubation, shivering and Aldrete recovery scores were evaluated and recorded.

Results: Peripheral tympanic membrane temperatures during the operation and aldrete recovery scores were higher in the patients were heated during surgery than the others. After the operation, the mean temperature of the tympanic membrane was 36.59±0.12 °C in the heated group, while 35.94±0.16 °C were recorded in the non-heated group (p= 0,039). Aldrete recovery scores and shivering scores after the operation were higher in the heated group than the non-heated group (p=0,001 for aldrete; and p=0,042 for shivering). None of the patients had shivering in the heated group, while four patients had shivering in the non-heated group.

Conclusion: In this study, we have clearly demonstrated that peripheral heating is preventing postoperative shivering and expediting postoperative recovery.

Key words: Intraoperative surface warming, body temperature, heating, shivering, postoperative recovery.

Introduction

Post-anesthetic shivering is one of the common complications of anesthesia, and is seen with a rate of 5-65% following general anesthesia whereas with an approximate rate of 33% after epidural anesthesia (1, 2). An increased metabolism involved by shivering results in increased carbon dioxide production with oxygen consumption, and as a result of these changes left ventricular workload elevates. While the decreased arterial O₂ saturation due to shivering is tolerated in patients without systemic disorder, it leads to increased mortality and morbidity in patients with cardiopulmonary disease (1). Postoperative shivering induces tightness, pain, bleeding and increased frequency of infection at the surgical incision site resulting in a prolonged hospitalization period (3). Shivering is significant during the postoperative period, particularly in patients at high risk (4). Therefore patients should be treated rapidly and effectively. Although the etiology of postoperative shivering is not definitively known hypothermia developed during the operation is the reason which is frequently held accountable (5, 6). The benefits offered by peripheral warming in order to prevent postoperative shivering are variable.

The purpose of this study is to evaluate the effects of intraoperative skin surface warming on postoperative shivering and recovery scores.

Materials and methods

The study was initiated after the approval of Ethical Committee and obtaining written informed consent of all patients. Eighty seven voluntary patients of ASA I-II risk group who were in the age range of 16-65 years and for whom open cholecystectomy operation was planned were enrolled in our study. While the patients without a history of any known allergies who received general anesthesia and whose duration of operation was 50-70 minutes were included in the study, the patients with an inflammatory disease and a known chronic systemic disease who were subjected to an emergent operation were excluded from the study.

The patients were randomly divided into two groups by closed envelope method in our prospective, randomized clinical study. The patients who received peripheral warming process were classified as group I, whereas the patients who were not heated were classified as group II. Four patients from heated group and three patients from non-heated group were excluded from the study due to extended operating time and complications. The anesthesiologist in the recovery room was blinded of study groups. The patients who did not receive premedication were taken into the operating room and their vascular access was opened by a 20 G intravenous (IV) cannula. Infusion was initiated at a rate of $8 \text{ mL kg}^{-1} \text{ sa}^{-1}$ by a crystalloid which was previously kept at room temperature. In the pre-operative period, a digital peripheral calorimeter was placed in the middle section of sternum in all patients. HR, SBP, DBP, MBP, SpO_2 and peripheral temperatures were followed by using a monitor (Dräger Infinity Vista XL Monitor, Germany) before the induction and at intervals of 5 minutes following the induction. Simultaneously, tympanic membrane temperatures (Braun Instant Thermometer IRT 1020, Germany) and room temperatures (TT T-ECHNI-C, TM1011) were recorded. The patients in the heated group were applied peripheral warming process at 37°C by using the pad of the heating device (STOCKERT Heater-Cooler System 3T, Germany) covering the entire operation table during their operations. In order to avoid the potential complication of burns in patients, a covering was placed between the heating pad and the patients. No warming process was applied for

the patients in the other group. All patients were given a standard anesthesia procedure. All patients were covered in a similar way by using identical covers in accordance with the sterility conditions before surgery was initiated. The patients were excluded from the study when the duration of operation was prolonged due to the complications. After the operation was completed the patients were taken into recovery room following extubation and given $2 \text{ L min}^{-1} \text{ O}_2$ by using a mask. Warming process by warming pads was not applied to the patients in the recovery room. However, they were covered with the same standard blankets. By using a monitor (Nihon Kohden BSM-4113K Monitor, Japan), HR, SBP, DBP, MAP, and SpO_2 values and tympanic membrane temperatures (Braun Instant Thermometer IRT 1020, Germany) of the patients were measured by a different anesthetist, who did not know in which group the patients were involved, at minutes 5-10-15 as of they were taken into the recovery room. In the recovery room, Aldrete recovery scores and shivering scores (0: no shivering, 1: One or more of: piloerection, peripheral vasoconstriction, peripheral cyanosis without other cause but without visible muscular activity, 2: Visible muscular activity confined to one muscle group, 3: Visible muscular activity in more than one muscle group, 4: Gross muscular activity involving the entire body) were evaluated and recorded at minutes 5-10-15 (7, 8). The patients with an Aldrete recovery score of ≥ 9 were sent to the relative services.

The potential complications, such as bradycardia, hypotension, decreased oxygen saturation, nausea, vomiting, and apnea that may develop in the patients followed up in the recovery room were interfered as necessary.

All data was recorded in an electronic environment by full access of only authors who were not blinded. Student's t-test and Chi-square test were employed to analyze the continuous variables and categorical variables, respectively, and an inter-group comparison was conducted. All data was evaluated by using a computer program, SPSS 13.0, in order to detect whether any statistically significant difference was observed within and between the groups. A p-value of <0.05 was considered significant for the statistical difference.

Results

Demographic data and preoperative values of the patients were summarized in Table 1. Statistically significant difference was not observed when the demographic data and preoperative values were compared between the groups. No significant difference was found between the groups in terms of HR, SBP, DBP, MBP, SpO₂, tympanic membrane temperatures, peripheral temperatures, and room temperatures during the preoperative period.

Patients during operation SBP, DBP, MAP compared to values not significantly different between them ($p > 0.05$) (Figure 1).

There were no statistically significant differences about the room temperatures between groups. Tympanic membrane temperature and skin temperatures of heated group were found to be statistically significantly higher ($p=0,0001$, $p=0,014$) (Figure 2).

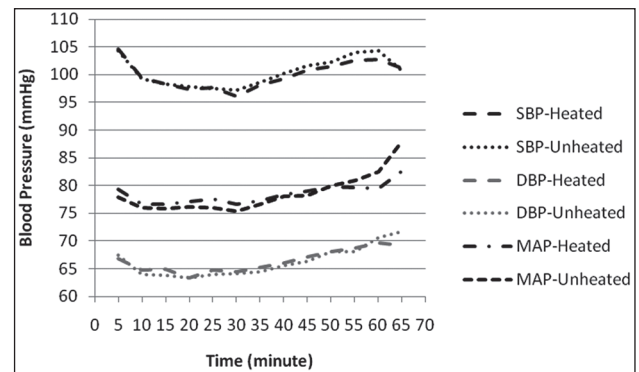


Figure 1. Blood pressure values during operation

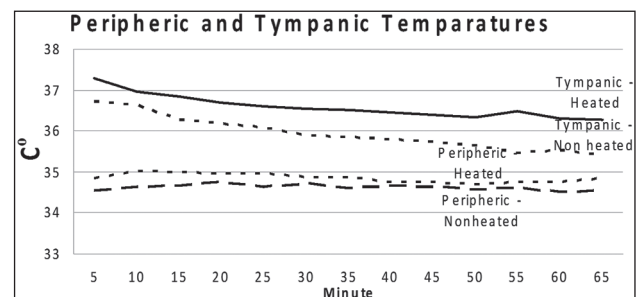


Figure 2. During operation, the temperature differences between the groups

Table 1. Demographic characteristics of the patients and the preoperative values

	Unheated Group Mean $\pm$ SD (n=40)	Heated Group Mean $\pm$ SD (n=40)	P Value
Age (year)	44,05 $\pm$ 13,46	45,48 $\pm$ 13,11	0,633*
Sex (M/F)	5 (%12,5) / 35 (%87,5)	7 (%17,5) / 33 (%82,5)	0,531**
Height (cm)	160,60 $\pm$ 6,66	160,78 $\pm$ 6,48	0,717*
Weight (kg)	76,08 $\pm$ 11,90	79,90 $\pm$ 18,73	0,519*
Body mass index (kg/m ²)	29,60 $\pm$ 4,95	30,91 $\pm$ 7,06	0,866*
ASA I / II	36 (%90,0) / 4 (%10,0)	33 (%82,5) / 7 (%17,5)	0,330**
Preoperative mean skin temperature (°C)	34,65 $\pm$ 0,62	34,58 $\pm$ 0,49	0,607*
Preoperative mean core temperature (°C)	36,92 $\pm$ 0,24	36,97 $\pm$ 0,28	0,419*
Preoperative mean room temperature (°C)	21,27 $\pm$ 0,84	21,52 $\pm$ 0,90	0,206*

*Student t test; **Chi-square test

Table 2. The values during operation

	Unheated Group Mean $\pm$ SD (n=40)	Heated Group Mean $\pm$ SD (n=40)	P Value*
Duration of surgery (min)	57,43 $\pm$ 4,95	57,88 $\pm$ 5,45	0,700
Heart rate (bpm)	69,22 $\pm$ 6,61	68,32 $\pm$ 5,79	0,519
SaO ₂ (%)	99,64 $\pm$ 0,53	99,75 $\pm$ 0,46	0,301
Peroperative mean skin temperature (°C)	34,62 $\pm$ 0,54	34,86 $\pm$ 0,24	0,014
Peroperative mean core temperature (°C)	35,94 $\pm$ 0,16	36,59 $\pm$ 0,12	0,0001
Peroperative mean room temperature (°C)	21,39 $\pm$ 0,74	21,60 $\pm$ 0,84	0,248

* Student t test

While postoperative mean tympanic membrane temperature was 36.26 ± 0.13 °C for all patients (non-heated group: 35.94 ± 0.16 °C and heated group: 36.59 ± 0.12 °C) a significantly higher tympanic membrane temperature was detected in the heated group in comparison with the non-heated group ($p=0.0001$).

Postoperative Aldrete recovery scores and shivering scores were observed to be higher (for Aldrete; $p=0.001$, for shivering; $p=0.042$) in the heated group compared to the non-heated group. The average Aldrete recovery scores of the patients in the non-heated group were 5.68, 8.0, and 9.6 for minutes 5-10-15, respectively, as of they were taken into the recovery room. The average Aldrete recovery scores of the patients in the heated group were 7.25, 8.65, and 9.9 for minutes 5-10-15, respectively, as of they were taken into the recovery room (Figure 3).

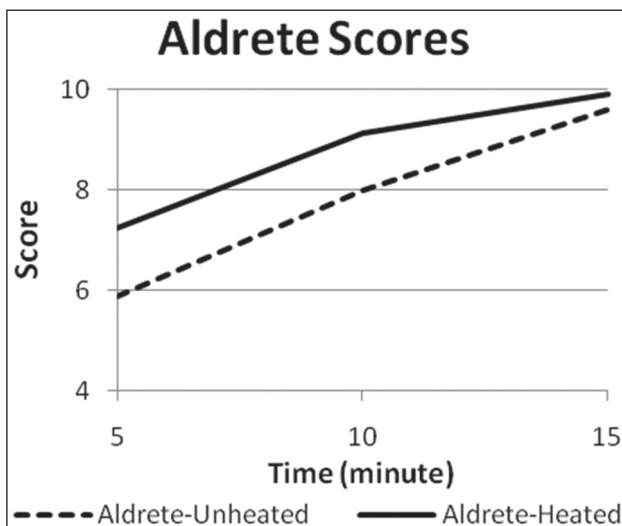


Figure 3. Postoperative recovery aldrete scores

Shivering was not observed in any of the patients in the heated group. Four female patients experienced shivering in the non-heated group. Among these patients, the shivering level score was 1 in three patients and 2 in one patient at postoperative minute 5, 1 in two patients and 2 in two patients at postoperative minute 10, and 1 in two patients at postoperative minute 15. Treatment for shivering was not needed in any of these patients (Figure 4).

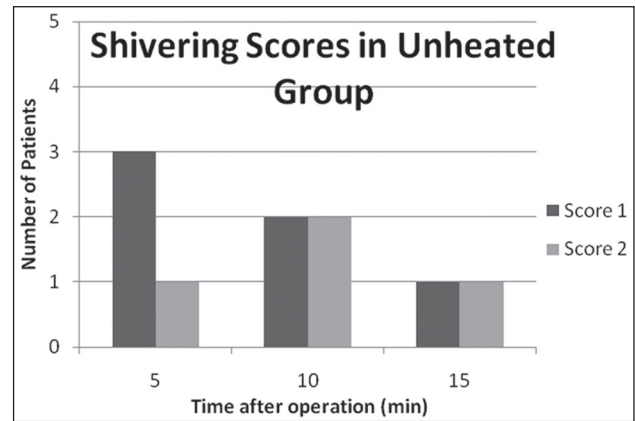


Figure 4. Scores of postoperative shivering of unheated group

Discussion

In the present study, we have determined that peripheral warming applied during the operation accelerates the postoperative recovery and prevents shivering which is a common post-anesthetic complication. None of the patients experienced shivering in the heated group, whereas shivering was observed in four patients in the non-heated group.

The normal value of the core temperature is in the range of 36 – 37.5°C in humans. The core temperature which is lower than 36°C is defined as hypothermia. In almost all patients who received anesthesia may have a temperature decrease by 1-3°C depending on the type of anesthesia, the type of surgery, the size of surgery, and the temperature of the operating room. As in the post general anesthesia, the patients who received regional anesthesia and developed hypothermia may experience shivering (3).

The development of hypothermia follows a specific course during the general anesthesia. In the first hour the core temperature decreases up to 1-1.5°C. This initial hypothermia is followed by a slower and linear decrease. Consequently, temperature goes through the plato phase and the core temperature remains unchanged (7). In our particular study, the mean duration of surgery was 57.65 ± 4.70 minutes (heated group: 57.88 ± 5.45 ; non-heated group: 57.43 ± 4.95 min.). Although the tympanic membrane temperatures, room temperatures, and peripheral temperatures measured in the preoperative period were similar, the tympanic membrane temperatures measured during the operation showed more decreases in the non-heated

group which was resulted in a statistically significant difference between two groups ($p < 0.019$).

Frank et al. (9) examined shivering and total body oxygen consumption in 110 elderly patients who had surgery in the early postoperative period. The average total body oxygen consumption of the patients who experienced shivering was 38% more than the patients without shivering. Despite the similar core temperatures, the male patients were observed to have a higher ratio of clinically identifiable shivering and higher total body oxygen consumption than that of the female patients.

Sajid et al. (10) reviewed 19 clinical trials in the literature concerning perioperative warming. They concluded that perioperative warming is effective in preventing pain, wound site infection, and postoperative shivering following operation. In addition, they reported that the systemic warming of the patient is associated with less perioperative blood loss through the inhibition of coagulopathy induced by hypothermia during surgery, and concluded that several surgical disciplines of perioperative warming may routinely be applied for all patients in order to eliminate the results caused by hypothermia.

Xu et al. (11) covered all patients with operation blankets in a study they performed with 40 patients. They heated the liquids given to patients by using a liquid heater during the operation and the patients by a forced-air heating system. They evaluated blood loss, blood transfusion requirements, extubation times, and postoperative shivering scores with the core temperatures at every 20 minutes during the operation. They found insignificant difference between the groups for blood loss and blood transfusion. They provided that extubation time was significantly shorter in the heated-group (18 ± 6 minutes in the heated-group, 26 ± 10 minutes in the non-heated group; $t = -3.364$, $P = 0.002$), and found that the core temperature was statistically significantly higher in the heated group at the end of the operation ($36.4 \pm 0.4^\circ\text{C}$ in the heated group and $35.3 \pm 0.5^\circ\text{C}$ in the non-heated group, $t = 7.547$, $p < 0.001$). While six patients experienced postoperative shivering in the non-heated group none of the patients experienced shivering in the heated group. They concluded that the efficient use of the liquid heating system and forced-air heating system will help to maintain perioperative

normothermia, to shorten the extubation time, and to reduce postoperative shivering.

Alfonsi et al. (12) performed a study in which they divided the patients into two groups. They covered the patients in the first group ($n=9$) with a blanket, whereas the patients in the second group ($n=9$) had air-heater blankets covered on their whole body. They determined that the average skin temperature ($35.7 \pm 0.4^\circ\text{C}$ - $33.2 \pm 0.8^\circ\text{C}$, $P < 0.0001$) and core temperature were higher ($35.7 \pm 0.2^\circ\text{C}$ - $36.4 \pm 0.2^\circ\text{C}$, $P < 0.0001$) in the heated group. They suggested that thermal comfort was increased by active warming, and reported that the shivering time was similar in both groups (heated group = 37 ± 11 minutes, non-heated group = 36 ± 10 minutes), although the oxygen requirement was significantly decreased.

Due to postoperative shivering may cause unpredictable complications and prolongation of postoperative recovery, it should be prevented. We conclude that intraoperative skin surface warming may prevent postoperative shivering and its complications, with shortening the postoperative recovery time.

References

1. Singh P, Dimitriou V, Mahajan RP, Crosley AWA. Double-blind comparison between doxapram and pethidine in the treatment of postanesthetic shivering. *Br J Anaesth.* 1993; 71: 685-688.
2. Konrad R, Schwarzkopf G, Hansjoerg H, Hartmann M, Fritz HG. A comparison between meperidine, clonidine and urapidil in the treatment of postanesthetic shivering. *Anaesth Analg.* 2001; 92: 257-260.
3. Sessler DI. Current concepts: Mild perioperative hypothermia. *N Eng J Med.* 1997; 336: 1730-1737.
4. Leslie K, Sessler D. Peri-operative hypothermia in the high-risk surgical patient. *Best Pract Res Clin Anaesthesiol.* 2003; 17: 485-498.
5. Kranke P, Leopold HE, Roewer N, Tramer MR. Pharmacological treatment of postoperative Shivering: A quantitative systematic review of randomized controlled trials. *Anaesth Analg.* 2002; 94: 453-460.
6. Wang JJ, Ho ST, Lee SC, Liu YC. A comparison among nalbuphine, meperidine, and placebo for treating postanesthetic shivering. *Anesth Analg.* 1999; 88: 686-689.

7. Claudia PB, Carmelita SP, Gary WB. Postanesthetic care in the critical care unit. *Crit Care Nurse* 2004; 24: 38-45.
8. Usta B, Gozdemir M, Demircioglu RI et al. Dexmedetomidine for the prevention of shivering during spinal anesthesia. *Clinics* 2011; 66: 1187-1191.
9. Frank SM, Fleisher LA, Olson KF et al. Multivariate determinans of early postoperative oxygen consumption in elderly patients. Effects of shivering, body temperature and gender. *Anesthesiology*; 1995; 83: 241-249.
10. Sajid MS, Shakir AJ, Khatri K, Baig MK. The role of perioperative warming in surgery: a systematic review. *Sao Paulo Med J.* 2009; 127: 231-237.
11. Xu L, Zhao J, Huang YG, Luo AL. The effect of intraoperative warming on patient core temperature. *Zhonghua Wai Ke Za Zhi.* 2004; 42: 1010-1013.
12. P. Alfonsi, KE. Nourredine, F. Adam et al. The Effect of Postoperative Skin-Surface Warming on Oxygen Consumption and the Shivering Threshold. *Anaesthesia.* 2003; 58: 1228–1234.

Corresponding Author

Cevdet Duger,

Department of Anesthesiology,

Cumhuriyet University School of Medicine,

Sivas,

Turkey,

E-mail: cevdetduger@gmail.com

Continuing education of intensive and emergency units nurses during clinical shifts

Abbasali Ebrahimian¹, Nader Khalesi¹, Maedeh Tourdeh²

¹ School of Health Management and Information Sciences, Tehran University of Medical Sciences, Tehran, Iran,

² School of Nursing and Allied, Semnan University of Medical Sciences, Semnan, Iran.

Abstract

Introduction: The aim of this study is to provide a new and practical method known as “nurse trainer” for constant training and ICU and emergency care during their clinical shifts.

Method: At first, using a pretest, the knowledge of nurses in emergency units and especially in interpreting arterial blood gases (ABG) and related nursing cares was determined. Then the nurse trainers, having carried out other professional activities, trained and answered the nurses’ questions when the unit workload had been lightened and the nurses had confronted questions about nursing and the interpretation of arterial blood gases. The post-test was conducted after 2 months, and the pretest and post-test results and their relationship were compared with some demographic variables.

Findings: Statistical tests showed a significant difference between demographic variables such as employment status, work history, working place and their need to attend in ABG training courses with ABG knowledge levels. Also, there was a significant difference between the nurses’ advantages of knowledge in pretest 10.55 ± 3.66 and post-test 18.92 ± 5.34 .

Conclusion: Results showed a significant effect of “nurse trainer” in enhancing nurses’ knowledge. Therefore, it is suggested that further studies be done in this field around other clinical issues so that, after identifying and removing barriers, we can implement this method and use it in training of nurses in ICU and emergency units.

Key words: Nurse Trainer, Nurse constant training, Clinical shift

Introduction

Training methods are one of the effective components of knowledge transfer (1) that vary with technological, social and cultural changes (2). Nowadays, the training is done in a way that the trainees

share the acquirement of the concept and are forced into mental, scientific, individual and communal activities. The emphasis is on active methods for achieving this goal (3). However, the lecture method is the commonest method among a variety of teaching methods that are used in training environments in the world, (4). The use of this method is so pervasive that in the majority of nurse retraining programs, still largely; the lecture method is used in its implementation even if the initial planning is based on another method like workshop method. But it seems that its efficiency is not enough to be used for constant training and keeping the nursing personnel ready. Because, this will not incite any critical thought and thought challenge and will be only effective more in memorizing materials, which will most likely go out of mind quickly (4). Also, factors such as excessive job preoccupation and being on compressed working shifts on the one hand, and matters relating to the personal and familial life of the nurses whose community mostly includes women, on the other hand, have precluded some of the nurses from participating in the retraining courses. Even the nurses, who manage to participate in such courses, do not have enough concentration to use the materials of the retraining course due to the fatigue of the previous shift or the stress and obsession of the next one. In a study, Sena Ebrahim (2010) showed that over one year, 14.5 % of the nurses had managed to participate in no retraining course and 61.8 % of them had missed at least one course (5). Besides the issues concerning the ability and inability of the nurses in participating in the retraining courses, the gap between the theory and practice has made it impossible for the nursing retraining courses, often taught in the form of new theoretical materials by the nursing specialists or the specialists of the other areas, to be effective in enhancing the practical knowledge of the nurses, and consequently, due to the non-use of the newly-learned materials in clinical environment, after a while, these materi-

als go out of mind. To solve this problem in nursing training, several methods have been proposed and used. Among the methods are: Ward sister, Mentor, Mentorship, Partnership, Preceptorship, etc. But in all of these methods, an experienced nurse or a nurse with higher academic qualifications have been used to train other nurses. Also, in most of these methods, the trainer is in charge of the students and the nurses of the unit simultaneously and is not a clinician (6). Furthermore, these methods have been mostly studied and used in the developed countries which have their specific nursing and caring infrastructure different than that of Iran. Therefore, it is likely that in the present state in which the nursing manpower of Iran is qualitatively and quantitatively peculiar, these methods cannot be used. Accordingly, it is imperative to use a method which is appropriate, to a great extent, for the nursing manpower state of Iran and can regularly update the nursing personnel and internalize the materials in their mind so optimally as to be used when needed. It seems that, the use of the training method "nurse trainer" can be more effective in enhancing the knowledge of the nursing personnel; concurrently, a research has been carried out with the purpose of investigating the impact of this method on nurse training. The results of this study can be used as a novel training method by the policy-makers and managers of nurse-training domain in the nursing area.

Method

The present study is quasi-experimental study with a pretest and post-test and without a control group. The study population consisted of all nurses working in hospital emergency departments, and especially Amir almomenin (AS) hospital in Semnan, who had at least a bachelor's degree in nursing. Based on the need assessment and the manager's and specialists' opinion poll, the interpretation of the Arterial blood gases and the nursing cares related to the title was selected to be studied. Research tools included a manipulated questionnaire consisting of two sections of demographic data and of measurement of the nurses' knowledge concerning the interpretation of the arterial blood gases. The questionnaire was consisted of 25 questions and 5 sections (including: Basic concepts, acidosis, alkalosis, mixed disorders, nursing care) which were re-

lated to the interpretation of the arterial blood gases. The validating method of the questionnaires was as such: the questionnaires were sent to a number of the specialists and trainers who were familiar to the title of the course and had training record, and their opinions were collected. For reliability, 10 members of the study population participated in a pilot study with a span of 2 weeks. The reliability coefficient of the questionnaire was 0.94 %, determined through the split-half method. At first using a questionnaire, the nurses' knowledge was analyzed in relation to the interpretation of arterial blood gases. After initial tests, one of the personnel working in the ICU and emergency unit, who had got a good mark and was motivated and skillful enough to train the others, was chosen to train the others (These individuals were excluded at this point and did not participate in the final test). In the next step, the chosen ones were given supplementary training and, after acquiring adequate skills for training the contents, were assigned as the trainers in the regular shifts of their work. Since the workload is not the same in different shifts, these persons had the opportunity to encourage the other personnel to learn the material when they were off work, and to teach them a part of the training contents and to answer their possible questions according to their needs, time schedule, and their mood. The data collected from the questionnaires, along with the demographic specifications of the personnel were entered in the SPSS software version 19 and were analyzed, using the analytical and descriptive statistics method (Paired t test and Pearson and Spearman correlation coefficients).

Results

52 nurses participated in the pretest and post-test. The average age of participants was 33.34 ± 8.36 and the average work experience was 10.19 ± 8.43 years. 32.7% of nurses (25 % once, and 5.8 % twice) had already participated in retraining courses of ABG interpretation. Of these, it was 3.8 % less than a year, 1.9 % less than two years and 25 % more than two years who had not participated in the retraining courses since their last participation. Other cases were investigated and their relationship with the subjects' scores in the pretest and post-test can be seen in Table 1. The average scores of nurses were in 10.55 ± 3.66 pre-test and 18.92 ± 5.34 post-

Table 1. Knowledge levels of intensive and emergency department nurses about ABG interpretation in pre-test and post-test and relation of these with some demographic variables

Knowledge levels			Very low		Low		Middle		Good		Excellent		P-Value		
Variables	Subgroups	No	%	Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test
Age	21-25	12	23.1	0	0	5	1	5	1	2	4	0	6	0.172	0.169
	26-30	10	19.3	0	0	2	0	7	1	1	5	0	4		
	31-35	12	23.1	3	1	4	0	4	1	1	7	0	3		
	36-40	6	11.5	1	0	1	0	4	0	0	0	0	6		
	41-45	6	11.5	0	0	4	0	1	0	1	4	0	2		
	>45	6	11.5	1	2	2	0	3	1	0	2	0	1		
Gender	Male	5	9.6	1	2	3	1	1	0	0	1	0	1	0.103	0.000*
	Female	47	90.4	4	1	15	0	23	4	5	21	0	21		
Employment Status	Formal	32	61.5	3	2	15	0	14	1	0	14	0	15	0.048*	0.424
	Informal	20	38.5	2	1	3	1	10	3	5	8	0	7		
Working place	Intensive care	26	50	0	1	4	0	17	2	5	11	0	12	0.000*	0.807
	Emergency department	26	50	5	2	14	1	7	2	0	11	0	10		
Work history	0-4	17	32.7	1	0	5	1	8	2	3	6	0	8	0.026*	0.464
	5-9	12	23.1	1	1	4	0	5	1	2	5	0	5		
	10-14	9	17.3	1	0	2	0	6	0	0	5	0	4		
	≥15	14	26.9	2	2	7	0	5	1	0	6	0	5		
University	Governmental	32	61.5	3	2	13	1	15	1	1	13	0	15	0.174	0.650
	Non-Governmental	20	38.5	2	1	5	0	9	3	4	9	0	7		
Previous participation in retraining the ABG	Yes	17	32.7	1	2	7	0	7	1	2	9	0	5	0.850	0.230
	No	35	67.3	4	1	11	1	17	3	3	13	0	17		
Training methods used in the former retraining	Workshop	4	25	0	0	1	0	2	0	1	2	0	2	0.254	0.303
	Lecture	6	37.5	1	1	3	0	2	0	0	4	0	1		
	Other method	6	37.5	0	1	3	0	3	1	0	2	0	2		
	Very high	4	7.7	0	0	3	1	1	0	0	2	0	1		
Need to attend in ABG training courses	High	7	13.5	1	2	4	0	2	1	0	3	0	1	0.001*	0.410
	Middle	13	25	4	0	5	0	4	1	0	8	0	4		
	Low	10	19.2	0	0	3	0	5	1	2	2	0	7		
	Very low	18	34.6	0	1	3	0	12	1	3	7	0	9		

Table 2. Relation of pre-test and post-test nurses scores about ABG interpretation

Knowledge levels Test items	Very low		Low		Middle		Good		Excellent		Mean		P-Value
	Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test	
Basic ABG	30	5	11	3	10	9	1	18	0	17	18.92±5.34	10.55±3.66	0.000
Acidosis	8	3	19	1	10	7	8	12	7	29			0.000
Alkalosis	9	5	15	5	24	6	4	13	0	23			0.000
Mixed disorders	19	3	12	6	9	14	10	13	2	16			0.000
Nursing care	21	5	22	4	7	11	1	13	1	19			0.000
Total score	5	3	18	1	24	4	5	22	0	22			0.000

test. The lowest score in the pretest was associated to basic concepts of ABG and the highest score was associated with acidosis. The lowest scores on the post-test were associated to alkalosis and the highest scores with acidosis. t paired test showed a significant difference between the scores of nurses in the five investigated sub-categories and the total score of the measurement tests of nurses' knowledge about ABG in pretest and posttest ($p = 0.000$) (Table 2).

Discussion

In the pretest, there was no significant relationship between age, gender and university levels and nurses' knowledge in ABG interpretation and the related nursing care. Other studies also have shown similar results (7, 8). These results show that keeping knowledge in its optimal level had no relation to age, sex and many other demographic variables. There was also no significant relationship between participation in the former retraining of ABG and the training methods used in the former retraining and the rate of nurses' knowledge on ABG interpretation and the related nursing cares. This suggests that participating in retraining with conventional styles and techniques nursing cannot alone meet information requirements of the nursing personnel. There was significant relationship between employment status and work experience of nurses and their knowledge of ABG. In that, there was a lower level of knowledge in the personnel with higher experience and stronger employment relationship. Similar studies have shown that there is a significant relationship between knowledge in different domains of experience and work experi-

ence (9-11). This represents a worrying situation, because it shows that tools and methods used for in-service training of nurses have not be efficient; this means that novice personnel who have just graduated from academic environments, are more informed. The knowledge of ICU personnel were higher than that of emergency personnel, and there was a significant relationship between the working place and the knowledge of the nurses. The findings of the special sections dealing with the ABG are more personnel. The finding showed the significantly notable relationship between the nurses' need to participate in the training courses and their knowledge level in the pretest and post-test. In that, the less need was felt in the pretest, the less was the knowledge level; and the less need was felt in the post-test, the more was the knowledge level. This suggests that nurse retraining should be devised based on coherent and comprehensive programs. Other studies also verify ongoing evaluations prior to the implementation of retraining programs (12, 13). In the post-test, there was no significant relationship between age, employment status, unit, place of employment, work experience, university, participation in previous retraining about ABG and teaching methods used in previous retraining and nurses' knowledge about ABG interpretation and nursing care. Once again this issue suggests that training overweighs any type of individual and demographic characteristics. It also reflects the impact of these remarkable new teaching methods used in the enhancement of knowledge of nurses with various demographic variables. But there was a significant relationship between sex and the nurses' knowledge about ABG interpretation and nursing care. The reason is due to the large number of fema-

le nurses compared with male nurses in this study, and perhaps the other reason is that since the nurse trainers in this study were women, men were shy to ask questions and increase their knowledge. The knowledge of nurses was not desirable regarding ABG interpretation in the pretest. Other studies have also confirmed this (7, 8). Researchers believe that significant shortage of staff nurses, high volume of workload in a shift, high and continuous shifts, lack of coherent programs for retraining, and inefficient teaching methods in organizing training programs are among the most important causes of this issue. There was significant difference between the scores of nurses before and after the retraining method of "nurse trainer." The researchers did not find a similar study in which this method would have been used to enhance the nurses' knowledge level in the ICU and emergency units. But almost similar studies have been used in the training of nursing students for promoting student knowledge, whose results support these findings (14, 15).

Conclusion

Results showed the significant effect of "nurse trainer" on the development of knowledge of the nurses in ICU and emergency department; this method can be used as a novel and effective method in enhancing the nurses' knowledge for ICU and emergency units. But certainty about the proposed use of this method needs further research and study. Therefore, it is suggested that after doing more research with more diverse methodologies and obviating potential defects, this method be used as an alternative method in retraining of nurses.

References

1. Heimlich JE, Norland E. *Teaching style: where are we now? New Directions for Adult and Continuing Education*. 2002; 93: 17-25
2. Holopainen A, Hakulinen-Viitanen T, Tossavainen K. *Nurse teacherhood: systematic descriptive review and content analysis. International Journal of Nursing Studies*. 2007; 44: 611-23.
3. Razavi s, Avijegan m. *Comparison of Lecture and Group Discussion Methods on Learning Anatomical Sciences: A Study in PhD students Iranian Journal of Medical Education. Iranian Journal of Medical Education*. 2012; 11(6):580-1.
4. Rafii F. *Educational Leadership / Supervision Model For Iranian Nursing Students*. Tehran: Iran University of Medical Science; 2002.
5. Ibrahim SA, Mahran SM. *Attributes of Nursing Staff Development in Port Said Hospitals Journal For Nursing Staff development*. 2010; 26(1):E6-E13.
6. Carol P, Lorraine E, Elaine S, Diane C. *Clinical education: A review of the literature. Nurse Education in Practice*. 2007; 7: 315-22.
7. Babamohammadi H. *A survey of Nursing Knowledge and Practice about Blood Product Transfusions in Kerman Hospitals Kerman University of Medical Science*; 1998.
8. Mohammadi GR, Ebrahimian AA. *Evaluating the knowledge of intensive care unit nursing staffs*. 2008. [Persian].
9. Mirzaee Saifabadi R. *a survey of Nursing Knowledge and Practice about Respiratory system Suction in Kerman Hospitals Kerman University and medical Science*; 1997.
10. Haghi M. *Comparison of Nurse And Nurse aid Knowledge about Psychotic Drug Administration Iran university of Medical Science*; 1997.
11. Mohamad jafari H, Vahidshahi K, Mahmudi M, Ab-baskhanian A, Shahbaznejhad L, Rnjbar M, et al. *Efficacy of continuing medical education on knowledge of general practitioners. Journal of Semnan University of Medical Sciences*. 2008; 9(4): 255-62.
12. Mohammadi MA, Dadkhah B. *Evaluation of Continuous Nursing Education Process in Ardebil Hospitals Journal of Ardebil University of Medical Sciences*. 2004; 5(3): 271-7.
13. Ebrahimian AA. *Nursing Development whit Education Based on Real Educational Needs. Iranian Journal of Medical Education*. 2005; 14: 123.
14. Ravanipour M, Kamali F, Bahreini M, Vahedparast H. *Facilitators and Barriers in Application of Peer Learning in Clinical Education according to Nursing Students. Iranian Journal of Medical Education*. 2011; 11(6): 569-79.
15. Gilmour JA, Kopeikin A, Douche J. *Student nurses as peer-mentors: Collegiality in practice. Nurse Education in Practice*. 2007; 7: 36-43.

Corresponding Author

Nader Khalesi,
School of Health Management and Information
Sciences,
Tehran University of Medical Sciences,
Tehran,
Iran,
E-mail: khalesi_nader@yahoo.com

Attitudes of nursing students towards older people in Turkey

Bilge Bal Ozkaptan¹, Birsen Altay², Huriye Demet Cabar¹

¹ Sinop University School of Nursing, Sinop, Turkey,

² Ondokuz Mayıs University Samsun School of Nursing, Turkey.

Abstract

Introduction: The attitudes of nurses towards older people in school period to be the important part of health team affect the work performance and the field of study after graduation. Therefore, this study was applied to define the attitudes of nurses towards older people and the relation of these attitudes with the experience of the students regarding older people and some demographic variables.

Methods: This study consisting of descriptive sectional type was implemented with 192 students that study in Sinop University, School of Nursing in 2010-2011 education year. Student description form that was prepared with the guidance of literature and the scale of Kogan's Attitudes Towards Older People (KAOP) were used as the data collection tools.

Results: The score rates that the students acquired by joining the research from the attitude scale towards older people are between 45-204 and the average score rate has been detected as 121.56 ± 13.60 . Significant difference has not been found out among the scores the students obtained from the scale according to age, class, place of living and hometown ($p > 0.05$). The students not having older people in their family had a more positive attitude towards older people than the ones having older people in their families and this difference was found out significant statistically ($p < 0.05$).

Conclusion: Consequently, with the attitudes of nursing students towards older people are slightly positive, taking place of geriatry subject more on the educational period will contribute to develop health of older people and improve more of positive attitudes.

Key words: Attitude, Aged, Nursing Students

Introduction

Lifetime in the world and in Turkey has expanded and so the share of old age population in the

population as a whole has gradually risen (1). Old age population growth rate is higher than general population growth rate in the world (2). In Turkey, 7.3% of the population is 65 aged and older (3). In our country, life expectancy at birth is 76.5 for women and 71.7 for men in 2009, which clearly shows that lifetime has expanded when compared to the previous years and it has been presumed that it will expand more in the future (4). This change in the demographic structure necessitates planning of services for the older people to improve the community health. Sociocultural structure of the society and its attitude and behaviours towards the elderliness are among the factors that affect the quality of these services offered to the old (5).

Aging process is a physiological incident defined as physical, mental and social regression of the person. Life quality of the older people is negatively affected because of the reasons like chronic diseases increasing in parallel with the elderliness, changes in lifestyle, retirement, loss of family members and loneliness, social and economical support loss, dependence on other people in daily life activities (6). Old age is a period in which attitude and values developed by the society towards these changes need to be evaluated (7). It is necessary to identify how the society and the individuals that will serve this group to develop health and social policies for the elder people perceive the old and what they expect from them. It is because of the fact that fallacies and negative attitudes towards growing old can cause a decrease in the quality and the efficiency of the services offered to the old people (8). The direction of these attitudes is closely related to past life of the individual, his/her cultural believes, values, educational background and motivation (1). Perception of elderliness of the individuals and so of the society may have an effect on the care for the old people and on the service offered to them (9).

Attitudes and perceptions of the individual, of the society and of the health professionals towards the old age and the old aged people are extremely important for the increasing old age population in our country in terms of having a healthy and productive old age period (10,11). Improvement of the care quality of the old people depends on the development of positive attitudes between the old aged and the health personnel (12). Especially attitudes and behaviours of the nurses who- in an integrated approach- have a role in every place the old people take part and who have a chance and responsibility for following people closely are of vital importance in improving old aged health (11).

Although in our country approaches arising from Turkish culture stiffen affection and respect for the old people and positive thoughts like taking the care responsibility of the old people, old people may be seen as a dependent group and a burden because of being nonproductive and their growing health problems. For this reason, working with the old people requires knowledge, skill, a particular patience and attention on this matter (5,8,11). Nursing curriculum and schools offering nursing education may play an important role in developing positive attitudes of nursing students towards growing old and the elderliness (8). Attitudes of the students towards the elderliness affect their field selection after the graduation and working performance. While developing positive attitudes by the students who have knowledge of the elderliness has a positive effect on working preference with the old people after the graduation and their performance, it has been observed that lack of knowledge of the elderly care reinforces negative attitudes towards the old people (13). First step to realize this is to make studies identifying opinions and attitudes of the students towards the old people.

Attitudes of the nursing students towards the elderliness based on their experiences with the family, social and cultural environment they live in and the old people can be developed in a positive way providing that they have knowledge of the issue through the education they will get in their four-year-pupilage process. Nurses who have knowledge of geriatrics and who hold positive views for the old people will have a positive effect on the quality of elderly care by working more willingly.

Aim

The aim of this study is to identify the attitudes of the nursing students towards the old people and the relation between these attitudes and experiences of the students with the old people and some demographic variables.

Methods

The population of this descriptive cross sectional type study was meant to involve total 230 nursing students who study in Sinop University School of Nursing in 2010-2011 academic year. It had been aimed to include this whole population to the study and there was no sampling selection. However, there were total 192 students-those who were in school at the time and those who were willing to participate- taking part in the study. As the data collecting tool, student description form that was prepared under the guidance of the literature relevant to the issue and Kogan's Attitudes Toward Older People (KAOP) were used (14). KAOP was developed by Nathan Kogan in 1961 and was declared to be used in the evaluations of the attitudes towards the old people in our country by Erdemir et al. (2010) and Uğurlu et al. (2011) (15,16).

Kogan's Attitudes Toward Older People is composed of 34 entries about the old people. While 17 of them express negative opinions about the old people, other 17 entries are positive. KAOP is a six point, likert type scale consisting of options as 'strongly disagree', 'a bit disagree', 'disagree', 'agree', 'a bit agree', 'strongly agree'. Points in the scale mean 1=strongly disagree, 2=a bit disagree, 3=disagree, 4=agree, 5=a bit agree and 6=strongly agree for the positive entries and vice versa for the negative ones. Sum of the negative and positive entries could either be separately calculated or total points of all the entries could be added and total score could be obtained. Maximum total score that can be obtained from the scale is 204 and the minimum one is 34. While 102 points show a neutral attitude towards the old person, higher points indicate positive attitudes; lower points indicate negative attitudes.

The data was evaluated in SPSS for Windows 14.00 statistic package. In the evaluation, descriptive statistics like percentage, average, standard deviation and Mann Whitney-U test, Kruskal Wallis

and t test for the independent variables were used. Statistical significance level was accepted as $p < 0.05$.

In the running of the study, the aim of the study was made clear to the students and their verbal and written consents were taken by paying attention to the willingness and voluntariness principles to participate in the study. There was also a permission from the high school directorate where the study data were compiled.

Results

Seventy six percent of the people participating in the study is girl, 24% of them boy. 71.4 % of them is at 18-22 age, 28.7% of them at 23-28 age and the average of age is 20.86 ± 1.56 . other demographic features of the student are shown in Table 1.

Table 1. Demographic features of the students

Demographic Features		N	%
Age	18-22 age	137	71.4
	23-28 age	55	28.7
Gender	Girl	146	76.0
	Boy	46	24.0
Class	1.Grade	51	26.6
	2.Grade	49	25.5
	3.Grade	49	25.5
	4.Grade	43	22.4
Income State	Low	22	11.5
	Middle	164	85.4
	High	6	3.1
Living Place	Dormitory	78	40.6
	At Home with the Family	9	4.7
	At Home with the Flatmates	105	54.7
Country	City Center	81	42.2
	Town	80	41.7
	Village	31	16.1
Total		192	100

According to Table 2, 75.5% of the students do not live with an old or more than one old person at home; 52.6% of them have an experience of living with the old people; 74.5% of them have never worked with the old people; most of them (70.8%) wants to work with the old people after the graduation; 65.1% of them say there is no old person in their family.

Scores that the students participating in the study got from the Attitudes Toward Older People scale changed between 45 and 204 points and the score average was 121.56 ± 13.60 . While the average score of the negative opinions about the elderliness that the students indicated in the scale was 57.64 ± 10.74 , the average score of the positive opinions was 63.91 ± 11.41 .

According to Table 3, when the relation between the demographic features and the average scores taken from the scale was examined, there was not a statistically huge difference between the average scores that the students got according to their age, class, living place and country ($p > 0.05$). When the average scores that the students got from the scale based on their gender were evaluated, male students (124.67 ± 17.38) had a higher score than the female students (120.58 ± 12.08), which means females students had a more positive attitude towards the old people. However, this difference was not found to be statistically meaningful ($p > 0.05$).

When the relation between the experiences about the old people and the average scores taken from the scale was examined, the score average (120.54 ± 14.45) of the students having people aged 65 and older in their family was lower than the score average (123.85 ± 11.38) of the students who do

Table 2. Experiences of the student with regard to the old people

Experiences with regard to the old people		n	%
Do you live with a person/the people aged 65 and older in your house?	Yes	47	24.5
	No	145	75.5
Have you ever lived with a person/the people aged 65 and older in the past?	Yes	101	52.6
	No	91	47.4
Do you have any experience as to working(care-treatment) with the people aged 65 and older in the past?	Yes	49	25.5
	No	143	74.5
Do you want to work(care-treatment) with the people aged 65 and older after the graduation?	Yes	136	70.8
	No	56	29.2
Is there a person or more than one person aged 65 and older in your family?	Yes	125	65,1
	No	67	34,9
Total		192	100

Table 3. The relation between demographic features and average scores taken from the scale

Demographic Features		Scale Average Score±Standard Deviation	p
Age	18-22 age	121.45±1.21	0.920
	23-27 age	121.84±1.61	
Gender	Girl	120.58±12.08	0.283
	Boy	124.67±17.38	
Class	1.Grade	118.84±19.44	0.371
	2.Grade	122.08±10.28	
	3.Grade	123.55±11.52	
	4.Grade	122.08±10.24	
Income State	Low	119.45±15.02	0.642
	Middle	121.68±13.47	
	High	126.00±12.77	
Living Place	Dormitory	120.21±14.50	0.954
	At home with the family	127.22±32.83	
	At home with the flatmates	122.08±9.84	
Country	City Center	121.83±14.25	0.282
	Town	121.01±14.60	
	Village	122.26±8.60	

Table 4. The relation between experiences with regard to the old people and average scores taken from the scale

Experiences with regard to the old people		Scale Average Score±Standard Deviation	p
Do you live with a person/the people aged 65 and older in your house?	Yes	120.30±12.57	0.206
	No	121.97±13.94	
Have you ever lived with a person/the people aged 65 and older in the past?	Yes	122.37±10.44	0.387
	No	120.66±16.43	
Do you have any experience as to working(care-treatment) with the people aged 65 and older in the past?	Yes	120.98±10.52	0.506
	No	121.76±14.54	
Do you want to work(care-treatment) with the people aged 65 and older after the graduation?	Yes	122.12±14.29	0.386
	No	120.20±11.79	
Is there a person or more than one person aged 65 and older in your family?	Yes	120.54±14.45	0.034*
	No	123.85±11.38	

* $p<0.05$

not have people aged 65 and older in their family. In other words, students with no old people in their family had a more positive attitude towards the old people and this difference was found to be statistically meaningful ($p<0.05$). The difference between the scores of the students that live with the people aged 65 and older in their house (120.30 ± 12.57) and those that do not (121.97 ± 13.94) was not found to be statistically meaningful ($p>0.05$). Even if students who stated that they had lived with old people in the past had a higher score when compared to those who had not, this difference was not statistically meaningful, either ($p>0.05$). Even if students

who stated that they want to work (care-treatment) with the people aged 65 and older were found to get a higher score than those who do not, this difference was statistically unimportant, as well ($p>0.05$) (Table 4).

Discussion

In the study made with the students of Health Sciences Faculty by Erdemir et al. (2010) in our country, it was confirmed that the points that the students got from the scale changed between 86-175 and the average score was 132.9 ± 14.74 and the students had

slightly positive attitudes towards the elderliness (15). In the study that was made with 191 taiwanese med students and 84 taiwanese nursing students, it was confirmed that nursing students' total points were 156.86 ± 17.56 from KAOP scale and they had a more positive attitude than the med students (17). In the study that was made with jordanian nursing students by Hweidi et al. (2006), KAOP score average of the students was 110.6 ± 21.79 (18). In the study by Yen et al. (2009), KAOP point average was 144.3 ± 17.89 and total points changed between 34 and 238. Half of the subjects had a higher point than the average score and they had a very positive attitude towards the old people (19). In our study, scores that the students got from the Attitudes Toward Older People scale changed between 45 and 204 and the average score of the sampling was 121.56 ± 13.60 . These results show that students' attitudes towards the old people were more positive in the study conducted in Jordan; on the other hand, students' attitudes towards the old people were less positive in the study conducted in our country by Erdemir et al. and in other studies conducted in other countries. This finding supports that attitudes and behaviours towards the old people may vary depending on society types and even on cultural and family features in the same society (20).

In a study made with the undergraduate students of Psychological Counseling and Guidance by Iwasaki et al. (2008), the score average of the negative views of the students about the elderliness was found to be 42.95 ± 7.46 and the score average of the positive ones was found to be 45.81 ± 6.13 (21). Similarly, in our study, too, the score average of the negative views of the students about the elderliness (57.64 ± 10.74) was lower than then the score average of the positive ones (63.91 ± 11.41).

In the study made with jordanian nursing students (2006), it was confirmed that male students and senior students had a more positive attitude towards the old people (18). In two different studies conducted by Kwan et al. (1994) and by Stewart et al. (2005), on the other hand, it was confirmed that female students had a more positive attitude than male students (22,23). Similarly, in the study made with med and nursing students by Wang et al. (2009), it was confirmed that female students (148.27 ± 18.97) had higher points than male students (140.47 ± 15.93) and second year students

(146.01 ± 18.59) had more positive views than senior students (140.05 ± 15.31) (17). In a study conducted in Sweden to evaluate the attitudes of 41 nurses and of 151 nursing student towards the elderliness (2001), it was confirmed that male students aged 25 and below had less positive attitudes towards the elderliness (24). In a study conducted in Greece with 390 freshmen and senior nursing students (2005), senior students had more positive attitudes than freshmen (25). Similarly, in the study made with med students by Hughes et al. (2008), when the attitude of the student was evaluated based on his/her class, it was stated that senior students had more positive attitudes towards the old people (26). In our country, in the study made with 399 nursing and physiotherapy and guidance students by Uğurlu et al. (2011), KAOP scale score of the girls (122.75 ± 12.50) was lower than the score of the boys (124.37 ± 12.69) and this difference was not found to be statistically meaningful. In the same study, there was not a big difference between scale points based on the classes (16). In another study conducted in our country to identify the opinions and views of the freshmen and senior nursing students about the elderliness and growing old (2010), almost half of the freshmen and senior students participating in the study delivered negative opinions and it was confirmed that senior students had more positive opinions and views about growing old and about the elderliness than freshmen (8). In our study, too, when the relation between average scores taken from the scale according to the gender was examined, it was found that male students (124.67 ± 17.38) had higher scores than the female students (120.58 ± 12.08); in that, male students had more positive attitudes towards the old people than female students; however, this difference was not found to be statistically meaningful ($p > 0.05$). Even if it was not statistically meaningful in our study, the average score of the senior students taking from the scale (122.08 ± 10.24) was found to be higher than freshmen (118.84 ± 19.44) ($p > 0.05$). This finding makes us think that the education that the students receive in the university has a positive contribution on the students and it affects their opinions about the old people in a positive way (5). Besides, the fact that senior students are elder and more mature than the freshmen might be effective in their more positive attitudes towards the old people.

According to the study by Yilmaz and Özkan to identify the attitudes of the nursing students towards the old discrimination (2010), it was stated that students who were born in places like village/town showed a more positive discrimination towards the old people than those born in central settlements (5). In village communities, old people's opinions are appreciated and they are respected and they have an important place in the village and in the family (20). In our study, too, even if it was not statistically meaningful, it was confirmed that students who live in villages (122.26 ± 8.60) had more positive attitudes towards the old people than those living in the city (121.83 ± 14.25) and in the county town (121.01 ± 14.60). This difference between attitudes towards the old people according to the settlements was thought to be caused by the facts that in small settlements, there are more extended families and the old people are more respected there and there is more close relationship and communication with the old people because of the cultural habits.

In the study conducted by Yilmaz and Özkan (2010), it was stated that spending more time with the old people had an effect on the nurses to have positive feelings for the old people and it showed that students living with the old people in their family developed positive feelings towards the old people (5). In the study conducted by Uğurlu et al. (2011), there was not a meaningful difference between the attitudes of the students who live with the old people (123.76 ± 11.56) and those who do not (123.42 ± 12.83) (16). In the literature, it was stated that those who had a close relationship experience with their grandfather and grandmother or with an old relative developed a more positive attitude (13). In our study, attitudes of the students who live with people aged 65 and older in their house (120.30 ± 12.57) and those who do not (121.97 ± 13.94) were similar. Besides, in our study, even if students who stated that they had lived with the old people in the past had higher scores than those who had not, this difference was not found to be statistically meaningful. In our study, it was stated that students who do not have an old family member in their family had more positive attitudes towards the old people than those who do and this difference was found to be statistically meaningful ($p < 0.05$). Having an old people in the family and

living with the old people and having close relationship with them and being all the time with them are different from each other and this affected the attitudes in different ways. Witnessing the negative effects of the elderliness may cause the development of negative attitudes as the experiences with the old people increase; on the other hand, getting a better understanding of the old people and making the communication with them stronger may lead to the development of positive attitudes.

In a study conducted in Sweden to identify the attitudes of 41 nurses and 151 nursing students towards the elderliness (2001), it was stated that participants had limited experiences with the old people (24). In our study, too, in a similar way with this study, most of the students (74.5%) stated that they had never experienced working (care-treatment) with the people aged 65 and older in the past.

In the study conducted by Wang et al. (2009), 75% of the nursing students stated that they were volunteer for working in geriatric nursing area after the graduation (17). In the study conducted in Scotland with 176 nursing students (16 of them male and 160 of them female) (2003), it was stated that the students had a positive approach towards working with the old people (27). In the study conducted in our country with the nursing students by Yilmaz and Özkan (2010), 74.3% of the students stated that they wanted to work with the old patients after the graduation (5). In our study, too, in a similar way with the literature, 70.8% of the students stated that they wanted to work with the old people aged 65 and older and the score average that these students got from the scale was higher than the others but this difference was not found to be statistically important ($p > 0.05$). As working with the old people requires a particular patience, attention, knowledge and skill, the more one wants to work in this field, the higher it will make the care quality of the old people (11). Covering geriatrics in the nursing education may affect positively the wish for working in geriatrics by making students have knowledge of and be skilled at this issue.

Conclusion

In conclusion, attitudes of the nursing students towards the old people are found to be slightly positive. On the other hand, students with no old people in their family are found to have a more positive

ve attitude when compared to the ones with the old people in their family. During nursing undergraduate and postgraduate education, it is suggested that in the curriculum and in application areas, more attention should be paid on the geriatrics and students should be supported for their participation in congresses, seminars and symposiums about the geriatrics. It is because of the fact that there is an important relation between positive attitude towards the old people and the knowledge. In other words, the more knowledge and skill level about the aging process and the old aged health increase, the more positive attitude towards the old people will develop and this will contribute to increasing life quality of the old people.

References

1. Akdemir N, Çınar Fİ, Görgülü Ü. Yaşlılığın Algılanması ve Yaşlı Ayrımcılığı, *Turkish Journal of Geriatrics* 2007; 10(4): 215-22.
2. Mandiracioğlu A, Dünyada ve Türkiye’de yaşlıların demografik özellikleri, *Ege Tıp Dergisi / Ege Journal of Medicine* 2010; 49(3): 39-45.
3. Adrese Dayalı Nüfus Kayıt Sistemi 2011 Yılı Sonuçları http://www.tuik.gov.tr/PreTablo.do?tb_id=39&ust_id=11 Erişim: 10 Ocak 2012.
4. Türkiye İstatistik Yıllığı 2010, Türkiye İstatistik Kurumu Matbaası, Ankara, Nisan 2011. ss: 92 www.tuik.gov.tr/IcerikGetir.do?istab_id=1
5. Yılmaz E, Özkan S. Hemşirelik Öğrencilerinin Yaşlı Ayrımcılığına İlişkin Tutumları. *Maltepe Üniversitesi Hemşirelik Bilim ve Sanatı Dergisi* 2010; 3(2): 35-53.
6. Günaydin R. Yaşlılarda Yaşam Kalitesinin Değerlendirilmesi, *Turkish Journal of Geriatrics* 2010; 13(4): 278-84.
7. Er D. Psikososyal Açıdan Yaşlılık, *Firat Sağlık Hizmetleri Dergisi*. 2009; 4(11): 131-44.
8. Kulakçı H. Hemşirelik Lisans Programı Birinci ve Dördüncü Sınıf Öğrencilerinin Yaşlılık ve Yaşlanmaya İlişkin Düşüncelerinin ve Görüşlerinin Değerlendirilmesi, *Dokuz Eylül Üniversitesi Hemşirelik Yüksekokulu Elektronik Dergisi* 2010; 3(1): 15-22. Erişim: 8 Ocak 2012 http://www.deu.edu.tr/UploadedFiles/Birimler/18280/15-22_pdf.pdf
9. Kodama H, Suda Y, Takahashi R, Nishimura M, Izumo Y, Watanabe M, Kudo H, Kudo H, Sasaki H. Family Relationships for Self-Care-Dependent Older People at Home. *Geriatrics & Gerontology International* 2007; 7(3): 252-57.
10. Vatan S, Gençöz T. Huzurevinde Yaşayan Sakinlerin Kuruma Yönelik Düşünce ve Beklentileri: Niteliksel Bir Çalışma. *Kriz Dergisi* 2002; 12(2): 19-32.
11. Hope KW. Nurses’ Attitudes Towards Older People: A Comparison Between Nurses Working in Acute Medical and Acute Care of Elderly Patient Settings. *Journal of Advanced Nursing* 1994; 20(4): 605-12.
12. Gözüm S, Tan M. Birinci Basamakta Çalışan Sağlık Personelinin Yaşlı Bakımına İlişkin Bilgi Görüş ve Uygulamaları. *Turkish Journal of Geriatrics* 2003; 6(1): 14-21.
13. Akin B, Seviğ Ü, Karataş N. Türkiye’de Gerontoloji Hemşireliği Eğitimi (II): Bir Sertifika Eğitim Programı Geliştirme Çalışması Deneyimler ve Eğitim Programı Önerisi. *C.Ü. Hemşirelik Yüksekokulu Dergisi* 2001; 5(1): 40-43.
14. Kogan N. Attitudes toward old people: The development of a scale and an examination of correlates. *Journal of Abnormal and Social Psychology* 1961; 62: 44-54.
15. Erdemir F, Kav S, Akgün Çitak E, Hanoğlu Z, Karahan A. A Turkish version of Kogan’s attitude toward older people (KAOP) scale: Reliability and validity assessment *Archives of Gerontology and Geriatrics* 2010; 52(3): e162-e165.
16. Uğurlu N, Karakaya MG, Çitak Karakaya İ, Subaşı Baybuğa M, Demir Uysal D, Acer N, Yakin B, Kogan N. Turkish Version of Kogan’s Old People Scale: A Validity And Reliability Study. *Turkish Journal of Geriatrics* 2011; 14(2): 145-53.
17. Wang CC, Liao WC, Kao MC, Chen YJ, Lee MC, Lee MF, Yen CH. Taiwanese Medical and Nursing Student Interest Levels in and Attitudes Towards Geriatrics. *Ann. Acad Med Singapore* 2009; 38: 230-36.
18. Hweidi, IM, Obeisat SM. Jordanian Nursing Students’ Attitudes Toward the Elderly. *Nurs Educ Today* 2006; 26: 23-30.
19. Yen CH, Liao WC, Chen YR, Kao MC, Lee MC, Wang CC. Chinese version of Kogan’s Attitude Toward Older People Scale: Reliability and Validity Assessment. *Int J Nurs Stud* 2009; 46(1): 37-43.
20. Konak A, Çiğdem Y. Yaşlılık Olgusu: Sivas Huzurevi Örneği. *C.Ü. Sosyal Bilimler Dergisi* 2005; 29(1): 23-63.
21. Iwasaki M, Jones, JA. Attitudes Toward Older Adults: A Reexamination of Two Major Scales. *Gerontology & Geriatrics Education* 2008; 29(2): 139-57.
22. Kwan AYH, Law BK. Attitudes of student/pupil nurse toward the aged in Hong Kong: implications for nursing education. *Hong Kong J Gerontol* 1994; 8: 43-51.

23. *Stewart JJ, Giles L, Paterson JE, Butler SJ. Knowledge and Attitudes Towards Older People: New Zealand Students Entering Health Professional Degrees. Phys Occup Ther Geriatr 2005; 23: 25-36.*
24. *Söderhamna O, Lindencronab C, Gustavssona SM. Attitudes Toward Older People Among Nursing Students and Registered Nurses in Sweden. Nurse Education Today 2001; 21(3): 225-29.*
25. *Lambrinou E, Sourtzi P, Kalokerinou A, Lemonidou C. Reliability and validity of the Greek Version of Kogan's Old People Scale. Journal of Clinical Nursing 2005; 14(10): 1241-247.*
26. *Hughes NJ, Soiza RL, Chua M, Hoyle GE, McDonald A, Primrose WR, Seymour DG. Medical Student Attitudes Toward Older People and Willingness to Consider a Career in Geriatric Medicine. Journal of the American Geriatrics Society 2008; 56(2): 334-38.*
27. *McKinlay A, Cowan S. Student Nurses' Attitudes Towards Working With Older Patients. Journal of Advanced Nursing 2003; 43(3): 298-309.*

Corresponding Author

Bilge Bal Ozkaptan,

Sinop University School of Nursing,

Ordu Koyu Mevkii,

Sinop,

Turkey,

E-mail: bilgebal57@hotmail.com

Conceptual skill in physicians: An overlooked basic competency

Khajavi Abdoljavad¹, Vatankehah Soudabeh¹, Maleki Mohammad Reza¹, Barati Ahmad¹, Alami Ali², Heyrani Ali¹

¹ Department of Health Services Management, School of Health Management and Information Sciences, Tehran University of Medical Sciences, Tehran, Iran,

² Social Development & Health Promotion Research Center, Gonabad University of Medical Sciences, Gonabad, Iran.

Abstract

Introduction: There is currently little effort to train physicians regarding leadership and management skills in medical education; however, it is acknowledged that attainment of such competencies is no longer an optional extra for doctors. Meeting this challenge is essential for healthcare system development. This study was conducted to assess general practitioners' (GPs') conceptual skill as one of the key components and basic management skills.

Methods: This was a cross-sectional study which conducted among new graduate GPs from Iran in 2009. Using a systematic sampling method, 141 samples were selected. A valid and reliable questionnaire with 23 questions in 6 domains was applied. The data were analyzed with SPSS software.

Results: A total of 141 questionnaires were completed. Of the 141 GPs, 29.8% had a desirable level of conceptual skill, and the others had a moderate level. Ranging from 23 to 115, the mean scores of men and women were 80.74 (SD 7.18) and 80.76 (SD 6.57), respectively ($P=0.983$). The total score for the married GPs (18% were married) was 85.52 (SD 3.32), while it was 79.72 (SD 7.01) for the singles ($P<0.001$). This correlation was supported by linear regression results ($P<0.001$). The mean rank order of conceptual skill domains indicated that, the highest and lowest ranks were assigned to goal setting and achieving, and strategic thinking and planning domains, respectively.

Conclusion: The results suggest that more attention be paid to training physicians in management skills. Also, further research on the assessment of these skills in physicians is recommended. It would be useful to adapt the physicians' competencies to the changing healthcare system.

Key words: Physicians, Conceptual skill, Management skills, Medical education

Introduction

Today's ever-changing healthcare environment requires new roles and responsibilities for physicians. It is believed that healthcare system improvement considerably depends on physicians' active engagement not only in their professional activities but also in their leadership and management roles (1). Increasing complexity in healthcare system also suggests a growing need for physicians who have leadership and management competencies (2-4). Similarly, the Kennedy Report (5) emphasized, there is a need for all physicians to undertake management training. They could then perform their professional and managerial roles, effectively.

Traditionally, medical education is focused on clinical and professional skills (6). Formal training in management skills is often lacking in medical education curricula, due to little attention to these skills (7-10). However, it is generally accepted that management skills should be learned by all doctors to perform their professional roles more effectively (11). The Royal College of Physicians (12) has well recognized this issue and recommended medical schools take on the responsibility to develop physicians with management skills. It is also recommended that the UK General Medical Council revises the "Tomorrow's Doctors" document to enhance managerial skills among general practitioners (GPs). These are the reasons why Clark and Armit (11) believed that "attainment of competency in management and leadership will no longer be an optional extra for physicians".

However, there is much debate on the nature and components of management skills (10, 13, 14). As a

pioneer, Katz (15) introduced a typology with three main categories of management skills consisting of technical, human, and conceptual skills. He generally stated, technical and human skills are about substances and individuals, respectively, while conceptual skill implies intellectual capabilities of the individuals which focused on ideas and concepts. So, the conceptual skill is generally defined as “the ability to see an organization as a whole or to have a systemic viewpoint” (16).

Although there are differences between newer approaches to managerial skills and the Katz approach, more or less they follow the Katz’s categorization (13, 17-19). For instance, to develop a competency assessment tool in healthcare administration, Robbins and Bradley (13) delineated four managerial skills consisting of technical, industry knowledge, analytic and conceptual reasoning, and interpersonal and emotional intelligence. Smith (18) considered another classification of management skills consisting of interpersonal, action, information management, and analytical skills to identify competencies for effective performance of physician-managers. In this study, doctors assessed themselves at the lowest level in analytic skill compared with other skills. Another research which was done to design a model for training hospital managers, displayed 14 components in the conceptual skill category including existing vision, focusing on crucial issues, analyzing problems, and making decision in uncertain conditions (17). This research showed that, among management skills, the conceptual skill had the greatest impact on job performance of hospital managers. Moreover, Moore and Rudd (19), articulated the conceptual skill into six different domains consisting of creating vision, strategic thinking and planning, decision making, creative thinking, setting and achieving goals, and organizational change. This brief review indicates that the above-mentioned differences are also reflected in the healthcare literature.

Despite the recognition of the importance of managerial skills for physicians, there is often no systematic training of these skills in undergraduate medical education curriculum (4, 11, 20, 21); the curriculum, which provides a foundation for future learning and practice of medical students (22). There is currently also no systematic training of management skills in the GP curriculum in Iran

(23). According to the relatively extensive search by the authors (MEDLINE & CINHALL databases and Scopus citation database in the period of 1990-2011), there are only a few studies which have assessed physicians’ management skills. So, this study conducted to evaluate conceptual skill, as one of the basic and key components of managerial skills, among new graduate GPs from medical schools in Iran in 2009 and to determine relationships between the skills and some of their baseline characteristics.

Materials and methods

This was a cross-sectional study which conducted among the Iranian GPs in 2009. Our study population was all GPs who currently graduated from Iran’s Universities of Medical Sciences and for his/her name registration, referred to Medical Council of our country. According to pilot study results, we systematically selected 141 samples to conduct the research. Gathering the data, we used a two-part valid and reliable questionnaire. The first part was related to general information of the respondents consisting of gender, marital status, and graduating date. Using the second part of the questionnaire, with a total of 23 questions, the respondents’ conceptual skill was assessed via a 5-point rating scale (we will be glad to send the questionnaire to interested readers).

Based on Moore and Rudd’s research (19), we considered six domains for conceptual skill consisting of creating vision, strategic thinking and planning, decision making, creative thinking, goal setting and achieving, and organizational change. We scored each question from 1 (very low agreement) to 5 (very high agreement). So, total range of the respondent’s score was measured between 23 and 115. According to the range, we then categorized the GPs into three levels comprising of weak (<54), moderate (between 54 and 84), and high (desirable) (>84). Using SPSS software (version 16), we analyzed the data with $P < 0.05$ as level of significance. Validity of the questionnaire was determined through content and face validity, and its reliability was assessed by Cronbach’s Alpha coefficient (0.69).

To run the research, the researchers achieved agreement of the Medical Council’s directors. Before beginning the data collection process, we

also verbally obtained the physicians' consent to participate the study. The samples were informed of their rights if they wanted to cease their participation during the interview.

Results

We used 141 questionnaires to analyze the data. Of the 141 GPs, 51.8% (73/141) were men and 48.2% women. Based on marital status, 82.3%

(116/141) of the GPs were single, and the others were married. The mean age of the respondents was 26.8 years (SD 1.68; range 25-34). Mean scores of the conceptual skill in men was 80.74 (SD 7.18) and in women, it was 80.76 (SD 6.57) ($P=0.983$). It was also 85.52 (SD 3.32) and 79.72 (SD 7.01) in the married and single samples, respectively ($P<0.001$).

In general, the conceptual skill of 70.2% (99/141) (Mean 77.46; SD 5.30) of the physicians was in moderate level, and for the others (29.8%)

Table 1. The respondents' conceptual skill levels and its associations with gender and marital status ($N=141$)

Variables		Conceptual skill levels		P-Value*
		Moderate (54-84) No (%)	Desirable (>84) No (%)	
Gender	Male	46 (63%)	27 (37%)	0.053
	Female	53 (78%)	15 (22%)	
Marital status	Married	13 (52%)	12 (48%)	0.028
	Single	86 (74%)	30 (26%)	

* X^2 test statistics

Table 2. Mean scores of the conceptual skill domains and its associations with the respondents' gender ($N=141$)

Conceptual Skill Domains (No of Questions)	Gender		P-Value*
	Male (n=73) Mean (SD)	Female (n=68) Mean (SD)	
Creating Vision (5)	17.38 (2.60)	17.59 (2.17)	0.614
Strategic Thinking and Planning (6)	19.99 (2.72)	20.09 (3.19)	0.838
Decision Making (2)	7.55 (1.55)	7.47 (1.03)	0.725
Creative Thinking (5)	17.14 (2.61)	17.26 (1.91)	0.742
Goal Setting and Achieving (2)	7.71 (2.18)	7.78 (1.52)	0.832
Organizational Change (3)	10.97 (1.32)	10.57 (1.53)	0.107
Total score	80.74 (7.18)	80.76 (6.57)	0.983

* Independent t-test statistics

Table 3. Mean scores of the conceptual skill domains and its associations with the respondents' marital status ($N=141$)

Conceptual Skill Domains (No of Questions)	Marital Status		P-Value*
	Single (n= 116) Mean (SD)	Married (n= 25) Mean (SD)	
Creating Vision (5)	17.09 (2.40)	19.32 (1.28)	<0.001
Strategic Thinking and Planning (6)	19.86 (2.98)	20.84 (2.67)	0.133
Decision Making (2)	7.41 (1.31)	8.00 (1.26)	0.040
Creative Thinking (5)	17.10 (2.39)	18.08 (1.50)	0.006
Goal Setting and Achieving (2)	7.68 (1.95)	8.04 (1.57)	0.327
Organizational Change (3)	10.68 (1.49)	11.24 (1.30)	0.084
Total score	79.72 (7.01)	85.52 (3.32)	<0.001

* Independent t-test statistics

(Mean 88.50; SD 2.54), it was in high (desirable) level. According to the findings presented in table 1, there were no significant associations between the conceptual skill levels and the respondents' gender ($P= 0.053$). While there was a significant relation between the levels of conceptual skill and marital status ($P= 0.028$).

Tables 2 and 3 show the mean scores of different domains of the GPs' conceptual skill in terms of gender and marital status, respectively. There were no significant associations between gender and the different domains in table 2, but, we found significant relations between marital status and creating vision ($P<0.001$), decision making ($P= 0.040$) as well as creative thinking domains ($P= 0.006$) which are presented in table 3. Table 4 shows the weighted mean rank order for the conceptual skill domains based on gender, marital status and the total respondents. The results indicated the rank order was the same in all groups, and the highest and the lowest ranks were assigned to goal setting and achieving,

and strategic thinking and planning domains, respectively. Figure 1 also represents the weighted mean of the conceptual skill domains in terms of the respondents' marital status.

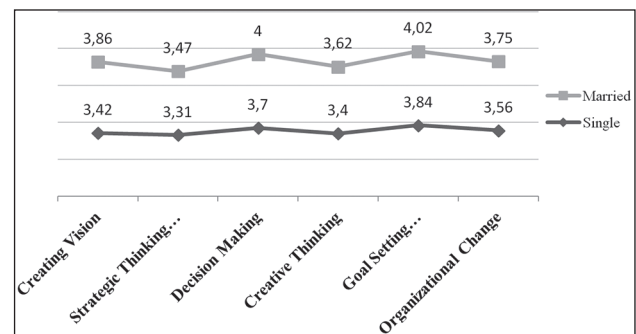


Figure 1. Weighted mean of the conceptual skill domains in terms of the respondents' marital status

Since conceptual skill level of individuals may be improved with increasing age (2), it is expected that the significant association between marital status and conceptual skill which are presented in

Table 4. The weighted mean rank order for conceptual skill domains in terms of gender, marital status, and the total respondents ($N= 141$)

Conceptual Skill Domains	Weighted mean (SD)					Rank*
	Gender		Marital Status		Total (N=141)	
	Men (n= 73)	Women (n= 68)	Single (n= 116)	Married (n= 25)		
Goal Setting and Achieving	3.86 (1.091)	3.89 (0.762)	3.84 (0.975)	4.02 (0.784)	3.87 (0.944)	1
Decision Making	3.77 (0.773)	3.74 (0.515)	3.70 (0.656)	4.00 (0.629)	3.76 (0.660)	2
Organizational Change	3.66 (0.465)	3.52 (0.510)	3.56 (0.497)	3.75 (0.433)	3.59 (0.490)	3
Creating Vision	3.48 (0.521)	3.52 (0.433)	3.42 (0.480)	3.86 (0.256)	3.50 (0.480)	4
Creative Thinking	3.43 (0.521)	3.45 (0.383)	3.40 (0.478)	3.62 (0.300)	3.44 (0.458)	5
Strategic Thinking and Planning	3.33 (0.453)	3.35 (0.532)	3.31 (0.497)	3.47 (0.445)	3.34 (0.491)	6

* The rank order is exactly the same in all groups and the total respondents

Table 5. Univariate and multiple linear regression results for correlation between the respondents' conceptual skill and marital status after controlling age variable

Variables	Univariate Linear Regression Results				Multiple Linear Regression Results	
	Un-standardized		Standardized Beta	P-Value	Standardized Beta	P-Value
	Beta	SE				
Marital Status	5.796	1.438	0.323	<0.001	0.345	<0.001
Age	-0.638	0.342	-0.156	0.064	-0.194	0.016

tables 1 and 3 is confounded with age variable. So, we first calculate the mean age and standard deviation of the single (26.72; SD 1.58) and the married (27.20; SD 2.08) GPs. There was no significant difference between the mean ages of the groups ($P= 0.193$). To control potential confounding effect of age, we also run a linear regression model. Table 5 shows the results. In spite of controlling the age effect we could see there is still significant association between the respondents' marital status and their conceptual skill scores ($P<0.001$).

Discussion

All doctors, to be considered an effective doctor in the future, will be needed to obtain competence in clinical as well as management skills (11). Currently, training the latter skills is not integrated in undergraduate medical education in most countries such as Iran (4, 11, 20, 21, 23). In this research, we evaluated the conceptual skill among the GPs who graduated from Iranian universities.

According to our results, the conceptual skill status of a majority of the GPs (70%) was in moderate level and for the others, it was in high level. The mean score of the married physicians was significantly higher than the single ones. There were also significant association between the GP' conceptual skill levels and their marital status so that the married subjects had more desirable of the skill level than the singles. In this study, the mean rank order for conceptual skill domains showed that, the highest and lowest ranks were allocated to goal setting and achieving, and strategic thinking and planning, respectively.

As noted above, our findings indicated that the level of conceptual skill among 70% of the GPs was moderate. This would be logical because there is no comprehensive program to train and develop managerial skills in Iran's medical education system. In a research which was done to recognize essential eligibilities for effective performance of physician-managers, the respondents' score for conceptual skill was also lower than the other domains of management skills (18). Our result would also be comparable with Smith and Young's results (14). They indicated, the conceptual skill of physicians is not usually strong, because they often focus on their own professional

duties and didn't comprehend how relations their works with other related activities. Considering management skills training deficiency in medical core curriculum, it seems the Katz's emphasize (15) on being required these skills could be a plausible explanation for our results.

Chuang (7) believed that because of this gap in medical training, physicians could not appropriately know the current complex and fragmented healthcare system. She indicated that adding healthcare management training to current curriculum of medical students could bridge the gap. Medical trainees also emphasized necessity to learn management knowledge and skills in various studies (10, 24, 25). In addition to the importance of meeting these needs, timing of training is also important. In Brouns et al results (24) for instance, residency period had been considered as appropriate time, while Parvizi et al (4) and Balderson and MacFadyen (21) believed training management skills should be started from the beginning of medical training period. This could then facilitate managerial roles of GPs as active and effective decision makers in healthcare systems.

Based on the conceptual skill domains, our results showed that the top two ranks were assigned to goal setting and achieving, and decision making domains. Comparable with our findings, Smith and Young (14) believed that as medical students and physicians continuously and implicitly facing with goal setting and decision making in diagnosis and treatment process, they are usually strong in these domains. This was also supported by a survey conducted in Finland wherein the respondents reported their personal professional experiences as the most important basis for their decision making (26). In deed, it may be associated with the nature of medical practice.

But contrary to our results, Smith (18) found that levels of the physicians' skills in organizational change and creative thinking domains among physicians were higher than for goal setting and achieving, and decision making domains. This disagreement may be because of differences in methods, assessment tools, and discrepancies in medical education programs. Another plausible explanation would be related to the variations in personal experiences between two samples. On the other hand, in smith's research, similar to

this study, the lowest rank was assigned to strategic thinking and planning domain. One possible cause for this finding could be due to lack of training. Schwartz and Pogge (9) believe acquiring such skills would be possible through systematic training. Besides, in response to the changing environment of healthcare delivery, physicians not only need to learn strategic planning, but also they should engage in conducting the programs to ensure the success of these programs (9, 27, 28). Bearing in mind these requirements and our results, learning such skills could be considered by medical education authorities.

In this study also, the relationship between baseline characteristics and the conceptual skill of the GPs showed a notable result worthy of elaboration. There was a significant relationship between the respondents' marital status and their conceptual skill scores. Indeed, there was not only a significant association between mean scores of the single and married physicians, but also the percentage of the married GPs who had a desirable level of conceptual skill was significantly higher than the unmarried GPs. O'Connor et al (29), and Parakandi and Asokan (30) also reported almost similar results. According to Litmanen et al (2), with increasing age, management skills level of individuals may be improved. So, the relation between marital status and conceptual skill of our respondents would probably be confounded with age. Using a regression model, adjusted for age, we still found a significant association between the GPs' marital status and their mean conceptual skill score. Although we have no clear explanation for this relationship, one could argue that being married gives a certain degree of maturity and this could lead to higher levels of conceptual skill. As a general rule, the researchers know cross-sectional study only suggest eventual relations among variables. Thus, it seems longitudinal researches will be needed to evaluate this association, properly.

Limitations

It was the first study in Iran which assessed conceptual skill, as one of the complex management skills, among the GPs. According to the sampling method, our results would have an appropriate generalizability. However, we were facing with some

limitations in this study. First, we could not broadly compare our results with other research results, resulting from little researches which measured physicians' managerial skills in the literature. Second, we could not find a valid and reliable tool to measure conceptual skill and our questionnaire was probably one of the first tools in this field. Inherent complexities of conceptual skill, as a subjective skill, lack of agreement for its domains, and diversity in operational definition of this synthetic managerial skill were some difficulties to design a relevant questionnaire. Hence, we suggest developing and revising the tool in future studies.

Conclusion

Changes in healthcare environment demand new requirements, including leadership and management skills, for physicians. According to the results of this preliminary study, less than one-third of GPs who graduated from Iranian universities have a desirable level of conceptual skill. So, we suggest that, like other researchers (2, 3, 7, 10, 11, 23, 24), management training programs would be incorporated into the medical education curricula. Indeed, there were a few researches to measure managerial skills among medical graduates. It seems running more studies in this subject not only could identify physicians' current level of management skills, but also help to develop effective educational interventions and more adaptation of the physicians' competencies to the changing healthcare system.

Acknowledgments

The authors gratefully acknowledge the financial support for this work that was provided by Tehran University of Medical Sciences. We also wish to thank all participants for kindly dedicate their time and efforts.

References

1. Chadi N. *Medical leadership: doctors at the helm of change*. *McGill J Med*. 2009; 12(1): 52-7.
2. Litmanen T, Ruskoaho J, Vänskä J, Halila H, Patja K. *Does the need for professional competencies change during the physician's career?--A Finnish national survey*. *Med Teach*. 2011; 33(5): 275-80.

3. Ackerly DC, Sangvai DG, Udayakumar K, et al. Training the next generation of physician-executives: an innovative residency pathway in management and leadership. *Acad Med*. 2011; 86(5): 575-9.
4. Parvizi N, Shahaney S, Martin G, Ahmad A, Moghul M. Instigating change: trainee doctors' perspective. *BMJ Qual Saf*. 2011.
5. Kennedy I. *The Report of the Public Inquiry into children's heart surgery at the Bristol Royal Infirmary 1984-1995*. Norwich: The Stationery Office; 2001.
6. Clark J, Morgan DM. Improving the effectiveness of health services: The importance of generating greater medical engagement in leadership. 2007; [17 screens] Available at: URL: <http://www.institute.nhs.uk>. Accessed February 21, 2012.
7. Chuang E. Expanding medical student and resident knowledge of health economics, policy, and management. *Acad Med*. 2011; 86(11): e1.
8. Kumpusalo E, Virjo I, Mattila K, Halila H. Managerial skills of principal physicians assessed by their colleagues. A lesson from Finland. *J Health Organ Manag*. 2003; 17(6): 457-62.
9. Schwartz RW, Pogge C. Physician leadership: essential skills in a changing environment. *Am J Surg*. 2000; 180(3): 187-92.
10. Busari JO, Berkenbosch L, Brouns JW. Physicians as managers of health care delivery and the implications for postgraduate medical training: a literature review. *Teach Learn Med*. 2011; 23(2): 186-96.
11. Clark J, Armit K. Attainment of competency in management and leadership: no longer an optional extra for doctors. *Clinical Governance: An International Journal*. 2008; 13(1): 35-42.
12. Royal College of Physicians of L. *Doctors in society : medical professionalism in a changing world: report of a working party, December 2005*. London: Royal College of Physicians of London; 2005.
13. Robbins CJ, Bradley EH, Spicer M. Developing leadership in healthcare administration: a competency assessment tool. *J Healthc Manag*. 2001; 46(3): 188-202.
14. Smith E, Young A. The practitioner as manager. In: Young AP, Cooke M, eds. *Managing and implementing decisions in health care*. New York: Bailliere Tindall; 2002. PP: 112-27.
15. Katz RL. *Skills of an effective administrator*. Boston, Mass.: Harvard Business Press; 2009.
16. Peterson TO, Van Fleet DD. The ongoing legacy of R.L. Katz. *Management Decision*. 2004; 42(10): 1297-308.
17. Raeissi P, Nasiripour AA. Management Development in Health Care Setting: A Training Model for Hospital Managers. *J Res Health Sci*. 2007; 2(2): 42-55.
18. Smith DM. *Physician managerial skills: Assessing the critical competencies of the physician executive [dissertation]*. United States -- Ohio: Case Western Reserve University; 1990; PP: 215.
19. Moore LL, Rudd RD. Leadership skills and competencies for extension directors and administrators. *Journal of Agricultural Education*. 2004; 45(3): 22-33.
20. Wass V. Doctors in society: medical professionalism in a changing world. *Clin Med*. 2006; 6(1): 109-13.
21. Balderson S, MacFadyen U. Management training for doctors: an in-house approach. *J Manag Med*. 1994; 8(6): 17-9.
22. General Medical C. *Tomorrow's doctors : recommendations on undergraduate medical education*: General Medical Council; 2003.
23. *Specifications, Program and Course syllabus of General Medical Education*. 1985; [141 screens] Available at URL: http://scume.behdasht.gov.ir/uploads/172_275_Sarfasl_64.pdf. Accessed February 7, 2012.
24. Brouns JW, Berkenbosch L, Ploemen-Suijker FD, Heyligers I, Busari JO. Medical residents perceptions of the need for management education in the postgraduate curriculum: a preliminary study. *Int J Med Educ*. 2010; 1: 76-82.
25. Kaur N, Singh T. Introducing medical students to health care management. *Med Educ*. 2009; 43(11): 1090-1.
26. Elina V, Juhani L, Tiina TJ, Kari M, Irma V, Mauri I, et al. Doctor-managers as decision makers in hospitals and health centres. *J Health Organ Manag*. 2006; 20(2-3): 85-94.
27. Schwartz RW, Cohn KH. The necessity for physician involvement in strategic planning in healthcare organizations. *Am J Surg*. 2002; 184(3): 269-78.
28. Gatrell J, White T. Doctors and management - the development dilemma. *J Manag Med*. 1996; 10(2): 6-12.
29. O'Connor SJ, Trinh HQ, Shewchuk RM. Determinants of service orientation among medical students. In: Friedman LH, Goes J, Savage GT, editors. *Adv Health Care Manag*. Amsterdam ; London: JAI, an imprint of Elsevier Science; 2000. p. 217-49.
30. Parakandi M, Asokan T. Impact of Demographic Variables on Managerial Skill Inventory. In: Hoque T, editor. *Proceedings of the 4th International Business and Social Science Research Conference*; 2012 Jan 5-7; Dubai, UAE: WBI Press; c2012.

Corresponding Author
 Vatankhah Soudabeh,
 School of Medical Management and Information,
 Tehran University of Medical Sciences,
 Iran,
 E-mail: abj-khajavi@razi.tums.ac.ir

The effects of self-perceived fatigue on functional mobility and balance in the community-dwelling elderly

Zeliha Baskurt¹, Ferdi Baskurt¹, Celal Haydar Demir²

¹ Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Suleyman Demirel University, Isparta, Turkey,

² Erbag Park Surgical Medical Centre, Erbag, Tokat, Turkey.

Abstract

Objective: Although fatigue is common among the elderly people, little is known concerning its impact on functional mobility and balance. The aim of this study was to investigate the effect of self-perceived fatigue on functional mobility and balance performances in the community-dwelling elderly people.

Methods: The sample consisted of 99 community dwelling elderly people of age between 65 years to 90 years (mean = 69.55, SD± 7.2). Fatigue was measured with the Turkish version of Checklist Individual Strength (CIS-T). The fatigued elderly group defined as a CIS-T total score >76. The Timed Up and Go (TUG) test was used to evaluate the functional mobility. Balance performance was evaluated with the Berg Balance Scale (BBS).

Results: The fatigued group consisted of 54 elderly people (54.5%). There were statistically significant differences between the fatigue and nonfatigue groups regarding TUG and BBS scores ($p<0.05$). Fatigue (CIS-T total and four dimensions of CIS-T) showed a significant correlation with functional mobility and balance performances ($p<0.01$).

Conclusions: We found that fatigue, as measured with the CIS-T, was associated with poor functional mobility and balance performances. These results suggest that assessment of fatigue should be considered for the clinical interventions in community-dwelling elderly population.

Key words: Fatigue, balance, functional mobility, elderly

Introduction

Fatigue is a subjective feeling of low vitality that disrupts daily functioning [1]. Fatigue is belie-

ved to be a common complaint among older adults [2]. Epidemiology of this symptom indicated that as many as 27–50% of community-dwelling older people complain of moderate to severe levels of fatigue [3-5].

Fatigue affects a person's health, reduces performance. Fatigued individual may present with a lower physical capacity [6,7]. The devastating consequences of fatigue are especially detrimental to older people, who have more seriously depleted reserves to make up for physical deconditioning [8]. Fatigue might be an early symptom of physical deconditioning or even underlying pathological changes in older people [9,10]. Liao and Ferrell found that fatigue was independently predicted by poor walking capacity among older people [9].

Assessment of fatigue is important in gerontological perspective. However, fatigue in elderly people is not routinely evaluated and has only been considered in a very limited number of studies. Literature is recommended that capturing such complex phenomenon among older people require detailed assessment on characteristics and quantification of fatigue, the key biological parameters and predisposing factors, as well as the associated distressing feelings, along with limitations on physical activities [8].

Also, the assessment of functional mobility and balance is an essential component of any geriatric assessment of older adults [11]. Functional mobility and balance in the elderly is fundamental to maintaining functional independence. Balance and mobility impairments have a tremendous impact on general health status and quality of life [12]. Due to a decrease in the physiological functions related to aging, the balance and mobility functions may be limited in elderly people [13].

The results of several studies demonstrate the significance of fatigue in elderly people. Until now, the associations between fatigue and functional mobility or balance have not been studied. It is not known whether fatigue in elderly people is associated with impaired balance and decreased mobility. Therefore, the purpose of this study was to examine the effect of fatigue symptoms on functional mobility and balance in the community-dwelling elderly. We hypothesized that increased fatigue would be associated with decreased mobility and balance performances.

Material and Methods

Subjects

The investigated population consisted of 99 subjects aged 65-90 years with an average age of 69.55 years (S.D=7.2). The study was conducted in Isparta, Turkey. A total of participants were living at their own homes. Subjects included in this cross-sectional and comparative study were eligible community-dwelling adults aged 65 years or older.

Inclusion criteria were: (a) to be able to perform the functional mobility balance tests, (b) had no medical conditions, cognitive problems and speech or hearing loss which would interfere with participation in the present study, and (c) being ambulatory independently or with a walking aid. (i.e a cane, walker).

Exclusion criteria were: (a) having an established definite diagnosis (i.e., neurological, psychiatric, or cognitive illnesses), (b) having communication difficulties, (c) having any visual or hearing problems, and (d) having an acute disease. (e) being non-ambulatory (cannot walk with or without a walking aid)

All the participants gave their informed consent for participating in the study. Demographic data was collected in order to describe the characteristics of the study sample (age, height, weight, marital and educational status).

Instruments

Berg Balance Scale (BBS) was used to evaluate of balance ability. The BBS is a performance-based measure designed to monitor performance during balance activities in community-dwelling and institutionalized older adults. The scores on the 14

items are combined for a total score, which can range from 0 to 56, with a higher score relating to better performance [14].

The Timed Up and Go (TUG) test was used to evaluate the functional mobility of the participants. The TUG is a test of easy and quick application that does not require special equipment and that could be easily included as part of the routine evaluation of elderly individuals. The TUG test measures in seconds the time taken by an individual to get up from a chair, walk a distance of 3 m, turn 180° and return to the chair, sitting down again. Two timed tests were performed and the final result was calculated as the mean of these two times [15,16].

Fatigue was measured with the *Turkish version of Checklist Individual Strength (CIS-T)*, a 20-item self-report instrument. The validity and the reliability of the Turkish version of CIS was established by Ergin&Yildirim [17]. The statements refer to aspects of fatigue experienced during the previous 2 weeks. The CIS-T covers several aspects of fatigue, such as subjective fatigue (eight items, for example, "I get tired very quickly"); concentration (five items, for example, "Thinking requires effort"); motivation (four items, for example, "I feel no desire to do anything"); physical activity (three items, for example, "I don't do much during the day"), and a total score. Items are scored on a seven point Likert scale (1 = Yes, that is true to 7=No, that is not true). The total score can range from 20 to 140. Higher scores indicate a higher degree of fatigue [18]. A cut-off score (a CIS total score which is a summation of the four aspects higher than 76) was used to distinguish individuals fatigue and nonfatigue [19,20]. The researcher administered CIS-T. Most subjects self-completed the CIS-T. For those who had difficulty reading or writing, the researcher read out the questionnaires and recorded their responses. The researcher supervised and gave advice to the subjects on how to complete the questionnaires, but gave no advice either directly or indirectly that might influence their response to the questions.

Statistical analysis

Data were analyzed statistically using the SPSS program for Windows, version 17.0. Results for continuous variables were given as mean $\pm$ standard deviation and categorical variables were gi-

ven as number and frequencies. A Chi-square test was used to compare the qualitative variables. For the comparison between the two groups the Student *t*-test for independent was used. Correlations between CIS-T, TUG, and BBS were calculated with Pearson correlation analysis. The statistical significance was considered at 0.05.

Results

All the participants completed all the selected measures and survey. The fatigued group consisted of 54 elderly people (54.5%). The basic characteristics for the fatigued and nonfatigued elderly subjects, separately, are presented in Table 1. There were statistically significant differences between the fatigue or nonfatigue groups regarding age, gender, education and marital status. ($p < 0.05$) (Table 1)

There were significant differences with respect to in TUG and BBS scores between the two groups. TUG scores were significantly higher in fatigued group compared with the nonfatigue group ($p < 0.05$). BBS scores were significantly lower in fatigued group compared with the nonfatigue group ($p < 0.05$) (Table 2)

The total CIS-T and the CIS-T subscales scores for all of the participants presented Table 3.

Table 3. Fatigue levels in the elderly (N=99)

	mean $\pm$ SD
CIS-Subjective Experience of Fatigue	30.87 $\pm$ 14.14
CIS-Reduction of Concentration	20.51 $\pm$ 8.62
CIS-Reduction of Motivation	19.55 $\pm$ 5.10
CIS-Physical Activity Level	12.31 $\pm$ 5.66
CIS-T total	83.26 $\pm$ 29.10

The relationship of the TUG scores and BBS scores to total CIS-T score and the CIS-T sub-

Table 1. Sociodemographic and physical variables related to fatigue in the elderly

	Fatigue (N=54, 54.5 %)	Nonfatigue (N=45, 45.5 %)	p	All Groups (N=99)
Age (year) (mean $\pm$ SD)	71.86 $\pm$ 7.28	67.62 $\pm$ 6.63	0.003	69.55 $\pm$ 7.22
Gender (n /%)				
Female	35/64.8	15/33.3	0.004	50/50.5
Male	19/35.2	30/66.7		49/49.5
Marital status (n /%)				
Never married	2/3.7	1/2.2	0.023	3/3.03
Married	39/72.2	29/64.4		68/68.6
Divorced	2/3.7	-		2/2.02
Widow	11/20.3	15/33.3		26/26.2
Education (n /%)				
Not literate	3/5.5	18/40	0.036	21/21.2
Primary school	34/62.9	23/51.1		57/57.5
Middle school	8/14.8	3/6.6		11/11.1
High school	9/16.6	1/2.2		10/10.1
Height (cm)	162.54 $\pm$ 6.98	167.61 $\pm$ 6.82	0.001	165.35 $\pm$ 7.30
Weight (kg)	76.20 $\pm$ 9.80	75.22 $\pm$ 12.85	0.675	75.75 $\pm$ 11.24
BMI (kg/m²)	28.54 $\pm$ 5.33	27.24 $\pm$ 4.16	0.189	27.83 $\pm$ 4.75

BMI= body mass index.

Table 2. The functional mobility and balance performance related to fatigue in the elderly

	Fatigue (N=54, 54.5 %) mean $\pm$ SD	Nonfatigue (N=45, 45.5 %) mean $\pm$ SD	p	All Groups (N=99) mean $\pm$ SD
TUG (seconds)	20.87 $\pm$ 3.25	16.51 $\pm$ 3.69	.001	18.88 $\pm$ 4.07
BBS	38.88 $\pm$ 10.89	51.27 $\pm$ 7.36	.001	45.64 $\pm$ 11.00

TUG: Timed Up and Go; BBS: Berg Balance Scale

Table 4. Correlation analysis between CIS-T scores and the performance parameters (N=99)

	TUG	BBS
	Correlation Coefficient	Correlation Coefficient
CIS-Subjective Experience of Fatigue	.601*	-.600*
CIS-Reduction of Concentration	.419*	-.478*
CIS-Reduction of Motivation	.367*	-.396*
CIS-Physical Activity Level	.490*	-.581*
CIS-T Total	.576*	-.616*

*Correlations significant at the 0.01 level

scales scores of the community-dwelling elderly are presented in Table 4. Based on Pearson correlation analysis, there was a significant positive correlation between TUG scores and CIS-T total and four dimensions of CIS-T. Similarly, a significant negative correlation was found between the BBS scores and CIS-T total and four dimensions of CIS-T ($p < 0.01$).

Discussion

Our study has documented a high prevalence of fatigue in this population. Using a published cut-point on the CSI that has been used by others [19,20], we found that 54.5 % of the older respondents had fatigue. The prevalence of self-reported fatigue among community-dwelling older adults varies widely in literature. On the lower end of the spectrum, a survey of a general medical practice in England found that 8% of subjects ages 64-75 years reported chronic fatigue lasting ≥ 6 months [21]. A large survey of community-dwelling individuals across 10 European countries found that, on average, 27% of subjects age 50-64 years and 37% of subjects ≥ 65 years old had reported exhaustion within the past month [22]. It may not be surprising that the prevalence of self-reported fatigue varies so widely across studies. The variability in fatigue prevalence is likely the result of a variety of factors, including differences in measurement tool, choice of time horizon (eg, present versus past week), selection of cutpoints defining fatigued from nonfatigued, and characteristics of the study population [23].

In the study, it was found that some demographic characteristics of community-dwelling elderly have effects on fatigue and performance measurements. Accordingly, it was found that functional

mobility and balance performances in females is lower compared with males and married patients experience fatigue more severely compared with single patients. There are many studies in the literature stating that there is a correlation between gender and fatigue [24,25]. The reason for this result may be responsibilities inside family. Females' traditional responsibilities within a family such as to take care of grandchildren, cooking, etc. and the responsibilities of being a mother/grandmother and a wife reduce their energy and may cause that they experience fatigue more severely.

In accordance with the literature on the subject, functional status has been found to be related to fatigue. The intensity of fatigue increases as the functional performances of daily activities by elderly individuals decreases [26]. Avlund et al. showed that tiredness in daily activities (measured by the Lower Limb-T Scale) is associated with balance [27]; and functional limitations measured by performance tests [28]. Also, earlier studies shown that old persons who feel tired in their daily activities are more sedentary than persons without tiredness [28,29], Murphy et al. demonstrated that fatigue is negatively associated with physical activity after controlling for other factors and more functional mobility impairment is related to decreased physical activity [30]. It is well known that physical activity has several longterm physiologic benefits: improved muscle strength, stimulating flexibility of joints, prevention or postponement of the age-associated decline in balance and coordination and postponement of declines in velocity of movements [31]. The present results in our study is likely the result of a variety of factors, including reduced exercise tolerance and physical activity or other age-related declines in the muscle, nerve and sensory system.

Fatigue has a multidimensional structure: physical, cognitive and emotional. Numerous instruments for measuring self-reported fatigue have been published [2,32,33]. Available fatigue instruments typically assess one or more dimensions of the fatigue experience. These unidimensional or multidimensional scales evaluate such characteristics as severity, impact, situation specificity, quality, duration, frequency, possible triggers, and/or distress [34]. According to Smets et al. the use of unidimensional instruments excludes the possibility of a more complete description of fatigue [34]. Therefore, we have chosen the multidimensional CIS-T for this study. The CIS was designed to measure several aspects of fatigue which is in line with our definition of fatigue. It consists of four dimensions: the subjective experience of fatigue and reduction in motivation, reduction in activity, and reduction in concentration. The current study aimed to evaluate the different dimensions of fatigue and its impact to functional mobility and balance performances among community-dwelling elderly. Because impact is directly related to function, we believe our instrument was an appropriate choice. Fatigue as measured with the CIS-T might provide a useful way to detect elderly people at high risk of impaired mobility and balance function.

Strengths of the study are that the analyses are based on well-validated measures of fatigue (CIS-T) and objective measures of functional mobility and balance performance. These measurements were done by trained professionals in standardized conditions.

When interpreting the present results, some limitations of the study should be considered. First, due to the crosssectional design, this study cannot address whether the observed relationships are causal. For example, poor functional mobility and balance performances may cause fatigue but fatigue may also lead to poor functional mobility and balance. Second, our assessment of fatigue was based on self-report. Third, the sample size was relatively small. Despite these limitations, this study contributes to the literature on the fatigue in elderly people. This research alerts researchers and health care providers alike to the varying manifestations of fatigue in elderly people.

Conclusions

The results in the present study indicate that it is important to take complaints about fatigue, as these people are at a higher risk of poor functional mobility and balance performances than others. It is recommended to include the measure in the preventive work among the community-dwelling elderly as a key point that may prompt referral to further geriatric evaluation and effective intervention. As seen through the data, community-dwelling elderly need advices of health professional for coping effectively with the fatigue. Further research is required to better understand the role of fatigue in elderly people in order to identify strategies to reduce its impact.

References

1. Reyes-Gibby CC, Aday LA, Anderson KO, Mendoza TR, Cleeland CS. Pain, depression, and fatigue in community-dwelling adults with and without a history of cancer. *J Pain Symptom Manage* 2006; 32: 118-128.
2. Eldadah BA. Fatigue and fatigability in older adults. *PM&R* 2010; 2: 406-413.
3. Hellstrom Y, Persson G, Hallberg IR. Quality of life and symptoms among older people living at home. *J Adv Nurs* 2004;48 (6): 584-593.
4. Reyes-Gibby CC, Mendoza TR, Wang S, Anderson KO, Cleeland, CS. Pain and fatigue in community-dwelling adults. *Pain Med* 2003;4 (3): 231-237.
5. Wijeratne C, Hickie I, Brodaty H.. The characteristics of fatigue in an older primary care sample. *J Psychosom Res* 2007; 62 (2): 153-158.
6. Tiesinga LJ, Dijkstra A, Dassen TWN, Halfens RJG, van den Heuvel WJA. Are nurses able to assess fatigue, exertion fatigue and types of fatigue in residential home patients? *Scand J Caring Sci* 2002; 16 (2): 129-136.
7. Trendall J. Concept analysis: chronic fatigue. *J Adv Nurs* 2000; 32(5): 1126-1131
8. Yu DSF, Lee DTF, Man NW. Fatigue among older people: a review of the research literature. *Int J Nurs Stud* 2010; 47: 216-228
9. Liao S, Ferrell BA. Fatigue in an older population. *J Am Geriatr Soc* 2000;48 (4): 426-430.
10. Bautmans I, Njemini R, Predom H, Lemper JC, Mets T. Muscle endurance in elderly nursing home residents is related to fatigue perception, mobility, and circulating tumor necrosis factor-alpha, interleukin-6, and heat shock protein 70. *J Am Geriatr Soc* 2008; 56 (3): 389-396.

11. Rose DJ, Jones CJ, Lucchese N. Predicting the probability of falls in community-residing older adults using the 8-foot up-and-go: the new measures of functional mobility. *J Aging Phys Act* 2002; 10: 466-475.
12. Ruwer SL, Rossi AC, Simon LF. Balance in elderly. *Rev. Brass. Otorrinolaringgol.* 2005; 71: 298-303.
13. Aslan BA, Cavlak U, Yagci N, Akdag B. Balance performance, aging and falling: a comparative study based on a Turkish sample. *Arch Gerontol Geriatr* 2008; 46: 283-292
14. Bogle Thorbahn LD, Newton RA. Use of the Berg Balance Test to predict falls in elderly persons. *Phys Ther* 1996; 76 (6): 576-83.
15. Podsiadlo D, Richardson S. The Timed "Up & Go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc* 1991; 39: 142-148.
16. Boulgarides LK, McGinty SM, Willett JA, Barnes CW. Use of clinical and impairment-based tests to predict falls by community-dwelling older adults. *Phys Ther* 2003; 83: 328-339.
17. Ergin G, Yildirim Y. A validity and reliability study of the Turkish Checklist Individual Strength (CIS) questionnaire in musculoskeletal physical therapy patients. *Physiother Theory Pract* 2012; (Early Online) 1-9
18. Vercoulen JH, Alberts M, Bleijenberg G. The Checklist Individual Strength (CIS). *Gedragstherapie* 1999; 32: 131-136.
19. Bültmann U, De Vries M, Beurskens AJHM, et al. Measurement of prolonged fatigue in the working population: determination of a cutoff point for the Checklist Individual Strength. *J Occup Health Psychol* 2000; 5: 411-16.
20. Swaen GMH, van Amelsvoort LGPM, Bültmann U, Kant IJ. Fatigue as a risk factor for being injured in an occupational accident: results from the Maastricht Cohort Study. *Occup Environ Med* 2003; 60(Suppl 1): i88-i92.
21. Aggarwal VR, McBeth J, Zakrzewska JM, Lunt M, Macfarlane GJ. The epidemiology of chronic syndromes that are frequently unexplained: Do they have common associated factors? *Int J Epidemiol* 2006; 35: 468-476.
22. Santos-Eggimann B, Cuenoud P, Spagnoli J, Junod J. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. *J Gerontol A Biol Sci Med Sci* 2009; 64: 675-681.
23. White PD. How common is chronic fatigue syndrome; how long is a piece of string? *Popul Health Metr* 2007; 5: 6.
24. Kobayashi H, Demura S, Nagasawa Y. Gender difference of subjective symptoms of fatigue among Japanese adolescents. *Environ Health Prev Med* 2003; 8: 41-46.
25. Mollaoglu M, Fertelli TK, Tuncay FO. Fatigue and disability in elderly patients with chronic obstructive pulmonary disease (COPD). *Arch Gerontol Geriatr* 2011; 53: e93-e98
26. Soyuer F, Senol V. Functional outcome and depression in the elderly with or without fatigue. *Arch Gerontol Geriatr* 2011; 53: e164-e167.
27. Era P, Avlund K, Jokela J, Gause-Nilsson I, Heikkinen E, Steen B, Schroll M. Postural balance and self-reported functional ability in 75-year-old men and women—a cross-national comparative study. *J Am Geriatr Soc* 1997; 45: 21-9.
28. Avlund K, Schroll M, Davidsen M, Løvborg B, Rantanen T. Maximal isometric muscle strength and functional ability in daily activities among 75-year-old men and women. *Scand J Med Sci Sports* 1994; 4: 32-40.
29. Avlund K, Osler M, Damsgaard MT, Christensen U, Schroll M. The relationships between musculoskeletal diseases and mobility among old people. Are they influenced by socio-economic, psychosocial and behavioral factors? *Int J Behav Med* 2000; 7: 332-9.
30. Murphy SL, Smith DM, Clauw DJ, Alexander NB. The impact of momentary pain and fatigue on physical activity in women with osteoarthritis. *Arthritis Rheum* 2008; 59(6): 849-856.
31. Avlund K, Damsgaard MT, Sakari-Rantala R, Laakkonen P, Schroll M. Tiredness in daily activities among nondisabled old people as determinant of onset of disability. *J Clin Epidemiol* 2002; 55: 965-973.
32. Hann DM, Jacobsen PB, Azzarello LM, et al. Measurement of fatigue in cancer patients: development and validation of the Fatigue Symptom Inventory. *Qual Life Res* 1998; 7: 301-10.
33. Smets EM, Garssen B, Bonke B, et al. The multidimensional fatigue inventory (MFI). Psychometric qualities of an instrument to assess fatigue. *J Psychosom Res* 1995; 39: 315-25.
34. Vestergaard S, Nayfield SG, Patel KV, Eldadah B, Cesari M, Ferrucci L, et al. Fatigue in a representative population of older persons and its association with functional impairment, functional limitation, and disability. *J Gerontol A Biol Sci Med Sci* 2009; 64A(1): 76-82.

Corresponding Author
Zeliha Baskurt,
Suleyman Demirel University,
Health Sciences Faculty,
Physiotherapy and Rehabilitation Department,
East Campus,
Cunur-Isparta,
Turkey,
E-mail: zelihabaskurt@sdu.edu.tr

Nutritional status and possible causes of obesity in preschool children

Biljana Ilic¹, Zoran Igrutinovic², Mile Despotovic¹, Hristos Aleksopoulos¹, Svetlana Milovanovic¹, Slavica Markovic²

¹ College of Health Education Cuprija, Cuprija, Serbia,

² Pediatrics Clinics, Clinical Center Kragujevac, Kragujevac, Serbia.

Abstract

Introduction: Monitoring the nutritional status of children is a multi-useful activity as it helps in analyzing the current state of health of children and can serve as a prognostic factor in their future health.

The aim of our study was to analyze the nutritional status of preschool children in a systematic review of enrollment in primary school in Čuprija, diagnosis of obese children, as well as analyzing the relationship between obesity in preschool children and their parents and analyzing children's obesity and parents' educational level, as the socioeconomic status of their parents.

Methods: The study involved 212 children and their parents, where nutritional status is verified using the percentile values of BMI. The height and weight of children is a measure of trained medical personnel and the data on height, weight and level of education were collected based on questionnaires completed by parents.

Results: The prevalence of obesity in children for enrollment in first grade is 5.19%. Obese girls were 5.6% and 5.7% of obese boys.

BMI in children is not a statistical significant correlation with BMI of both parents, but deserves more attention the fact that 9.43% of children with elevated body mass 27 have parents who are with BMI <25 kg/m² and 5.66% of children found to be obese and 17 have a parent with a BMI <25 kg/m².

Conclusion: The results of this study clearly indicated the existence of the problem of excessive weight gain in enrollment of children in primary school compared to the parental body weight and level of parental education.

Key words: BMI (body mass index), preschool children, obesity, parents

Introduction

Lifestyle changes, both in industrialized and in developing countries, have led to altered lifestyle and diet. The combined effects of these changes have important implications for the health of children and adults and contribute to its negative impact on the health of populations at all levels.

Obesity is a worldwide more than doubled since 1980. In 2008, 1.5 million adults 20 and older were obese. Of these, over 200 million men and nearly 300 million women were obese. Even 65% of the world's population lives in countries where overweight and obesity is killing more people than hunger⁸.

Child obesity has not been properly diagnosed and inadequately tested. Nearly 43 million children under 5 years old in 2010 had an overweight eighth it is estimated that in the category of children aged 5 to 17 years 155 million with excess weight and 30 to 45 million gojazno⁶ Child obesity is becoming a global problem. The prevalence of childhood obesity in the last ten years in some countries increased by two to three times in some up to almost four times. In Canada rose from 11% to over 30% of the boys in Brazil rose from 4% to 14%¹.

Some studies have shown that the risk factors in children of school age usually associated with low physical activity and factors that promote the family - the level of parental education, parental obesity, the job of parents, household size, ...

Particular attention should be paid to solving the problem of obesity in children, because many studies show that a large number of obese adults were obese in children's ages², which is brought about a number of health problems these people such as type II diabetes, cardiovascular disease, osteoporosis, some types of cancer (endometrial, breast, colon), ...

Additionally increased risk from breathing difficulties, fractures, hypertension, early signs of car-

diovascular disease, insulin resistance, possible psychosocial problems (low self-esteem, depression, eating disorders), premature death and disability.

Studies have shown that children aged 7 years who were obese (BMI > 95 percentile) in 43% of cases in girls and 63% of the boys will be obese and 30 years.⁷

Measures to prevent many cases of obese children have good performance so children become aware of their problems and want to change. Children with elevated body weight in 57,1% of the cases he wants to change their eating habits in obese children the percentage was 68,4%.²

The biggest prevention efforts in addressing childhood obesity should be near children in the early days of their lives, including the prenatal period, postnatal suckling period and the transition to a modified adult diet.

The most important task of parents in the early development of the habit of being carriers of nutrition and their changes in early childhood. Demonstrated the influence of environment on child nutrition and the emergence of obesity, particularly the way in which parents feed and parental behavior in the third occurrence of childhood obesity.

Mothers have much greater impact on the nutrition of children compared to fathers, as more and more concerned about the preparation and conduct of children in food intake, while fathers have an impact on the imposition of fast food meals in children⁴. Research conducted with 236 children in one area of Poland showed that exist between obesity of children aged 3-15 years with family or environmental factors, including faulty eating habits fifth.

According to WHO definition of overweight and obesity are defined as abnormal or excessive fat accumulation which may endanger health.

Body mass index (BMI) is a simple index is the ratio of the weight and height, and is commonly used to classify overweight and obesity. It is defined as the ratio of body mass and the square of height in meters (kg/m²)

Materials and methods

The study involved 212 children and launched by parents who have access to a systematic review of enrollment in primary school in the municipality Čuprija, during February and March 2009. Of the

total number of girl children were 107 (50.47%) boys and 105 (49.53%). Was measured anthropometric parameter of height and weight in all patients. Height was measured vertical statometrom, expressed in centimeters (cm) and the results are rounded to 0.5 cm. Body weight was measured by electronic scale floor and expressed in kilograms (kg) and the results are rounded to 0,5 kg. During all measurements the children were in their underwear. The work uses data obtained during a survey of parents were related to information about their anthropometric characteristics. Respondents have voluntarily participated in the survey. The data were entered into the information system were anonymous to all respondents.

Nutritional status of parents have expressed through the calculation of BMI: TM (kg)/TV (m)². Children whose BMI was above the 95th percentile for their age and gender are designated as overweight, and increased body weight as indicated by BMI = 85-95. percentile. Parents with a BMI below 25 kg/m² are classified in a group of people with normal weight, with BMI between 25 and 30 kg/m² in the group with elevated body weight, while those with a BMI greater than 30 kg/m² defined as obese parents.

After analysis and processing of the results obtained by appropriate methods of descriptive statistics, data are presented as the mean value, SD standard deviation, a difference of values obtained were evaluated by χ^2 test.

Results

The study was done of the child sample of 212 preschool children and their parents. Ratio of the number of boys and girls was balanced. (Figure 1)

In a systematic review of the enrollment in primary school children were on average high 119.81 ± 5.82 cm (range 101.5-135 cm), average 24.38 ± 6.04 kg (range 13.5-58.5 kg) and had an average BMI = 16.8229 ± 2.9939 kg/m² (range 11.65172-32.09877 kg/m²).

The values of BMI with elevated body mass, there were 21 (9.9%) and 11 obese (5.19%).

The average BMI of mothers was 23.1463 ± 3.81657 kg/m² (range 15.427-42.01534 kg/m²) and fathers 26.4429 ± 3.63497 kg/m² (range 18.0055-37.8775 kg/m²).

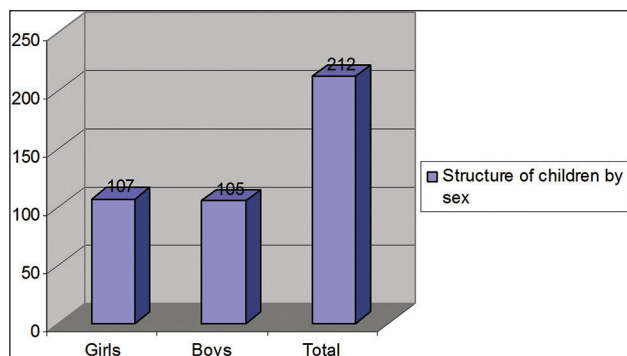


Figure 1. Structure of children by sex

With the increase of body weight were 10 girls (9.3%) (BMI had 18.8972-20.72135 kg/m²), while overweight girls were 6 (5.6%) (had a BMI > 20.72135 kg/m²). (Figure 2)

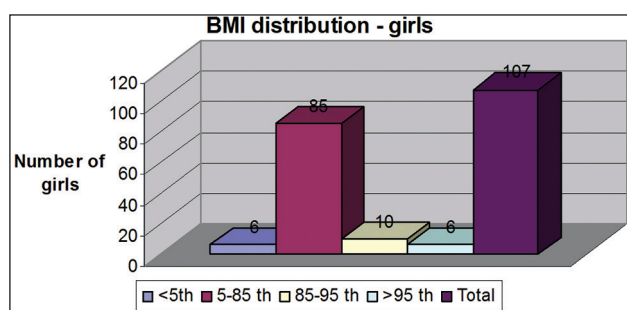


Figure 2. BMI distribution-girls

In boys with elevated body mass were 10 boys (9.5%) (had a BMI kg/m² 19.20456-23.52614) while the obese boys were 6 (5.7%) (had a BMI > 23.52614 kg/m²) (Figure 3)

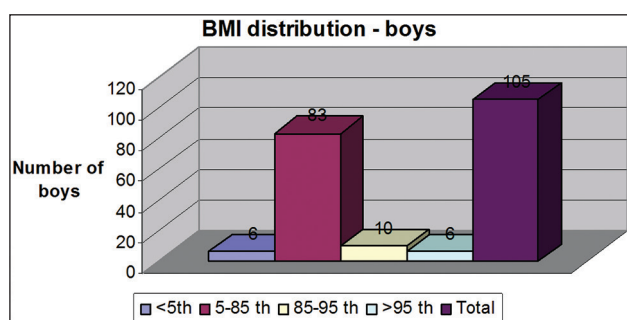


Figure 3. BMI distribution-boys

In mothers, 159 of 212 mothers had a BMI <25 kg/m², which is 75% and 51 had a BMI > 25 kg/m², which is 24.05% while the two mothers had BMI = 25 kg/m².

84 of 212 fathers had a BMI <25 kg/m², which is 39.6%, and 128 had a BMI > 25 kg/m², which is 60.4 %. (Figure 4)

Obese mothers had 51 children (24.06%) (BMI > 25 kg/m²) and obese fathers 128 children (60.4%) (BMI > 25 kg/m²). According to the χ^2 test children have significantly more obese than obese mother, father ($\chi^2 = 33,128$, $df=3 > \chi^2_{(0.05, 3)} = 7,815$).

When two children have both parents BMI > 25 kg/m² (of which a child with an elevated body mass and a child is obese) in 14 children who have parents with a BMI <25 kg/m², 8 is a child with an elevated body weight and 6 children are obese.

The influence of parents' BMI was not statistically significant at BMI values of children ($\chi^2=1,829$ $df=3 < \chi^2_{(0.05, 3)} = 7,815$)

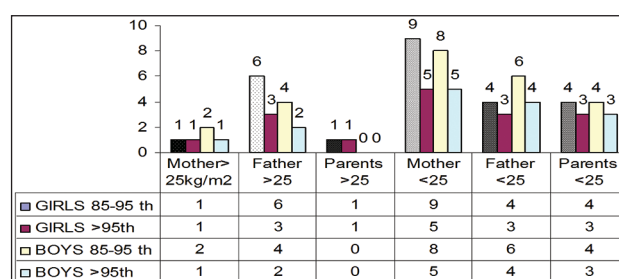


Figure 4. Relationship of BMI for children and parents

Out of 20 children who have increased body weight (10 boys and girls) 27 parents with a BMI <25 kg/m², 17 of which were mothers with a BMI <25 kg/m² and 10 were fathers of children.

In 12 obese children (6 girls and 6 boys) were 17 parents with a BMI <25 kg/m², of which there were eight mothers and 9 fathers. (Figure 5)

Comparing the education levels of parents and children's BMI was found that the level of parental education has no statistically significant effect on the BMI of children, $\chi^2=7,825$ $df=7 < \chi^2_{(0.05, 7)} = 14,067$

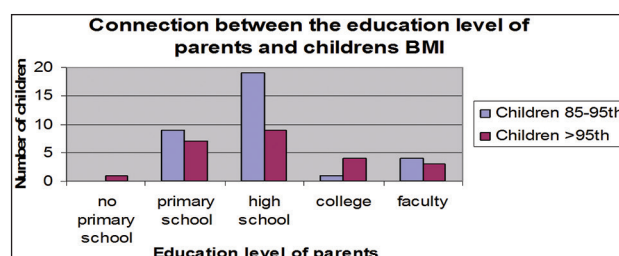


Figure 5. Connection between the education level of parents and children's BMI

It was found that fathers' education level had a statistically significant effect on the BMI of boys ($\chi^2 > \chi^2_{(0.05, 3)}$) and BMI in females ($\chi^2 > \chi^2_{(0.05, 3)}$). The

highest BMI ($18,49 \pm 3,08$) are boys whose father has a college education level and the lowest BMI ($16,18 \pm 0,71$) is for fathers with college level education. The girls have the highest BMI ($18,39 \pm 2,24$) for fathers with higher education and the lowest BMI ($15,99 \pm 2,01$) are the fathers with primary education.

The education level of mothers has a statistically significant effect on the BMI of boys ($\chi^2 > \chi^2_{(0,05, 3)}$) and the BMI of girls ($\chi^2 > \chi^2_{(0,05, 3)}$). The highest BMI ($18,38 \pm 3,73$) with boys whose mothers have higher levels of education and the lowest BMI ($17,00 \pm 3,89$) of mothers with primary education level. The girls have the highest BMI ($18,11 \pm 4,65$) in mothers with higher education and the lowest BMI ($16,02 \pm 1,96$) are in families with mothers with primary education.

Frequently children (277) live in families where the parents of secondary level education (65,33%). Children with excess body weight (8,96%) and obese children (4,245 %) usually live in families where the parents of secondary level education.

Rarest children with excess body weight living in families where parents with higher education (0,235%) and least frequently obese children live in families with parents who have only primary school (0,235%).

Discussion

Obesity is a growing threat to human health and increasingly takes the form of epidemics in many countries. Particularly worrisome phenomenon of excess weight and obesity in children.

Obesity is a worldwide more than doubled since 1980. In 2008, 1.5 million adults 20 and older were obese. Of these, over 200 million men and nearly 300 million women were obese. Even 65% of the world's population lives in countries where overweight and obesity is killing more people than hunger.⁸

Obesity is a predisposing factor for the development of many chronic diseases such as cardiovascular disease, hypertension, early atherosclerosis, diabetes mellitus type II, endocrine, orthopedic, psychosocial disorders, ...⁸ Special attention should be paid to solving the problem of obesity in children, because many studies show that a large number of obese adults were obese in children's age², which is brought about a number of health problems these people.

Obesity is a multifactorial problem that is caused by hereditary factors, social conditions, lifestyles, eating habits and physical activity levels, as well as differences in the environments where the child lives. Obesity is determined by the parents risk for developing obesity in children via genetic and environmental factors within the family. Obesity in adulthood depends on whether parents were obese, and the degree of obesity in childhood. Top risk for developing obesity in adulthood are the parents of overweight and obesity in the period from three to ten years because it is considered that obesity in the period after ten years is exclusively associated with excessive energy intake.⁶

The results of tests conducted in 212 children, who were on a systematic review of the enrollment in primary school show that the 10 girls and 10 boys with the increase of body mass which is 9,43% while the child is 12, with 6 girls and 6 boys are obese. This means that the overall prevalence of obesity in 5,66% of the children. in the former Yugoslavia, where children are living similar anthropometric, South Slavic ("continental type") has so far been little communication about this topic: Obesity has been found 1972 to 7,8% of schoolchildren in Novi Sad⁹, with 14.8% of children enrolled in the first primary school in Croatia 2008th.¹⁰

Towards the end of the last century in the U.S. was 13% of children with excessive body weight at the age of 6-11 years, in China 11,3%, aged 6-9 years, in Brazil the same age, even 17,4% in Australia and the age of 7 - 5 years only 4,7% of boys and only 5,5% girls.¹⁰

It is obvious that the overall prevalence of the examined children obesity our population of 5,66% is still considerably lower than the prevalence of obesity in Western Europe and the USA.

It is curious that the number of boys with excessive body weight and the number of obese boys identical to the number of girls who have excessive body weight and those who are obese, suggesting that sex is not a predominant factor in the prevalence of obesity perception of general. BMI in children is not a statistical significant correlation with BMI of both parents because it is only 2 children found to have both parents with a BMI > 25 kg/m², which is some disturbing information. More attention deserves the fact that 20 children (9,43%) which increased with body mass 27 have parents who are with BMI < 25

kg/m² in 12 children (5,66%) was found to be obese and to have 17 parents with a BMI<25 kg/m².

A positive correlation between the incidence of obesity parental BMI and BMI of boys and girls in our study, which confirms that the BMI of children dependent on parents' BMI. Some studies have shown that children of obese parents and parents with higher body weight have a high risk of developing obesity in the period from seven to 33 year. Some researchers have shown that it is even more important if both parents are obese, compared to a situation where only one parent is obese. It is also found that obesity is a significant predictor of parents in the development of childhood obesity.¹¹

Recent studies have shown that parental involvement in education on obesity is of crucial importance for success, which suggests that the preventive measures and targets are children and parents and not be considered as only childrens.¹²

It is important to emphasize the impact of inaccurate perceptions of obesity, because the mothers in one study incorrectly identified the status of 84% of normal weight children, 52% of excess body weight and 14% obese. In the Italian study identified factors associated with incorrect identification of overweight children: lower maternal education, living in a region with high prevalence of obesity, sex of the child and child BMI.¹³

Another study has shown that family factors were significantly associated with overweight children and obesity in school children: more parental education, living in high-income family and a small number of children in the family.¹⁴

It is very important to conduct research in the younger age groups of children and involve them in prevention programs work together with parents.

It is essential and mark those with excessive body weight (BMI 85-95 kg/m²) who are potential obese children as well as monitor for obese children (BMI> 30 kg/m²).

Conclusion

The incidence of obesity in children for enrollment in first grade was 5,19% and excessive body weight is 9.9%. With the increase of body weight were 10 girls (9,3%) while the 6 girls were obese (5,6%). In boys with elevated body mass were 10 boys (9.5%) while the obese boys were 6 (5,7%).

Suggesting that there is a great uniformity of the presence of excessive weight and obesity in this group of children.

BMI in children is not a statistical significant correlation with BMI of both parents because it is only 2 children found to have both parents with a BMI>25 kg/m², which is some disturbing information. More attention deserves the fact that 20 children (9, 43%) which increased with body mass 27 have parents who are with BMI<25 kg/m² in 12 children (5, 66%) was found to be obese and to have 17 parents with a BMI<25 kg/m².

Comparing the education levels of parents and children's BMI was found that the level of parental education has no statistically significant effect on the BMI of children, but it was found that fathers' education level had a statistically significant effect on BMI in the BMI of boys and girls. As the education level of mothers has a statistically significant effect of BMI on the BMI of boys and girls.

The results of this study showed clearly the existence of the problem of excessive weight gain in enrollment of children in primary school compared to the parental body weight and level of parental education. It is clear that genes can not change, but we strive to increase physical activity, reduced energy intake and changes in factors that may contribute to the excessive weight and obesity on a date from the environment.

References

1. Flynn MA, McNeil DA, Maloff B, Mutasingwa D, WuM, Ford C, et al. Reducing obesity and related chronic disease risk in children and youth: a synthesis of evidence with „best practice“ recommendations. *Obes Rev* 2006; 7 Suppl 1: 7-66
2. Ramic E, Kapidzic-Durakovic S, Karic E, Batic-Mujanovic O, Alibasic E, Zildzic M. Influence of Lifestyle on Overweight and Obesity in School-age Children. *Med Arh* 2009; 63(5): 280-3
3. Anzman SL, Rollins BY, Birch LL. Parental influence on children's early eating environments and obesity risk: implications for prevention. *Int J Obes (Lond)* 2010 Jul; 34(7): 1116-24, Epub 2010 Mar 2
4. Johannsen D, Johansen MN. Influence of parents eating behaviors and child feeding practice on children's weight status. *Obesity (Silver Spring)* 2006 Mar; 14(3): 431-9

5. *Weker H. Simple obesity in children: A study on the role of nutritional factors. Med Wieku Rozwoj 2006 Jan-Mar; 10(1): 3-19*
6. *Plourde G. Preventing and managing pediatric obesity. Canadian Family Physician, 2006; 52: 322-8*
7. www.who.int/mediacentre/factsheets/fs311/en/
8. *Dinarevic S, Brankovic S, Hasanbegovic S. Relation of diet and physical activity to obesity in children in elementary schools. Journal of Health Sciences 2011; 1(1): 44-9*
9. *Markovic S, Igrutinovic Z, Kostic G, Vuletic B. The state of nutrition and possible factors of etiopathogenesis of the obesity among school children. Journal of Medicine Serbian Medical Society 2008; 42(1): 7-14*
10. *Jakic M. Correlation between body mass index of children enrolled in first grade, and BMI of their parents. Croatian Journal of Public Health 2008, vol 4 (15)*
11. *Bukara – Radujkovic G, Zdravkovic D. Determinants of body mass index in Children and Adolescents. Archives of Serbian Medical Society 2008. 1(07-14)*
12. *Reinehr T. Effectiveness of lifestyle intervention in overweight children. Proc Nutr Soc 2011. Nov; 70(4): 494-505. Epub 2011 Aug 1*
13. *Binkin N, Spinelli A, Baglio G, Lamberti A. What is common becomes normal: The effect of obesity prevalence on maternal perception. Nutr Metab Cardiovasc dis 2011 Dec 31*
14. *Mustanq MU, Gull S, Shahid U, Shafique MM, Abdullah HM Shad MA, et al. Family-based factors associated with overweight and obesity among Pakistani primary school children. BMC Pediatr. 2011 Dec 16; 11: 114*

Corresponding Author

Biljana Ilic,

College of Health Education Cuprija,

Cuprija,

Serbia,

E-mail: jobi98yu@yahoo.com

Improvement of anxiety resources scale of school-age children with oncological disease under condition of illness and hospitalization

Selver Guler¹, Huriye Demet Cabar²

¹ Hospital of TAM-MED, Gaziantep, Turkey,

² Sinop University, School of Nursing, Sinop, Turkey.

Abstract

Objective: This methodological study was aimed to improve “Anxiety Resources Scale” (ARS) of school-age children with oncological disease under condition of illness and hospitalization.

Material and Methods: After obtaining prior written approval, the study was conducted in Gaziantep Kocatepe Primary School (GKPS) and Gaziantep University Oncology Hospital (GUOH) between May and September in 2007. The sample of study was selected by using simple random sampling technique from GKPS and GUOH. Totally 300 which school age children composed of; 80 healthy children sketchiness scale-test-again for, 30 out-patients, 30 hospitalized patients and 160 healthy children joined the study.

Results: The reliability and validity coefficient of “Anxiety Resources Scale of school-age children with oncological disease under condition of illness and hospitalization” was calculated as 0.92. *The analysis revealed that factors* explained 52, 7% of the variance. Results were evaluated with a significance level of $p < 0.05$ and confident interval of 95%.

Conclusion: The findings obtained via investigation revealed that the scale of anxiety resources of the school age children with oncological diseases requiring hospitalization is valid and confidential, so it could be used for such purposes.

Key words: School-age, oncological diseases, anxiety, hospitalization, scale.

Introduction

In all communities parents regard their children as precious gifts. Healthy children mean healthy communities (1). The population of Turkey in 2003 was estimated by Turkey Demographic and Health Survey at 71 million which placed it as number 20

in population among the 193 nation in the world. According to the demographic statistics report of Turkish Statistical Institute in 2003, 5-14 year-old-children constitute 18% of the whole population (2, 3).

School-aged children desire to be successful in school and to manage a good communication with their peers. Self-perceiving at this age may have positive effects on child's success, social interaction and emotional state (4).

Oncological diseases can cause mental and physical difficulties in children as well as families. Children suffering from oncological disease become more anxious as the disease exacerbates or progresses. Among this problems posttraumatik stress disorder are usually encountered. (5,6).

In Likert Type Scales, overall rating score and scaling models are used. It is assumed that each item measures only one attitude (7).

Material and Methods

The study was conducted in Gaziantep Kocatepe Primary School (GKPS) and Gaziantep University Oncology Hospital (GUOH) between May and September in 2007. Study population included the school-aged children who were attending Gaziantep Kocatepe Primary School, the school-aged children with oncological disease hospitalized in Gaziantep University Oncology Hospital and the school-aged children who were undergoing an outpatient treatment. Sample group was chosen by the use of random sampling method and then it was distributed into groups in accordance with the research processes.

To improve the scale, following criteria were determined for test-retest and reliability-validity analyses; -being a healthy school-aged children (aged 7-11), -being a school-aged children hospitalized due to oncological disease (aged 7-11), - being

a school-aged children undergoing outpatient treatment due to oncological disease (aged 7-11), - not having anxiety disorders, -not having physiological disorders, -not having substance or drug abuse problems, -not having mental illness, having good communication skills and - being willing to participate.

In accordance with the literature, number of item of the scale was determined as 44. The draft scale was asked specialists' opinion. After receiving feedback, number of item of the scale was determined as 37. Draft scale was applied to 80 school-aged children who were attending Gaziantep Kocatepe Primary School twice with a two week interval. Internal consistency Cronbach Alpha value of the scale was analyzed. According to the test-retest application, standardized item alpha was calculated in the first and second applications as 0.92 and 0.94 respectively. The Cronbach Alpha coefficient of the scale was determined as 0.93.

Item analysis was applied to the 37-item scale. Spearman's Correlation Analysis was used to determine the total item score of the draft scale of "Anxiety Resources Scale of School-age Children with Oncological Disease under Condition of Illness and Hospitalization". In accordance with the item analysis, item (number 11) that did not meet the criteria was excluded. Spearman's Correlation Analysis was used for each question in test-retest process. Spearman's correlation coefficient was 0.92.

In the second phase, 36-item "Anxiety Resources Scale of School-age Children with Oncological Disease under Condition of Illness and Hospitalization" and Inquiry Form were applied to hospitalized (n=30) and outpatients (n=30) school-aged children at Gaziantep University Oncology Hospital. On the other hand school-aged children (n=160) who were attending Gaziantep Kocatepe Primary School were applied "Anxiety Resources Scale of School-age Children with Oncological Disease under Condition of Illness and Hospitalization".

In accordance with the results of factor analysis, items in the scale were grouped into five independent factors. *The analysis revealed 5 factors that explained 52,7% of the variance.*

These factors were as follows,

1. Anxiety resources related to self care problems and physical needs that can occur due to the illness.

2. Anxiety resources related to hospitalization.
3. Anxiety resources related to school, family and environment.
4. Anxiety resources related to illness.
5. Anxiety resources related to social activities

After these processes "The Anxiety Resources Scale of School-age Children with Oncological Disease under Condition of Illness and Hospitalization" was developed.

The values on the scale range from zero to three. The items in the scale were scored as follows; three indicates severe anxiety, two indicates anxiety, one indicates mild anxiety and zero means that there is no anxiety. Higher total scale scores indicate severe anxiety.

For statistical analyses, SPSS for Windows 15.0 (Statistical Package for Social Science) was used in the analyses of the data. Mean and *Standard deviation tests* were used as *descriptive statistical methods* and One-way ANOVA and Tukey's HSD Tests were used for comparison of quantitative data. Student's t-test was used for comparing the means of two groups. Items in the scale were classified by the use of item analysis. Chi-Square test and Fisher Exact Chi Square test were used in the comparison of qualitative data. Results were evaluated with a significance level of $p < 0.05$ and confident interval of 95%.

Results

In the study of "Anxiety Resources Scale of School-age Children with Oncological Disease under Condition of Illness and Hospitalization" findings were dealt with following subtitles; findings related to the demographic characteristics of the school-aged children, findings related to the anxiety level and condition of illness/hospitalisation of outpatients/hospitalized school-aged children and findings related to the Anxiety Resources Scale.

When age and gender distribution were analyzed it was revealed that, 12(40.0%) of outpatient children were 7-8 years old, 13(43.3%) were 9-10 years old and 5(16.7%) were 11 years old [9(30.0%) were female and 21(70.0%) were male]. Twelve (40.0%) of hospitalized children were 7-8 years old, 13(43.3%) were 9-10 years old and 5(16.73%) were 11 years old [13 (43.3%) were female and

17(56.7) were male]. 64(40.0%) of healthy children were 7-8 years old, 64(40.0%) were 9-10 years old and 32(20.0%) were 11 years old [83 (51.9%) were female and 77 (48.1) were male].

When outpatient/hospitalized children's education levels were analysed, it was revealed that 11(18.3%) of outpatient children were attending to schools, 14(23.3%) were not attending to scho-

Table 1. Distribution of children with oncological disease concerning age and gender (n=220)

Characteristics		Out-patients (n=30)	Hospitalized (n=30)	Healthy (n=160)	Statistical Analysis
Age	7-8 years old	12 (40.0%)	12 (40.0%)	64 (40.0%)	$\chi^2=0.339$ $p=0.987$
	9-10 years old	13 (43.3%)	13 (43.3%)	64 (43.3%)	
	11 years old	5 (16.7%)	5 (16.7%)	32 (20.0%)	
	total	30 (100%)	30 (100%)	160 (100%)	
Gender	female	9 (30.0%)	13 (43.3%)	83 (51.9%)	$\chi^2=5.114$ $p=0.078$
	male	21 (70.0%)	17 (56.7%)	77 (48.1%)	
	total	30 (100%)	30 (100%)	160 (100%)	

Table 2. Distribution of ill children with oncological disease concerning demographic characteristics (n=220)

Characteristics		Patients (n=60)		Statistical Analysis
		N	%	
Education Level (Child)	attending a school	11	18.3	$\chi^2=4.873$ $p=0.087$
	absentee due to the illness	14	23.3	
	left to school due to the illness	35	58.3	
	total	60	100.0	
Education Level (Mother)	literate	30	50.0	$\chi^2=11.628$ $p=0.003^*$
	primary school	29	48.3	
	high School	1	1.7	
	total	60	100.0	
Education Level (Father)	literate	7	11.7	$\chi^2=3.128$ $p=0.372$
	primary school	41	68.3	
	high School	11	18.3	
	university	1	1.7	
	total	60	100	

χ^2 Ki-kare test

* $p<0.01$

Table 3. Distribution of children with oncological disease under condition of hospitalisation (n=60)

Characteristics		Out-patients (n=30)	Hospitalized (n=30)	Statistical Analysis
The person who informed the patient that he/she is going to be hospitalized	mother	18 (60.0%)	15 (50.0%)	$\chi^2=1.558$ $p=0.459$
	father	2 (6.7%)	5 (16.7%)	
	medical staff	10 (33.3%)	10 (33.3%)	
	total	30 (100%)	30 (100%)	
The person that the patient wants as a hospital attendant during the hospitalization	mother	22 (75.9%)	23 (75.9%)	$\chi^2=3.818$ $p=0.148$
	father	8 (24.1%)	4(13.8%)	
	medical staff	0 (0.0%)	3(10.3%)	
	total	30 (100.%)	30 (100.%)	
The person that the patient wants as a hospital attendant during the painful process	mother	22 (75.9%)	24 (82.1%)	$\chi^2=1.823$ $p=0.402$
	father	8 (24.1%)	5 (14.3%)	
	nurse	0 (0.0%)	1 (3.6%)	
	total	30 (100.0%)	30(100.%)	

χ^2 Ki-kare test

Table 4. Distribution of children with oncological disease under condition of hospitalisation and anxiety states of parents (n=60)

Characteristics		Out-patients (n=30)	Hospitalized (n=30)	Statistical Analysis
Are you worried about staying in the hospital?	yes	25 (83.3%)	20 (66.7%)	$\chi^2=2.222$ $p=0.136$
	no	5 (16.7%)	10 (33.3%)	
	total	30 (100.0%)	30 (100.0%)	
Are you worried about your parents' concern?	yes	22 (73.3%)	19 (63.3%)	$\chi^2=0.693$ $p=0.405$
	no	8 (26.7%)	11 (36.7%)	
	total	30 (100.0%)	30 (100.0%)	

χ^2 Ki-kare test

ols due to the illness and 35(58.3%) left school due to the illness. When outpatient/hospitalized children's parents' education levels were analysed, it was revealed that 30(50.0%) of outpatient children's mothers were literate, 29(48.3%) graduated from primary school and 1(1.7%) graduated from high school. 7(11.7%) of outpatient children's fathers were literate, 41(68.3%) graduated from primary school, 11(18.3%) graduated from high school and 1(1.7%) graduated from university.

When the way of obtaining information about hospitalization was analysed it was revealed that 18(60.0%) of the patients were informed by their mothers, 2 (6.7%) were informed by their fathers and 10(33.3%) were informed by the medical staff. On the other hand, 15 (50.0%) of hospitalized patients were informed by their mothers, 5 (16.7%) were informed by their fathers and 10(33.3%) were informed by the medical staff. 22(75.9%) of outpatient wanted his/her mother as a hospital attendant and 8(24.1%) wanted his/her father. 23(75.9%) of hospitalized patients wanted his/her mother as a hospital attendant, 4(13.8%) wanted his/her father and 3(10.3%) wanted medical staff. 22(75.9%) of outpatient patients wanted his/her mother as a hospital attendant, 8(24.1%) of hospitalized patients wanted his/her father and 1(3.6%) wanted nurses during the painful processes.

When outpatient and hospitalized patients' replies to the question of "Are you worried about staying in the hospital?" were analysed it was revealed that 25(83.3%) of outpatients replied "yes" 5(16.7%) replied "no". On the other hand 20(66.7%) of hospitalized patients replied "yes" and 10 (33.3%) replied "no". When outpatient and hospitalized children's parents' concerns were analysed, it was revealed that 25(83.3%) of the

outpatients replied "yes" and 5(16.7%) replied "no". On the other hand 16(53.3%) of hospitalized patients replied "yes" and 11(36.7%) replied "no". The validity-reliability of draft scale was confirmed by the validity and reliability analysis.

Discussion

No previous study involving the scale of school-age children with oncological disease under condition of illness and hospitalization was found in the literature. Therefore we have nothing to discuss here. In this chapter, we are going to deal with the findings related to the demographic characteristics of the school-aged children, findings related to the anxiety level and condition of hospitalization of outpatients/hospitalized school-aged children and findings related to the anxiety resources scale.

According to the data concerning gender differences, it was found that the number of males exceeded the number of girls. These findings were similar that those found in the report of Turkey Demographic and Health Survey (TDHS-2003) (2).

When education levels of outpatients/hospitalised children with oncological disease were analysed it was revealed that great majority of children left school or were non-attendant due to the illness. Findings in Numerical Children Warning Report (expressing that 31.9 % of males and 21.2 % of females were non-attendant due to their illness) support our study findings (8). In a previously conducted study by Erdem (2006), it was revealed that 30% of seriously ill students were non-attendant, 20% of seriously ill students left school and 63.3% of the students could not able to attend school regularly for treatments and controls. These findings support our study results (9).

These findings revealed the urgent necessity of establishing schools at hospitals.

When parents of children education levels were analysed, it was revealed that great majority of parents were literate and primary school graduate. No significant difference was observed statistically between outpatients' and hospitalized patients parents in terms of education level ($p<0.01$). The number of primary school graduate parents in outpatients group was higher than those found in hospitalized patients group. The number of literate parents in hospitalized patient group was higher than those found in outpatient group. These results run parallel with the reports of Turkey Demographic and Health Survey (TDHS-2003). A study conducted by Erdem (2006) it was determined that great majority of parents were secondary school graduate. This finding shows that there may be regional differences in levels of education (2, 9).

In our study, we determined that the great majority of outpatients and hospitalized patients wanted his/her mother as a hospital attendant during the painful processes. This finding shows that emotional connection between mothers and children is stronger.

When the respondents' replies to Anxiety Resources Scale were analysed, the great majority of the children marked "I am worried that I might separate from my family and my friends", "I am worried that my family members might get tired due to my illness" and "I am worried about the extend of healing period." items. Other studies have stated that school-aged children prefer spending time with their peers more than others but changes in state of health (e.g. under condition of illness and hospitalisation) make the children more anxious. These findings support our study results (10, 11, 12, 13, 14, 15).

When subgroup scores of school-aged children with oncological disease concerning "anxiety of children and parents" were analysed, no difference was observed between two groups. This result revealed that school-aged children become anxious about hospitalisation and parental concerns make children more anxious. Literature and other studies likely showed that hospitalisation and parental worry lead to the children anxiety (11, 14, 16, 17, 18, 19, 20, 21, 22,23).

Conclusion

The findings obtained via investigation revealed that the scale of anxiety resources of the school age children with oncological diseases requiring hospitalization is valid and confidential, so it could be used for such purposes (Annexe 1).

References

1. *Unicef Dünya Çocuklarının Durumu- 2005.* http://www.unicef.org/turkey/dcd05/_dcd05b.html (Erişim: 30.03.2008)
2. *Türkiye Nüfus ve Sağlık Araştırması.* <http://www.hips.hacettepe.edu.tr/tnsa2003/basin.htm> (Erişim: 16.12.2007)
3. *Türkiye Başbakanlık İstatistik Kurumu.* <http://www.die.gov.tr> (Erişim: 22.03.2008)
4. *Yavuzer H.: "Eğitim ve Gelişim Özellikleri İle Okul Çağı Çocuğu" 10. Basım, Remzi Kitapevi, İstanbul,13-54, 2004.*
5. <http://www.omucocuk.gen.tr/bilim/onko/soru/soru.htm> Erişim: 22.01.2008
6. *Arıkan K. Kanser Hastalarında Psikolojik Destek. Klinik Gelişim 2004; 17: 77-86.*
7. *Tavşancıl E. Tutumların Ölçülmesi ve SPSS ile Veri Analizi. Ankara: Nobel Yayınları, 2002.*
8. *Sayısal Çocuk Uyarı Raporu* http://www.cocukvakfi.org.tr/sayisal_rapor2.htm#h1 (Erişim: 29.01.2008)
9. *Erdem E. "Kanserli Çocuğu Olan Ailelere Evde Verilen Hemşirelik Hizmetlerinin Değerlendirilmesi" Hacettepe Üniversitesi Sağlık Bilimleri Enstitüsü Doktora Tezi, Ankara, 2006.*
10. *Beser (Gördeles) N, Öz F. Kemoterapi Alan Lenfomalı Hastaların Anksiyete depresyon Düzeyleri ve Yaşam Kalitesi. C.Ü. Hemşirelik Yüksek Okulu Dergisi, 2003; 7(1): 47-58.*
11. *Çavuşoğlu H. Hastaneye Yatan Çocuk ve Aile Üzerindeki Etkileri, Çocuk Sağlığı Hemşireliği. Bizim Büro Basımevi, Ankara, 1995.*
12. *Ataman (Keyik) Z. Okul Çağı Çocuklarının Tıbbi İşlem Korkularına Yönelik Verilen Bilginin Etkisinin İncelenmesi. Dokuz Eylül Üniversitesi Sağlık Bilimleri Enstitüsü Yüksek Lisans Tezi, İzmir-2006.*
13. *Gültekin G, Baran G. 9-14 Yaş Grubu Akut Ve Kronik Hastalığı Olan Çocukların Denetim Odağı Düzeylerinin İncelenmesi. Türk Pediatri Arşivi 40: 211-20, 2005.*

14. Akçay C. *Kanser Hastalarında Destek Tedavile-ri-1. XIII. TPOG Ulusal Pediatrik Kanser Kongresi, Hemşire Programı 184-185.*
15. Mu PF, Ma FC, Hwang B, Chao YM. *Families of Children with Cancer: The Impact on Anxiety Experienced by Fathers.* *Cancer Nurs* 2002; 25(1): 66-73.
16. Eşki A. *Ben Hasta Değilim, Çocuk Sağlığı ve Hastalıkların Psikososyal Yönü, Nobel Tıp Kitabevi, 1999.*
17. Toros F, Tot Ş, Düzovalı Ö. *Kronik Hastalığı Olan Çocuklar, Anne Ve Babalarındaki Depresyon ve Anksiyete Düzeyleri.* *Klinik Psikiyatri* 2002; 5: 240-247.
18. Karakavak G, Çırak Y, *Kronik Hastalıklı Çocuğu Olan Annelerin Yaşadığı Duygular” İnönü Üniversitesi Eğitim Fakültesi Dergisi* 2006; 7(12): 95-112.
19. Kavaklı A, Pek H, Bahçecik N. *Çocuk Hastalıkları Hemşireliği 2. Baskı. Çevik Matbaacılık, İstanbul 1998.*
20. Kebudi R. *Terminal Dönemde Kanserli Çocuk ve Ailesine Yaklaşım. Türk Onkoloji Dergisi* 2006; 21(1): 37-41.
21. Schwamborn D, Wendel K. *A Child-Centred Management Concept For Families Of Children With Cancer in the Terminal Phase. Cooperation with the Established Physician Monatsschr Kinderheilkd,* 1993; 141(4): 272-6.
22. Helseth S, Ulfsaet N. *Having a Parent with Cancer: Coping and Quality of Life of Children During Serious Illness in the Family.* *Cancer Nurs* 2003; 26(5): 355-62.
23. Gönener, HD. *Okul Yaş Dönemi Çocuğu Olan Ebeveynlerin Hastalık ve Hastaneye Yatma Durumunda Ebeveynlerin Endişe Kaynakları Ölçeğinin Geliştirilmesi ve Çocukların Endişe Kaynakları İle Etkileşimi. Marmara Üniversitesi Sağlık Bilimleri Enstitüsü, Doktora Tezi, İstanbul, 2003.*

Corresponding Author
Huriye Demet Cabar,
Sinop University,
School of Nursing,
Ordu Koyu Mevkii,
Sinop,
Turkey,
E-mail: gonener@hotmail.com

Annexe 1**Anxiety Resources Scale**

Anxiety resources scale of school-aged children with oncological disease

The aim of this scale is to determine the anxiety resources of the school-aged children with oncological disease under condition of illness and hospitalization. Expressions related to anxiety resources of school-aged children are given below. Please read each expression carefully and mark the best choice corresponding to the severity of anxiety. Please just mark only one choice.

Your replies will be scored as follows;

3- severe anxiety 2- anxiety 1- mild anxiety 0- no anxiety

EXPRESSION	Severe anxiety	Anxiety	Mild anxiety	No anxiety
1. I am worried that I might separate from my family and my friends	()	()	()	()
2. I am worried that my friends might not like me again	()	()	()	()
3. I am worried that my close friends might not come closer for fear that catching infection	()	()	()	()
4. I am worried that my friends might not visit me	()	()	()	()
5. I am worried that my friend might miss me due to my absentee	()	()	()	()
6. I am worried that my teachers might not love me again	()	()	()	()
7. I am worried that I might fail in the exams	()	()	()	()
8. I am worried that I might forget course subjects due to my absentee	()	()	()	()
9. I am worried that I might not play game again	()	()	()	()
10. I am worried that my mother will not be able to take care my brother/sister	()	()	()	()
11. I am worried that my brother/sister might diverge from me	()	()	()	()
12. I am worried that my family members might get tired due to my illness	()	()	()	()
13. I am worried that I will have to wear mask continuously	()	()	()	()
14. I am worried that my friends might not like me due to hair loss	()	()	()	()
15. I am worried that my social environment might find my hair loss strange	()	()	()	()
16. I am worried that I might not comb my hair again	()	()	()	()
17. I am worried that my friends might exclude me	()	()	()	()
18. I am worried that I might get bored in hospital room	()	()	()	()
19. I am worried that I might not eat a well-balanced diet	()	()	()	()
20. I am worried that I might not elimination myself while I am in hospital	()	()	()	()
21. I am worried that I might not have a bath while I am in hospital	()	()	()	()
22. I am worried that I might catch an infection while I am in hospital	()	()	()	()
23. I am worried that I might not watch TV while I am in hospital	()	()	()	()
24. I am worried that I might not brush my teeth regularly	()	()	()	()
25. I am worried that I might not sleep due to noise	()	()	()	()
26. I am worried that I might get bored because of standing for long hours	()	()	()	()
27. I am worried that my illness might get worse	()	()	()	()
28. I am worried that I might suffer from painful process	()	()	()	()
29. I am worried that I might not eat my favourite foods such as candy and chocolate	()	()	()	()
30. I am worried that other might catch infection	()	()	()	()
31. I am worried about my disfigurement	()	()	()	()
32. I am worried that everybody might feel pity for my illness	()	()	()	()
33. I am worried that I might not be informed about my illness	()	()	()	()
34. I am worried about long period of disease	()	()	()	()
35. I am worried about delay in my physical development	()	()	()	()
36. I am worried about the extend of healing period	()	()	()	()

Ethical performance in delivery of sexual and reproductive health services: A Delphi study focused on the right of confidentiality

Tahmineh Farajkhoda¹, Robab Latifnejad Roudsari², Mahmoud Abbasi³

¹ Department of Midwifery, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran,

² Research Center for Patient Safety & Health Quality, Department of Midwifery, School of Nursing and Midwifery, Mashhad University of Medical Sciences, Mashhad, Iran,

³ Shahid Beheshti Medical Law & Ethics Research Centre, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Abstract

Introduction: Advancement in technology has brought notable changes in current methods of diagnosis and treatment in Sexual and Reproductive Health (SRH), which itself has created ethical issues including confidentiality protection for the clients and health care professionals to deal with in SRH services.

Objectives: To develop an ethical guideline regarding confidentiality in SRH services in Iran.

Methods: This study was a modified three round Delphi of Iranian academics and clinicians which explored the perception and perspectives of 45 Iranian experts towards confidentiality in SRH services. Purposeful sampling was applied to data collection. Data were collected through sending a series of three questionnaires including a questionnaire contained open-ended questions in round 1. The data underwent three rounds of analysis until a consensus was reached.

Results: The panelists' views were organized to five categories related to confidentiality including 1) right to confidentiality 2) access to information 3) secure management of client's data 4) third party interests and 5) legal and illegal disclosure.

Conclusion: This study has set up an ethical guideline towards confidentiality in SRH services. It can guide health care providers to what they should do and should not do ethically in practice regarding confidentiality in SRH care services.

Key words: Sexual and reproductive health, confidentiality, ethical guideline

Introduction

Sexual and Reproductive Health (SRH) matters are the most global concern in the world (1). Advancements in knowledge and technology have brought a noticeable changes in screening, diagnosis and treatment methods in SRH (2, 3, 4). These changes have influenced the SRH issues of women such as infertility, prenatal diagnosis and treatment, safe motherhood and gynecological cancers. This situation has expanded opportunities for women's choices in decision making on their SRH. These new options have also created ethical issues for the women, health care professionals and related group of people to approach the ethical problems (5, 6).

SRH service users i.e. clients, physicians and other health care providers in SRH services, need a moral compass to guide them (7, 8). Providers have obligations to SRH service users based on women and SRH rights (1, 6, 9). What clients want are respect, technically competent care, fairness, free and informed decision making, privacy and confidentiality (1).

Confidentiality is very important in giving SRH care, because sexual and reproductive issues are sensitive subjects and could not be discussed the same in various families, communities, cultures or even genders (6, 4). Confidentiality is different from privacy, although they are often coupled as a single right. Privacy defines as a right of client but confidentiality is the duty of all health providers who receive client's private information. They do not have permission to disclose this information without clients' consent. (10, 11). It has been addressed in all the Bill of Rights and professional

codes of ethics in medical ethics literature (2, 4, 12, 13, 14).

Since the definition of confidentiality remains largely uncertain in operational terms, providers need to be trained on (4, 6, 15). Breaching confidentiality can produce serious ethical and legal problems. It is a sort of violence against client's human rights (2, 11, 16-19). Illegal breaching of confidentiality in civil law of Iran and other countries has been considered as a crime and is accompanied with fine. Providers must be aware of and familiar with different dimensions of confidentiality to protect clients' information and records (2, 20, 21).

World Health Organization (WHO), and WHO research group on patients' rights have emphasized on collaboration within countries regarding developing professional code of ethics. All countries should have a dynamic mechanism for dealing with ethical issues according to their concerns, priorities and diversities in their own social, cultural, economical and religious needs, backgrounds and contexts (10, 21).

In all cultures, medical practice is regulated by professional code of ethics. Training of health providers, institutional capacity building and promotion of code of ethics should be applied powerfully (6, 10, 22). In Iran, few studies regarding patients' Bill of Rights and code of ethics in medical sciences has been carried out (21, 23). The "Six Ethical Codes for Research" analysed by Khodaparast et al. in 2007 in Iran does not represent comprehensiveness (23). Parsapoor et al. (2009) in their study on attitude of Iranian physicians, nurses and patients towards necessity of respect to patient's rights reported that patients' right of confidentiality was mentioned as an essential right of each client by the majority of participants (24). Whereas most of the patients in the study of Bateni et al. (2011) had no awareness of right of confidentiality in medical care (25). While the right of confidentiality has been confirmed in other countries, patient's rights has many shortcomings in Iran. In this relation, Sarbaz & Kimiafar (2011) have suggested that main reviews in this field should be conducted (26). Yarmohammadian et al. (2010) have similarly recommended that further research should be carried out towards confidentiality in Iran (20). Mohammad Nejad et al. (2011) have also emphasized on expert meeting to assess barriers and to develop strategies in or-

der to implement the Bill of Patients' Rights and professional code of ethics in Iran (27). Likewise, Khodakarami & Jannesari (2009) have highlighted that developing professional code of ethics in SRH area regarding confidentiality is a necessity in Iran (28). Bayrami et al. (2007) in their study in Iran found that running a workshop on patient's rights for midwives increase their ethical performance towards respecting of the clients' confidentiality according to the female clients' viewpoints (2.5% in non-trained midwives vs 100% in trained midwives). These findings shows that increasing midwives' knowledge regarding their professional responsibility towards patient's rights including right to confidentiality can significantly increase their ethical performance (29). Therefore providers' instruction on confidentiality dimensions may help them to set up an appropriate SRH services for all clients (4, 28, 29).

At present, lack of professional code of ethics for physicians and other health care providers is a dramatic concern for medical practice In Iran. Considering the lack of code of ethics on confidentiality in SRH services, this study aimed to develop an ethical guideline in this relation in SRH care in Iran. It could be applied as a useful tool for solving ethical dilemmas, and also providing practical ethical guideline regarding respect to confidentiality in SRH care.

Method

This article is a part of a large sequential exploratory mixed method study (Creswell & Plano, 2007) (30) including a Delphi study and survey in relation to development of professional ethical guideline regarding SRH care in Iran. It was conducted between March 2010 and August 2011 in four Iranian universities of medical sciences which offered PhD course in Reproductive Health including Tehran, Shahid Beheshti, Isfahan and Mashhad universities of medical sciences. Ethics committee of Shahid Beheshti University of Medical Sciences approved the study protocol. In this paper the authors have presented a part of the results of the first phase of the study which was a modified Delphi study (Powell, 2003) (31). The Delphi method allows a panel of experts to generate ideas on a given topic and to reach a consensus on the relative importan-

ce of those ideas (Jones & Hunter, 1995) (32). The method is based on a structured and iterative process for extracting knowledge from the experts via a series of questionnaires with controlled opinion feedback (Adler & Ziglio, 1996) (33). There are typically three or four Rounds of questionnaires, with the responses to each questionnaire providing the material for the development of the subsequent questionnaire. The purpose of this process is to reach agreement among the group of experts on the specific statements (Powell, 2003) (31).

This study used a three-Round modified Delphi method to identify and reach agreement on the confidentiality in SRH through combination of qualitative and quantitative processes (Powell, 2003) (31). Sample size in Delphi study depends on experts' panel homogeneity, disciplines diversity and aims of the study. An average range between 10 to 50 experts has been recommended (31). For obtaining scientific and valuable data from stakeholders and providers in SRH services in the first Round of Delphi, 45 experts were included. The *Expert Panel* members were selected from four aforementioned medical universities based on their expertise in relation to SRH care and also according to the aims of study. They should have at least three years work experience in the related discipline. The panel consisted of five Obstetricians and Gynecologists, 15 SRH specialists, 10 Medical Ethicist, two General Practitioners (GP), six Midwives, two Family Healthcare Providers, three lawyers and two clergymen, who were invited to participate in this study by sending an E-mail. Written informed consent was obtained from all participants.

Data collection was carried out in three Rounds. Round 1 (qualitative part) was conducted using electronic communication. The first questionnaire containing few open-ended questions was distributed to the list of panels identified using the criteria explained above. The first questionnaire focused on general issues related to the confidentiality dimensions and its breaching circumstances in SRH. Participants were asked to provide thorough and detailed answers to the questions. All the responses obtained from the panelists were analyzed using content analysis. Content analysis is a standard research method in the health and social sciences that uses a set of procedures to make replicable and valid inferences from text based on

precise rules of coding (Krippendorff, 1980) (34). The first step of content analysis was performed to recognize the smallest meaningful unit by re-reading the participants' answers several times and then breaking the data down. Subsequently, through open coding, these meaningful words, phrases and sentences were labeled as codes. In the second step, all initial codes with the same general meanings were merged and arranged into subcategories and categories. Data analysis was initiated at the same time with the data collection and was continued until achievement of data saturation (Creswell & Plano, 2007) (30).

Selecting participants from diverse disciplines in order to maintain maximum variation, and also data (space, person), investigator and analytic triangulation were used in this study to achieve trustworthiness. Member check and peer debriefing were applied to preserve credibility of the findings. All study documents including all questionnaires and computer files in different Rounds of Delphi were saved for confirmability.

After merging the findings and making them validated with the results of a thorough literature review, the draft of ethical guideline was developed and delivered electronically to the expert panel members in Round 2 (quantitative part). They were asked to rate each item according to their views concerning importance of every statement in five-point Likert scale. Score one was defined as "not important" and five was considered as "very important". After data gathering face validity of each item was calculated and statements with impact score less than 1.5 were deleted according to Lacasse et al. (2002) (35). To determine Content Validity Index (CVI) of each statement and then CVI of all statements, Scale- Content Validity Index /Average Calculation Method (S-CVI/Ave) was used to calculate CVI (Polit & Hungler, 2006) (36). Participants were scored each item in a four- point Likert scale based on relevancy, clarity and simplicity (Waltz & Bausell, 1983) (37). According to S-CVI formula CVI was determined 0.9. Also appropriate writing style of each item were controlled and corrected statement-by- statement through face-to-face discussion with a number of expert panel members. Experts' new comments in Round 2 were integrated and at the end of Round 2, a refined draft of ethical guideline was achieved.

Round 3 (quantitative part) was accomplished in order to achieve final refinements and to attain the final agreement and consensus. Final version of ethical guideline was disseminated to the experts by E-mail. The results of Round 3 was accepted as ethical guideline in relation to confidentiality for SRH care providers.

Results

Experts participated in this study were 12 males and 33 females. Their ages ranged from 37 to 58 years old (mean age: 42.52 ± 5.46). Mean length

of work experience was 15.76 ± 5.20 years. In the first Round, all 45 panel members completed the questionnaire and responded to all the questions. This provided the investigator with a large variety of responses which facilitate the development of the second Round questionnaire. The overall response rate for the completion of questionnaires in Round two and three was 100%.

The results of the study presented in this article included five categories. The main categories were right to confidentiality, secure management of client's data, access to information, third party interests and legal and illegal disclosure (Table 1).

Table 1. Emergent categories

Right to confidentiality • Respect the right to confidentiality for clients who are/ are not competent to make decision legally and intellectually. About the later, the provider should discuss with their legal representatives regarding the limits of confidentiality. • Hold any information obtained from client in confidence and protect client's information from wittingly, unwittingly, or carelessly disclosure.
Secure management of client's data • Apply proper system for recording, storage, management and processing of client's information. The information must be relevant and up-to-date, should be gathered accurately and appropriately and processed fairly and lawfully. • Protect security of data against improper access, provide prompt access to serve the interests of the client and protect against accidental data loss or destruction of client's data. • Protect the information from unapproved access during electronic or other methods of recording and processing data. Health providers should arrange confidential records using numbers instead of clients' names and avoid using an alphabetical system. • Design a unique identification number for sexually transmitted diseases or Human Immunodeficiency Virus testing instead of disease name. • Set up a secure appointment system. • Use proper coverage for wrapping tests requested. • Provide secure anonymity of client's information available for medical research and health care system improvement.
Access to information • Respect the right of legally competent clients or their legal representative to have access to all information recorded about them, and correcting inaccurate data and objecting on. Client has the right of final control on information, confidentiality process and omitting some information. Provider should discuss with client about the potential harm of deleting requested information and should put a memo in client's record. Clients have the right of copying their medical information. • Avoid client's information to be used for various purposes without client's permission. • Pay attention that there is no need that every member of a health care team have the right to have access to all client's information; but when he/ she received the information he/ she has the same responsibility for maintaining its confidentiality. • Protect confidentiality of the client's information during students' education or research process.

Third party interests

- Discuss with woman in cases that delivery of SRH services without husbands' approval would provide husband with rights of divorce. In this case the provider should follow local laws or get advice and guidance from relevant authorities or associations.
- Offer client the opportunity to have couple counseling but give the test results to each partner separately.
- Inform the client about any circumstances that she cannot hide from her husband.
- Inform client about any SRH services which requires husband authorization such as infertility treatments, payment for health care services costs from husband's resources and when services need legally the husband's permission.
- Suggest to client for informing third party (husband or wife) when a client may transmit a disease (STD) after consulting with the client.
- Avoid some behaviors that may breach confidentiality such as leaving message to the client for visiting the provider via third party.

Legal and illegal disclosure**A- Legal disclosure**

- Breach confidentiality after discussion with client if there is a clear evidence of urgent, vital and non-reversal risk for the health of the client, and other persons, or when the disease should be reported, or in any circumstances which is requested by law.
- Divulge only necessary information that can prevent the harm and to the only persons who need to know such information.
- Consider the potential harms and risks of breaching confidentiality, if they are equal; provider should consult with responsible and expert persons in this relation before divulging the information.
- Consult with responsible and expert persons before divulging the information when there is a serious risk due to breaching confidentiality and there is no request by law.
- Inform the client about some of his/ her information which could be reported by provider and may be used in statistical analysis of health indices, before providing the services.
- Share the information with related colleagues after getting permission from the client just in order to provide better services.
- Divulge and report any marriage under legal age or violence against girls and women.
- Divulge surrogate mother about additional prenatal screening, and also chance and risks of multiple pregnancies.

B- Illegal disclosure

- Save and use client's voice or picture with client's permission.
- Avoid divulging client's confidential information to other relevant organizations and authorities without client's permission.
- Avoid divulging competent client's information including purpose of his/her visit, any information about his/her health status and test results to others (partner, parents, family members, friends, or co-workers) without client's permission.
- Avoid consulting the client in the presence of other clients, colleagues who are unrelated or other non-health staff.
- Avoid forcing a client to give consent his/ her information to be disclosed.
- Pay more attention to protect medical information of women who are exposed to violence, STDS, or special medical tests.
- Pay more attention to signs and cues that could threaten confidentiality like the titles of a clinic, the letter head on a client letter or the color of drugs.
- Inform the client regarding potential harmful consequences of revealing his/ her SRH information to irrelevant persons, staff and providers.
- Keep client information regarding infertility consultations and treatments (sperm/ oocyte donation, and surrogacy)

Right to confidentiality

Right to confidentiality was one of the main categories that most of experts included it in their answers. It mainly dealt with maintaining confidentiality as a principal right for all clients, irrespective of the extent of mental competency, according to the local, national and international laws. For instance one infertility fellow in this regard mentioned: "Right to confidentiality is a principle". A Medical ethicist pointed out to the respect to the right of confidentiality of vulnerable groups including adolescents and minorities.

Secure management of client's data

Secure management of client's data was another category that was emerged through data analysis and emphasized by the majority of experts. This category was related to the client's data management for the purpose of protection of client's information. experts in this study believed that clients' information should be saved in confidential manner in all circumstances when recorded either manually or electronically. For example a medical ethicist declared: "client's information and records should be kept in confidence". A midwife similarly stressed: "client's information should be registered and saved".

Access to information

Many experts addressed access to information as a priority in providing confidentiality in SRH services. Some issues regarding the persons who have the right to access to the client's information and also respecting the client's right to confidentiality in training and research processes were mentioned in relation to this category. For example a GP stated: "Provider should protect confidentiality of client in research and also students' education". The experts believed that providers should pay attention that client's family members and even colleagues do not entitle to have access to client's information without client's consent. A medical ethicist declared: "Provider should protect confidentiality of client's information from his/ her family members and relatives". One family health provider in this regard mentioned: "Provider should protect confidentiality of client from other coworkers". A SRH specialist pointed to the confidentiality protection in front of other clients: "Provider should protect confidentiality of the client in front of other clients".

Third party interests

Third party interests was a key element in confidentiality that most of the experts addressed to. This category concerned with the awareness of husband /wife of client's information and counseling with husband/wife in shared decision making in SRH services. A SRH specialist mentioned: "Provider should protect confidentiality of client's information from his/ her wife or husband." Also a clergyman declared: "Provider should encourage the client to discuss with his/ her wife or husband when it's necessary."

Legal and illegal disclosure

Legal and illegal disclosure of client's information were stressed as important factors by the majority of experts. They believed that every provider should be familiar with these issues in order to be able to maintain confidentiality. This category consisted of two groups of legal and illegal disclosure. The first group (legal disclosure) included participants' viewpoints concerning providers' performance regarding breach of client's confidentiality in cases of requisition by law, persons who should know client's confidential information, reportable diseases, and serious risk for health of other persons such as family members, health providers or community. Sharing the client's information with related colleagues was also mentioned by a number of experts. For example a SRH specialist believed that provider should share client's information with other related providers in order to provide optimum care after giving client's permission. Second group, i.e. illegal disclosure issues related to providers' unethical performance that could produce serious legal consequences. For instance a medical ethicist stated: "Provider should pay attention that breaching client's confidentiality is an unethical and unlawful practice." One Obstetrician-Gynecologist declared: "Provider should not release client's information to irrelevant persons or providers." Safety of health care without any physical, psychological, economical and social harm to client and compensation of any harm were addressed by the majority of experts. For example a midwife mentioned: "Provider should not act to harm client." Also a lawyer emphasized: "Provider should compensate any harm due to breaching client's confidentiality."

Discussion

The emergent categories concerning ethical guideline on confidentiality in SRH services were included right to confidentiality, access to information, security management of client's data, third party interests and legal and illegal disclosure of confidentiality.

The experts in this study believed that respecting the right to confidentiality in SRH care is very important. The right to confidentiality has been highly valued in the Bill of Rights and all codes of professional ethics and has a strong historic tradition since the time of Hippocrates (10, 12, 14, 21). It has been mentioned as an essential part of the client's autonomy and the cardinal principle of monotheistic religions including Islam (10, 14, 38, 39). The relation between the right to confidentiality and law in SRH care was stressed by the experts in this study. There is an adherence between ethical principles, human rights and law (6). Health care providers have encountered many challenges in wide and rapid changes in the health care delivery system (2, 3). Additionally, the interface between law and ethics as it affects professional practice is complex and confusing. It has altered and limited professional practice (2, 8, 22).

Protecting against violation of confidentiality in SRH care was mentioned as a key element by the experts. Secure care has an important role to save lives of women and men (40). Violation of confidentiality occurs frequently and habitually in medical settings in spite of global agreements of national laws and policies on patient's rights and endorsement (22). It is a dilemma that the clients even are uninformed of their right of confidentiality and also most of health care providers are similarly unaware of their duties to protect confidentiality (4, 21). Unwittingly violation of confidentiality was addressed by the experts in this study. They believed that health care providers should pay more attention to this matter. Health care providers may violate the clients' rights unwittingly or carelessly, whereas are unaware of its serious and unpleasant health consequences. Proper care and treatment require accurate information. Providers must ask clients a range of sensitive questions about their sexual behaviors or that of their partners. If clients are afraid of divulging confidential information, they might less

likely to reveal accurate information (4, 6, 41). Keeping client's information in confidence was declared as an important factor in respecting the right of confidentiality by the experts. It is a priority in clients' access to SRH information, counseling, and service deliveries that is well documented by research evidences. When a provider could not respect client's right to confidentiality, the client (especially vulnerable ones such as poor women and men; adolescents and HIV positives people) may give up care because of fearing of social stigma and related psychological trauma (4, 16-19, 42, 43). This situation could create delay in early diagnosis and treatment, incomplete treatment, or poor health outcomes and even death (4, 6, 9, 15). A lot of studies in SRH area have shown evidence of failure in performing proper actions by health care providers. International Planned Parenthood Federation (IPPF) (1995) has identified that the clients' SRH rights, including the right to confidentiality has been violated (11). According to the experts' views in this study, the client's right to confidentiality should be protected through instruction process. Though students in various health professions are trained for this purpose, but still confidentiality is not protected (9). The findings of this study were congruent with the results of several similar studies. For instance, Garbin et al. (2008) found that 44.29% of the respondents reported that they talk about their patients with their friends or spouses (44). However, Peng et al. (2011) reported that confidentiality indicators have got higher weight and rate compare to other indicators according to the patients' views (45).

Secure management of clients' data in all stages of SRH care was stated by the experts. It requires extraordinary protection (14). Advances in health sciences and computer technology have influenced the duty of providers to keep the client's information in confidence (2, 46). Applying a proper system for gathering and processing of client's information was declared as an important factor for managing of clients' data. This situation and possibility of sharing client's information have emerged a range of challenges related to confidentiality and its violation through sharing the information (2, 47). SRH care providers require learning about data management and applying them in their daily practice to provide proper information security (4, 15). Many alternatives have been recommended

for better keeping of confidentiality such as using cover sheets of faxes, extra paper of ultrasound tests requests and an appropriate location for computer and making data anonymised (2, 4, 6, 41).

Access to client's information was one of the most important issues mentioned by experts. Clients have the right to access and control their information (6, 12, 13, 15). In order to achieve optimal confidentiality, they should know "what they can and cannot do legitimately with their data" and "who should have access to the data and for what purposes" (41). Explicit clients' consent sometimes may accompany with unquantifiable biases (6, 15). National Health System (NHS) Information Authority's new draft code of practice for NHS staff (UK) and also the recommendations of the Confidentiality and Security Advisory Group for Scotland identified that access to identifiable data must be only on a "need to know" basis (48, 49). Consulting with clients about their information was pointed by the experts in this study. Patients should be aware that what happens to their information. They should know that some information may be shared beyond the immediate care team, when health information is used for planning, management, surveillance, and research. These data should be anonymised (6, 41).

Third party interests has been addressed as a problematic issue in protecting client's confidentiality in SRH care by the experts. It has been stressed in most of the articles concerning client's confidentiality too. Requests from third parties for health information about client have always been associated with legal concerns (6, 12, 13, 15). Providers have moral and legal duty, when one partner's disease (such as STDs/HIV) can transmit to another one. They may treat the patient through advising to use condom with or without informing his/her partner. Providers should be aware that their proper decision can provide interest for both patient and third party (6, 8, 15, 17).

Breaching confidentiality after discussion with client in any circumstances, which is requested by law was emphasized by the experts in this study. They believed that providers should divulge only necessary information that can prevent the harm and to the only persons who need to know. Criminal Code and the Code of Professional Ethics refer to legal and ethical importance of disclosure (50).

Since SRH matters are highly sensitive issues, disclosure of information should be discussed with clients. Occurrence of violation against confidentiality may imply that staff, providers, and supervisors lack understanding, information, and tools to deal with the ethical and practical issues of ensuring confidentiality in SRH settings (4). Providing adequate and correct information can accompany more accountability, better performance and providing effective SRH services that are expressed with respect, empathy, and commitment to protecting the confidentiality rights of clients.

Conclusion

This study has tried to set up an ethical guideline regarding confidentiality in SRH services. It will allow providers, supervisors, managers and policy makers to have a better realization of their personal and professional responsibilities and also duties on handling of client's information. Furthermore, it is believed to be useful to all health workers involved in SRH including obstetricians and gynecologists, general practitioners, health officers, midwives, nurses and even other health workers who deal with women, although not principally involved in reproductive health related works. It may be useful to all health workers and may help providers to be familiar with risks of breaching confidentiality in the new trend in SRH care.

Acknowledgement

This article is part of a PhD thesis in Reproductive Health, which has been approved by Shahid Beheshti University of Medical Sciences, Tehran, Iran.

The authors would like to thank all experts participated in this study and also Shahid Beheshti University of Medical Sciences, Vice Chancellor for Research for financial support of this project. Our special gratitude goes to Professor Sasha Dina from Virginia University, Dr Masoumeh Simbar, Associate Professor in Reproductive Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran and Dr Mohsen Fadavi, for their valuable comments in designing and conducting this research project.

References

1. United Nations Population Fund. Improving the quality of SRH care. UNFPA. Reproductive health. 2009. <http://www.unfpa.org>. <http://www.unfpa.org/rh/care.htm> [16 Aug 2011].
2. RJ Mann. The interface between legal and ethical issues in reproductive health. *Journal of Midwifery & Women's Health* 2004;49:182-187.
3. Sommerville A. Moral and ethical imperatives of health care technologies: Scientific, legal and socio-economic perspectives on use and misuse. The second National Bioethics Conference. *Indian Journal of Medical Ethics* 2007; 4: 11-13.
4. Program for Appropriate Technology in Health (PATH). Ensuring privacy and Confidentiality in Reproductive Health Services: A Training Module and Guide for Service Providers. Washington, D.C.: PATH 2003. www.path.org. http://www.path.org/files/RH_ensuring_privacy.pdf [17 Aug 2011].
5. Sharp ES. Ethics in reproductive health care: A midwifery perspective. *Journal of Nurse-Midwifery* 1998; 43: 235-45.
6. Cook RJ, Dickens BM. Considerations for formulating Reproductive health laws. World Health Organization. 2nd ed. 2000. <http://www.who.org>. http://www.who.int/topics/reproductive_health/en [17 Aug 2011].
7. Sabin JE, Cochran D. Confronting trade-offs in health care: Harvard pilgrim health care's organizational ethics program. *Health Affairs* 2007; 26:1129-34.
8. Poll R. Managing the public health risk of a 'sex worker' with hepatitis B infection: legal and ethical considerations. *Journal of Medical Ethics* 2011. (In press)
9. Ethiopian Society of Obstetricians and Gynecologists. Human right code of ethics for reproductive health workers practicing in Ethiopia. ESOG SRH Ethical Guideline. 2005. <http://www.esog.org>. <http://www.esog.org.et/ESOG%20SRH%20Ethical%20Guideline.htm> [17 Aug 2011].
10. World Health Organization. Ethics of medicine and health. EMRO technical papers series 4.WHO-EM/PHP/1/E/G/09.08/1000. 1998. <http://www.who.org>. <http://www.emro.who.int/rpc/pdf/PHP-1-E-G.pdf> [18 Aug 2011].
11. International Planned Parenthood Federation. Sexual & Reproductive Health & Rights. IPPF. 2006. <http://www.ippf.org>. <http://www.ippf.org/NR/rdonlyres/6C9013D5-5AD7-442A-A435-4C219E689F07/0/charter.pdf> [18 Aug 2011].
12. American Association of Physicists in Medicine. Code of Ethics for the American Association of Physicists in Medicine: Report of Task Group 109. *Medical Physics* 2009; 36:3-17.
13. British Association of Social Workers. The Code of Ethics for Social Work. 2002. <http://www.basw.uk>. <http://www.belfastforum.co.uk/index.php> [18 Aug 2011].
14. Antomás J, Huarte Del Barrio S. Confidentiality and the medical record. *Ethical-legal considerations. Anales del Sistema Sanitario de Navarra* 2011; 34: 73-82.
15. Federation International of Gynecology Obstetrics/FIGO. Ethical issues in obstetrics and gynecology by the FIGO committee for the study of ethical aspects of Human Reproduction and Women Health. 2009. <http://www.figo.org>. <http://www.figo.org/files/figo-corp/Ethical%20Issues%202009%20-%202012%20pdf.pdf> [18 Aug 2011].
16. Sussner KM, Edwards TA, Thompson HS, Thompson, HS, et all. Ethnic, Racial and Cultural Identity and Perceived Benefits and Barriers Related to Genetic Testing for Breast Cancer among At-Risk Women of African Descent in New York City. *Public Health Genomics* 2011. (In press)
17. Pavlin NL, Parker RM, Piggan AK, et all. Better than nothing? Patient-delivered partner therapy and partner notification for Chlamydia: the views of Australian general practitioners. *Bio Medical Central Infectious Diseases* 2010; 10: 274-7.
18. Owolabi RS, Araoye MO, Osagbemi GK, Odeigah L, Ogundiran A, Hussain NA. Assessment of Stigma and Discrimination Experienced by People Living with HIV and AIDS Receiving Care/Treatment in University of Ilorin Teaching Hospital (UITH), Ilorin, Nigeria. *Journal of the International Association of Physicians in AIDS Care* 2011. (In press)
19. Wu L, Colby E, Iongi-Filiaga A, Maskarinec GG. American Samoan women's health: experiences and attitudes toward breast and cervical cancer screening. *Hawaii Medical Journal* 2010; 69: 17-20.
20. Yarmohammadian MH, Raeisi AR, Tavakoli N, Nansa LG. Medical record information disclosure laws and policies among selected countries; a comparative study. *Journal of Research in Medical Sciences* 2010; 15: 140-9.
21. Joolae S, Tschudin V, Nikbakht-Nasrabadi A, Parsa-Yekta Z. Factors affecting patients' rights practice: The lived experiences of Iranian nurses and physicians. *International Nurse Review* 2008; 55: 55-61.
22. De Leeuw PW, Zaat JO, Verheugt FW. Hippocrates in the age of reality television. *Nederlands Tijdschrift voor Geneeskunde* 2008; 152: 785-6.
23. Khodaparast AH, Abdolazadeh A, Rasekh M. Critical Study of the "Six Ethical Codes for Research" in Iran. *Journal of Reproduction & Infertility* 2007; 37: 65-79. (In Farsi)
24. Parsapoor A, Mohamad K, Malek Afzali H. Physician, nurses and patient attitude toward necessity of respect to patient rights. *J Medical Ethics & History of Medicine* 2009; 4: 8-90. (In Farsi)

25. Bateni M, Sajadi Z, Hoseini M. Patient's Knowledge Rate of Illness Protocol. *Journal of Health Information Management* 2011; 7: 53-8. (In Farsi)
26. Sarbaz M, Kimiafar K. Comparison of Patient's Rights in Developed Countries and Suggestion a Proper Model for Iran. *Journal of Health Information Management* 2011; 8: 1-9. (In Farsi)
27. Mohammad Nejad E, Begjani J, Abotalebi G. Nurses awareness of patients rights in a teaching hospital. *Journal of Medical Ethics & History of Medicine* 2011; 4: 2-9. (In Farsi)
28. Khoda Karami N, Jannesary S. Pregnant women knowledge regarding bill of rights of pregnant women. *Journal of Medical Ethics & History of Medicine* 2009; 1: 51-58. (In Farsi)
29. Bayrami R, Pezeshki M, Ebrahimi M. A study of the influence of implementing patient's rights workshop for midwives on the women's viewpoints about parturient right respect. *The Journal of Urmia Nursing and Midwifery Faculty* 2007; 5: 92-9. (In Farsi)
30. Creswell JW, Plano CV. *Mixed Methods Research*. SAGE publications 2007.
31. Powell C. The Delphi technique: Myths and realities. *Journal of Advance Nursing* 2003; 1: 376-82.
32. Jones J, Hunter D. Consensus methods for medical and health services research. *Biomedical Journal* 1995; 311: 376-380.
33. Adler M, Ziglio E. *Gazing into the oracle: the Delphi method and its application to social policy and public health*. Bristol, PA: Jessica Kingsley Publishers. Ltd. 1996.
34. Krippendorff K. *Content analysis: An introduction to its methodology*. Newbury Park, CA: Sage 1980.
35. Lacasse Y, Godbout C, Series F. Health-related quality of life in obstructive sleep apnoea. *European Respiratory Journal* 2002; 9: 99-503.
36. Polit, D F, Hungler B P. *Nursing research: Principles and methods*. 7nd ed. Philadelphia: J. B. Lippincott 2006.
37. Waltz CF, Bausell RB. *Nursing research: Design, Statistics and Computer Analysis*. 2nd ed. Philadelphia: FA Davis Company 1983.
38. Beauchamp T, Childress JF. *Principles of biomedical ethics*. Oxford: Oxford university press 2001.
39. Shomali MA. Islamic bioethics: A general scheme. *Journal of Medical Ethics & History of Medicine* 2008; 1: 11-16.
40. Laner-Abass B. Poverty and maternal mortality in Nigeria: Towards a more viable ethics of modern medical practice. *International Journal for Equity in Health* 2008; 7: 11-19.
41. Chalmers J, Muir R. Patient privacy and confidentiality: The debate goes on; the issues are complex, but a consensus is emerging. *Biomedical Journal* 2008; 326: 725-6.
42. Deneyer M, Devroey D, De Groot E, Buyl R., Clybouw C, Vandenplas Y. Informative privacy and confidentiality for adolescents: the attitude of the Flemish paediatrician anno 2010. *European Journal of Pediatrics* 2011. (In press)
43. Helitzer DL, Sussman AL, de Hernandez BU, Kong AS. The "ins" and "outs" of provider-parent communication: perspectives from adolescent primary care providers on challenges to forging alliances to reduce adolescent risk. *Journal of Adolescent Health* 2011; 8: 404-9.
44. Garbin CA, Garbin AJ, Saliba NA, De Lima DC, De Macedo AP. Analysis of the ethical aspects of professional confidentiality in dental practice. *Journal of Applied Oral Science* 2008; 16: 75-80.
45. Peng D, Li XS, Zhang Q, Zhu CR, Zhang JY, Yuan P, Liu Y. Responsiveness evaluation of mental intervention services system in Wenchuan earthquake area. *Zhonghua Yu Fang Yi Xue Za Zhi* 2011; 45: 158-62.
46. McGinn CA, Grenier S, Duplantie J, et all. Comparison of user groups' perspectives of barriers and facilitators to implementing electronic health records: a systematic review. *Bio Medical Central Medicine* 2011; 9: 46-51.
47. Kim D, Schleiter K, Crigger BJ, McMahon JW, Benjamin MR, Douglas P. A physician's role following a breach of electronic health information. *Journal of Clinical Ethics* 2010; 21: 30-5.
48. NHS Information Authority. Confidentiality. The national consultation. <http://www.nhs.uk/confidentiality/pages/consultation> [28 Aug 2011].
49. Confidentiality and Security Advisory Group for Scotland. Protecting patient confidentiality—final report. Edinburgh: Scottish Executive Health Department. 2002. <http://www.show.scot.nhs.uk/sehd/publications/ppcr/ppcr.pdf> [28 Aug 2011].
50. Rueff Mdo C. Breach of confidentiality in medicine. *Acta Medica Portuguesa* 2010; 23: 141-8.

Corresponding Author

Robab Latifnejad Roudsari,
 Research Center for Patient Safety & Health Quality,
 Department of Midwifery,
 School of Nursing and Midwifery,
 Mashhad University of Medical Sciences,
 Mashhad,
 Iran,
 E-mails: LatifnejadR@mums.ac.ir,
 rlatifnejad@yahoo.com

Assessment of kinesthetic awareness and fine motor dexterity in music students with performance-related hand disorders

Zeliha Baskurt¹, Ferdi Baskurt¹, Bilge Kara²

¹ Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Suleyman Demirel University, Isparta, Turkey,

² School of Physical Therapy, Dokuz Eylul University, Izmir, Turkey.

Abstract

Objective: Kinesthetic sense and fine motor skills are extremely important when playing a musical instrument. The aim of this study was to determine differences in kinesthetic awareness and fine motor dexterity between music students with performance-related hand disorders (PRHDs) and healthy music students.

Methods: Assessments were administered to 20 music students with PRHDs and 20 healthy music students. For students with PRHDs, the visual analog scale (VAS) was used to assess pain levels, and the Disabilities of Arm, Shoulder and Hand (DASH) questionnaire was used to determine disability levels. Additionally, Fry's overuse grades were used to determine the severity of the PRHDs. Kinesthetic sense was evaluated with the Kinesthetic Awareness Test, and fine motor dexterity was measured using the Nine-Hole Peg Test in all subjects.

Results: Music students scored lower on kinesthetic awareness and fine motor dexterity performance than healthy controls ($p < 0.05$) with both affected hands. The correlation between scores for kinesthetic awareness and fine motor dexterity was significant ($p < 0.05$). Pain intensity, severity of symptoms and disability levels significantly correlated with kinesthetic awareness and fine motor dexterity test scores ($p < 0.05$).

Conclusions: These results suggest that tests of kinesthetic ability and fine motor dexterity should be considered in the assessment of musicians with PRHDs.

Key words: Music students, fine motor dexterity, kinesthesia, performance-related hand disorders, disability

Introduction

Musicians have an increased risk of developing performance-related hand disorders (PRHDs). This occurs because playing an instrument requires repeated exposure to fine coordinated movement of the hands and fingers, fast-paced forceful movements, stereotypical grasping and sustained awkward hand postures¹⁻³. Most studies on PRHDs indicate that this problem is highly prevalent and problematic among young music students, and in many cases, the disorder can terminate the career of a musician²⁻⁴.

The discomfort in PRHDs may arise from various structures including the musculotendinous unit, joint capsule, synovium and ligaments⁵⁻⁶. Despite uncertain etiology, there is general agreement that PRHDs occur when tissues are stressed beyond their anatomical and physiological limits⁷. PRHDs usually present with localized pain, tenderness and occasionally swelling of the muscle and tendon sheath. Other symptoms include sensory changes, loss of fine motor control (agility, speed and accuracy), coordination difficulty, difficulty moving a particular joint, motor weakness and easy fatigability of the muscles^{1-3,5,6}. The symptoms of PRHDs can decrease the performance quality in musicians⁸.

A predominant symptom of this disorder is pain, which may be acute or chronic⁹. The pain is likely caused by the activation of sensory receptors that are specialized in responding to tissue damage^{1,9}. Although injuries related to repetitive movement are often attributed to soft tissue inflammation and swelling resulting from cumulative microtrauma to the tendons and muscles^{6,10}, recent evidence points to abnormal sensory processing as a potential etiology¹¹. Sensory input generated during the performance of highly repetitive manual tasks can lead to the degradation of the somatic sensory

representation, which can then lead to the loss of peripheral sensory perception and neuromuscular coordination¹¹⁻¹². Musicians also complain of clumsiness, suggesting a possible motor control problem. Neuromuscular control is important to appreciate when treating individuals with even a slight impairment of this fine tuning⁶.

Kinesthesia is defined as the awareness of joint movement. It is dynamic and arises from sensory information from mechanoreceptors¹³. Kinesthetic awareness in the hand is essential for fine motor skills and a precondition for optimal muscular control and coordination. Impairment of kinesthetic sense has an impact on voluntary movement, posture maintenance and the execution of movement¹⁴⁻¹⁶. This sensation may be compromised after the onset of PRHDs.

An examination of fine motor dexterity, which refers to in-hand manipulations, provides a unique way of evaluating the neuromotor function of the entire hand because sensation and intrinsic hand strength combine to produce the manipulative skills that facilitate dexterous movements. Assessments of fine motor dexterity may be used to quantify and predict both ability and disability by gauging a musician's speed and quality of movement as the hand interfaces with an instrument related to performance¹⁷.

Although a number of studies have investigated hand function in patients with various musculoskeletal disorders^{18,19}, no reports exist regarding hand kinesthesia and fine dexterity in musician with PRHDs. Based on the studies reviewed, the effect of PRHDs on kinesthetic awareness and fine motor dexterity has not been clearly established. The purpose of this study was to investigate whether differences in kinesthetic awareness and fine motor dexterity exist between music students with PRHDs and healthy music students. We hypothesized that kinesthetic deficits and decreased fine dexterity would be present in the hands of musicians with PRHDs.

Materials and methods

Participants

A total of 40 music students participated in this study. All participants were recruited from the Dokuz Eylül University Conservatoire in Turkey.

They underwent a complete neuromusculoskeletal examination by an experienced physiotherapist. The participants were divided into two groups: injured and healthy.

The first group consisted of 20 music students suffering from pain, aches or discomfort related to playing an instrument, which was localized in the hand and/or wrists. To be included in the injured group, the subjects had to be involved in playing an instrument that required repetitive use of the hands and demonstrate unilateral or bilateral complaints of pain and tenderness in the hands or wrist as determined by palpation. The subjects could have no signs of neurological impairment due to nerve entrapment and focal dystonia. None of the subjects had any previous or present history of chronic or systemic diseases (e.g., diabetes mellitus and neurological disease), neck pains, or signs of disease in the shoulder and elbow joints (e.g., rotator cuff diseases and tennis elbow). The subjects who had serious hand trauma, surgical intervention, or intra-articular/muscular injection in the previous 6 months were not included in the study.

A second group consisting of 20 music students was recruited as the healthy controls. The healthy control group included musicians with no history of chronic or systemic disease, movement disorders, or inflammatory conditions that affected the upper extremity. They had to be free of physical complaints surrounding the hand, wrist, or elbow for at least 6 months prior to testing.

Table 1 presents detailed descriptive data on the subjects.

All of the subjects described themselves as strongly right-handed according to their writing hand. In the analysis, the affected limb (dominant or non-dominant) of the subject with PRHDs was matched with the corresponding dominant or non-dominant limb of the control subject.

Prior to participation in the study, all subjects signed an informed consent that was approved by the local ethics committee.

Measurements

Pain Intensity: Pain intensity was measured using the visual analogue scale (VAS), with 0 indicating 'no pain' and 10 indicating 'the worst imaginable pain'. Pain intensity was indicated on a ruler²⁰.

Grade of PRHDs: Fry's overuse grades were used to determine the severity of the PRHDs. The five grades of the scale are as follows: *grade 1*, pain occurs only when playing; *grade 2*, pain occurs when playing and for a short period afterward; *grade 3*, pain occurs when playing and for hours or days afterward; *grade 4*, pain is constant; and *grade 5*, pain is incapacitating and severely limits all activities²¹.

Disability: The subjects completed the self-administered, 30-item Disability of the Arm, Hand and Shoulder (DASH) questionnaire. We used the Turkish validated version of the DASH questionnaire. There are two optional scales of the DASH (sport/music and work). Each subject was instructed to rate their ability to do specific everyday activities from 1 (no difficulty) to 5 (unable), the extent to which their symptoms limited physical activities (1= not at all, 5= extremely), and the severity of any symptom they were experiencing (1= none, 5= extreme). The impact of their symptoms on sleep and feelings of confidence or capability was also assessed. If at least 27 of the 30 items are completed, a scale score can be calculated ranging from 0 (no disability) to 100 (most severe disability). The general section and performing arts module of the DASH questionnaire were used in this study²².

Kinesthetic Awareness: Eight different test positions devised by Lynch et al.¹⁵, and later adapted by Grant and Water²³, were used to assess the kinesthetic sense of the hand. The test was explained to the subjects before application, and the positions were practiced. The subjects who failed the practice test were excluded from the study with no other positions shown. The test was conducted in a quiet and well-lit room, with the subject comfortably seated using a table and chair of an appropriate height. A masking box was placed on the table to occlude the subject's vision while allowing the examiner to have a full view of the subject's hands. An internal shelf in the box supported the forearms along predetermined lines at an angle of 20 degrees to the edge of the table, with the hands hanging freely over the edge of the shelf. The level of kinesthetic awareness in the hands was measured by examining the subject's ability to copy hand positions. The accuracy of copying hand gestures was assessed. The test positions were assessed as follows:

- 0= failure to move the hand from the resting position;
- 1= no resemblance to the test position;
- 2=incomplete replication; this includes the use of the wrong fingers in the correct relationship, one finger out of place, inappropriate opposition, or a reversal of the gesture;
- 3=complete and accurate replication.

The test of kinesthetic awareness is scored from 0–24, with lower scores indicating more severe kinesthetic impairment.

Fine Motor Dexterity: The Nine-Hole Peg Test (9-HPT) was used to quantify dexterity. It is a timed measurement of fine dexterity and involves placing and removing nine pegs in a pegboard with nine holes. The subjects are scored on the amount of time it takes to place and remove all 9 pegs. Two trials for the affected hand were performed. The score was obtained using the average of the times required to perform the 2 trials. The mean time (in seconds) was used²⁴.

The participants were either not taking medication or on a stable medication that is not expected to influence sensory afferent function. Additionally, the participants were not allowed to use alcohol, analgesics and/or sleeping medicine in the 24 hours before measurement.

Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Science (SPSS), version 15.0 for Windows. All results were given as the mean $\pm$ standard deviation. Mann–Whitney U tests were used to compare variables between the two groups. Gender distribution between the groups, expressed in percentages, was compared using a chi-squared test. Spearman's correlation analysis was used to determine the variables correlating with kinesthetic awareness and 9-HPT performance. The level of significance was accepted as $p < 0.05$.

Results

The subjects' demographic and other characteristics are given in Table 1. There were no statistically significant differences between the groups related to physical and demographic characteri-

stics ($p>0.05$). Table 1 also shows the distribution of instruments used by the subjects.

Of the 20 subjects in the injured group, 8 subjects had PRHDs in the right hand, 5 in the left hand, and 7 subjects had PRHDs in both hands. The duration of pain experienced in the right hand ($n=15$) and left hand ($n=12$) was 22.76 ± 11.17 [6-48] months and 17.83 ± 8.37 [6-36] months, respectively. According to the grade of PRHDs, 2 subjects were in grade I, 6 subjects were in grade II, 4 subjects were in grade III, 2 subjects were in grade IV and 1 subject was in grade V for the right hand. For the left hand, 1 subject was in grade I, 7 subjects were in grade II, 3 subjects were in grade III and 1 subject was in grade IV.

The clinical parameters evaluated are presented in Table 2. A significant difference between music students with PRHDs and healthy controls was found for the kinesthetic awareness scores and the 9-HPT scores in both affected left and right hands ($p<0.05$). The affected hands demonstrated lower kinesthetic awareness scores (18.33 ± 2.52 vs. 23.35 ± 0.98 , for right hands; 18.91 ± 2.02 vs. 22.50 ± 1.10 , for left hands) and higher 9-HPT scores (19.40 ± 2.81 vs. 16.14 ± 1.01 , for right hands; 18.18 ± 1.26 vs. 16.53 ± 2.38 , for left hands) than corresponding healthy control hands.

The relationship of the kinesthetic awareness scores and 9-HPT scores to pain intensity, pain duration, severity of the symptoms and disability scores of the subjects in the PRHD group are pre-

sented in Table 3. Based on Spearman's correlation coefficient analyses, there was a significant correlation between kinesthetic awareness scores and 9-HPT scores.

There was a significant correlation between the kinesthetic awareness scores and pain intensity, the severity of the symptoms and the disability scores ($p<0.05$). Similarly, a significant correlation was found between the 9-HPT scores and pain intensity, the severity of the symptoms and the disability scores ($p<0.05$). No correlation was found between the kinesthetic awareness scores and pain duration, the 9-HPT scores and the pain duration ($p>0.05$).

Discussion

In this study, we investigated the effects of PRHDs on kinesthetic awareness and the fine motor performance of the hand. Statistically significant differences were detected in the affected hand of the musicians with PRHDs compared with the healthy controls using parameters such as the 9-HPT and kinesthetic awareness scores. The main finding of this study is that the music students' kinesthetic abilities and fine motor skills were significantly diminished in the affected hand compared with the healthy controls. These results support our hypothesis that PRHDs result in significantly impaired kinesthetic awareness and reduced fine motor dexterity.

Table 1. Characteristics of the Participants

	Injured (n=20)	Healthy (n=20)	p
Age (years, mean[SD])	17.20[1.73]	17.36[1.76]	0.793
BMI (kg/m ² , mean[SD])	19.81[1.87]	19.48[1.72]	0.636
Gender (n, Male/Female)	4/16	3/17	0.677
Main Instrument (n, a ¹ -2-3-4)	8-7-3-2	10-6-3-1	
Pain Intensity (VAS, 0-10)			
Affected Hand R (n/mean[SD])	5.53[2.32]	-	
L (n/mean[SD])	4.91[1.72]		
Disability (DASH, 0-100)			
Affected Hand R (n/mean[SD])	25.08[8.67]	-	
L (n/mean[SD])	24.14[12.43]		
Disability (DASH- PAM, 0-100)			
Affected Hand R (n/mean[SD])	40.16[17.44]	-	
L (n/mean[SD])	36.97[13.17]		

SD: Standard deviation, BMI: Body Mass Index, VAS: Visual Analog Scale, R: Right, L: Left

DASH: Disabilities of Arm, Shoulder and Hand; DASH- PAM: Disabilities of Arm, Shoulder and Hand- Performing Arts Module

a¹.Keyboards a². Strings a³.Woodwinds a⁴.Others

Table 2. The Comparison of Kinesthetic Awareness Test and 9-HPT Values of Injured and Healthy Groups

	Right Hand				Left Hand			
	Injured (n=15)		Healthy (n=20)		Injured (n=12)		Healthy (n=20)	
	Mean[SD]	Range	Mean[SD]	Range	Mean[SD]	Range	Mean[SD]	Range
Kinesthetic Awareness Test Score (0-24)	18.33[2.52]	15-24	23.35[0.98]	21-24	18.91[2.02]	16-24	22.50[1.1]	20-24
9-HPT (sec)	19.40[2.81]	15.66-24.73	16.14[1.01]	14.28-18.30	18.18[1.26]	15.73-20.73	16.53[2.38]	9.98-20.96
								0.000
								0.009

9-HPT: Nine-Hole Peg Test

The association between chronic musculoskeletal disorders and the loss of kinesthetic sense has been demonstrated in several studies²⁵⁻²⁷. However, kinesthesia has not been studied as extensively in PRHDs. There is only one study that has investigated the effects of PRHDs on kinesthetic deficits in the musician population. Byl et al. assessed sensory motor performance in the hands of musicians with repetitive strain injuries. Similar to our findings, they found impairment in hand kinesthesia in musicians with tendonitis compared with controls²⁸.

Motor performance during purposeful activities, such as playing an instrument, is dependent on the continuous flow of sensory information to guide the direction, force, and accuracy of movement²⁹. The activation and feedback from the somatosensory receptors in the skin, joints, and muscles provide the foundation for tactile perception, shaping the hand for object manipulation and finger movements³⁰. Somatosensory system feedback dysfunction results in the degradation of motor control of the hand²⁸⁻³¹. Nociceptive stimulation and pain may directly interfere with the central processing of proprioceptive input³² and thus contribute to the abnormal kinesthesia reported in individuals with PRHDs. Some studies have shown that stereotypical repetitive movement patterns produced cortical changes that may lead to impaired motor performance³³⁻³⁴. The mechanisms related to impaired kinesthetic sense, such as the inability to execute or copy the desired position, in the musicians with PRHDs in the present study are unclear. These changes may result in pain or central alterations in motor control.

Assessing dexterity is critical because dexterity is a central component of hand function¹⁷. There has not yet been a study on musicians with PRHDs examining fine motor dexterity. However, a few researchers have measured motor dexterity in patients with forearm/wrist musculoskeletal disorders. For example, Skinner et al. examined the differences in fine motor dexterity between 28 subjects with lateral epicondylitis and matched control subjects and found significant differences on both the Purdue Pegboard Test and the Complete Manual Dexterity Test¹⁹. Similarly, in the current study, we found that the time required to perform the motor pattern of the 9-HPT was significantly longer for music students with PRHDs

Table 3. The Correlations of the Between Pain Characteristics, Kinesthetic Awareness and Fine Motor Dexterity in Music Students with PRHDs

	9-HPT Correlation Coefficient	Kinesthetic Awareness Test Correlation Coefficient
Pain Intensity (VAS, 0-10)	.568**	-.799**
Pain Duration (months)	.072	.162
Severity of the symptoms (Grade1-5)	.619**	-.566**
Disability (DASH, 0-100)	.502*	-.514*
Disability (DASH-PAM, 0-100)	.484*	-.526*
Fine Motor Dexterity (9-HPT, sec)	-	-.447*
Kinesthetic Awareness Test (0-24)	-.447*	-

VAS: Visual Analog Scale; DASH: Disabilities of Arm, Shoulder and Hand; DASH- PAM: Disabilities of Arm, Shoulder and Hand- Performing Arts Module; 9-HPT: Nine-Hole Peg Test

* Correlations significant at the 0.05 level

** Correlations significant at the 0.01 level

than for healthy music students.

Kinesthetic awareness in the hands is important for fine motor skills because impairment of the hand's kinesthetic sense affects its performance¹⁴⁻¹⁶. Kinesthetic awareness and fine motor dexterity in the hand may also be closely related to performance when playing an instrument. The kinesthetic input may enhance playing by decreasing the amount of visual inspection required by the musicians. Adequate kinesthetic development and perceptual motor skills are the foundation for performance in instrument playing. Our findings support the existence of a relationship between impaired kinesthetic sense and fine motor skills. The impaired kinesthetic awareness found in this study is considered to be one of the factors behind the reduced fine motor dexterity observed in musicians with PRHDs.

Smeulders et al. evaluated the relationship between pain intensity and fine motor control among patients with chronic wrist pain. They found a significant difference in the fluency of motion due to disturbed motor control between the patients and controls, but there was no relationship between the pain and test scores¹⁸. In the present study, we found that pain intensity and the grade of PRHDs affected kinesthetic awareness and fine motor dexterity.

Disability represents the impact of a disorder on the ability of the individual to carry out activities in the manner or within the range that is considered normal³⁵. Physical function depends upon many physiological parameters, including muscle stren-

gth, muscle flexibility, range of motion, sensory input from the proprioceptive system and higher cortical function. Impairments in these parameters are likely contributors to disability³⁶. A relationship between impaired kinesthesia and disability has been found in patients with various musculoskeletal conditions through both objective measurement and specific patient-oriented measurements^{25,36-38}. Our data demonstrated significant correlations between disability points and both kinesthetic awareness and fine motor dexterity test scores. Because kinesthesia plays an important role in coordinating and refining motor activity, a link between kinesthetic deficits and disability might be expected. However, disability in musicians with PRHDs is multifactorial. Factors aside from kinesthetic deficits play a greater role in influencing the degree of disability. Severity of pain is a consistent predictor of disability together with psychological factors, including the pain coping, anxiety and the individual's well-being³⁵.

This study has demonstrated that kinesthetic awareness and fine motor dexterity are significantly decreased in the affected hand in musicians with PRHDs. However, further studies using different methods of kinesthetic sense and fine motor skills are needed to measure the loss of kinesthetic sense that is frequently associated with PRHDs in musicians. Furthermore, the effects of impaired kinesthetic sense and reduced fine motor dexterity on playing an instrument in musicians with PRHDs are not completely known.

Conclusion

Kinesthetic awareness and fine motor dexterity in the hand are important during instrument playing. Motor control for executing complex activities, such as playing an instrument, depends on afferent inputs and may be affected by extensive playing. Good sensorimotor function is important for reducing the risk of PRHDs in musicians. Early recognition of PRHDs and the appropriate responses are critical in minimizing the severity of health effects and maintaining a musician's ability to perform. Early detection of changes in kinesthetic sense and fine motor dexterity in musicians exposed to risky manual tasks associated with instrument use is important for a successful physiotherapy program. From this point of view, physical therapists should carefully evaluate kinesthetic sense and fine motor skill in each musician complaining of a PRHD before treatment. Additionally, these findings indicate that clinicians should consider hand treatment programs that include kinesthetic training. Improvement in kinesthesia and fine motor dexterity may lead to improvements in instrument performance.

References

1. Brandfonbrener AG. Musculoskeletal problems of instrumental musicians. *Hand Clin* 2003; 19: 231-239.
2. Akı E, Yakut Y. Overuse syndrome and related problems in professional and student string players. *Pain Clin* 2003; 15(3): 327-331.
3. Foxman I, Burgel BJ. Musician health and safety: preventing playing-related musculoskeletal disorders. *AAOHN Journal* 2006; 54: 309-316.
4. Kaufman-Cohen Y, Ratzon NZ. Correlation between risk factors and musculoskeletal disorders among classical musicians. *Occup Med (Lond)* 2011; 61(2): 90-95.
5. Hoppmann RA. Instrumental musicians' hazards. *Occup Med (Lond)* 2001; 16(4): 619-361.
6. Bejjani FJ, Kaye GM, Benham M. Musculoskeletal and neuromuscular conditions of instrumental musicians. *Arch Phys Med Rehabil* 1996; 77: 406-13.
7. Lambert CM. Hand and upper limb problems of instrumental musicians. *Br J Rheumatol* 1992; 31: 265-271.
8. Blum J. Examination and interface with the musician. *Hand Clin* 2003; 19: 223-230.
9. Brandfonbrener AG. The epidemiology and prevention of the hand and wrist injuries in performing artists. *Hand Clin* 1990; 6: 365-377.
10. Pitner MA. Pathophysiology of overuse injuries in the hand and wrist. *Hand Clin* 1990; 6: 355-364.
11. Tremblay F, Mireault AC, Letourneau J, Pierrat A, Bourrassa S. Tactile perception and manual dexterity in computer users. *Somatosens Mot Res* 2002; 19(2): 101-108.
12. Byl NN, Merzenich MM, Cheung S, Bedenbaugh P, Nagarajan SS, Jenkins WM. A primate model for studying focal dystonia and repetitive strain injury: effects on the primary somatosensory cortex. *Phys Ther* 1997; 77: 269-284.
13. Proske U. Kinesthesia: The role of muscle receptors. *Muscle Nerve* 2006; 34: 545-558.
14. Putzki N, Stude P, Konczak J, Graf K, Diener HC, Maschke M. Kinesthesia is impaired in focal dystonia. *Mov Disord* 2006; 21: 754-760.
15. Lynch MR, Raymer ME, Elvery JH, Walsh AL, Burns YR. The development of hand position sense. *New Zealand J Physiother* 1992; 20: 15-20.
16. Hwang SJ, Kentish M, Burns Y. Hand positioning sense in children with spina bifida myelomeningocele. *Aust J Physiother* 2002; 48: 17-22.
17. Yancosek KE, Howel D. A narrative review of dexterity assessments. *J Hand Ther* 2009; 22: 258-70.
18. Smeulders MJC, Kreulen M, Bos KE. Fine motor assessment in chronic wrist pain: the role of adapted motor control. *Clin Rehabil* 2001; 15: 133-141.
19. Skinner DK, Curwin SL. Assessment of fine motor control in patients with occupation-related lateral epicondylitis. *Man Ther* 2007; 12: 249-255.
20. Van Den Hout JHC, Vlayen JWS, Houben RMA, Soeters APM, Peters ML. The effects of failure feedback and pain-related fear on pain report, pain tolerance and pain avoidance in chronic low back pain. *Pain* 2001; 92: 247-257.
21. Fry HJH. Overuse syndrome in musicians: prevention and management. *Lancet* 1986; 27: 728-731.
22. Düger T, Yakut E, Ökstüz Ç, Yörükan S, Bilgütay S. ve ark. Kol, omuz ve el sorunları (disabilities of the arm, shoulder and hand-DASH) anketi Türkçe uyarlamasının güvenilirliği ve geçerliği. *Fizyoterapi-Rehabilitasyon* 2006; 17(3): 99-107.
23. Grant L, Watter P. Ability to copy hand positions at 10 and 12 years of age. *New Zealand J Physiother* 1998; 26: 21-25.

24. Grice KO, Vogel K, Le V, Mitchell A, Muniz S, Vollmer MA. Adult norms for a commercially available Nine Hole Peg Test for finger dexterity. *Am J Occup Ther* 2003; 57: 570-573.
25. Kara B, Yildirim Y, Karadibak D, Acar Ü. Evaluation of the kinesthetic sense and function of the hand in early period in operated cervical disc hernia. *Eur Spine J* 2006; 15: 992-997.
26. Lam SS, Jull G, Treleaven J. Lumbar spine kinaesthesia patients with low back pain. *J Orthop Sports Phys Therapy* 1999; 29: 294-299.
27. Hubbard TJ, Kaminski TW. Kinesthesia Is not affected by functional ankle instability status. *J Athl Train* 2002; 37(4): 481-486.
28. Byl N, Wilson F, Merzenich M, Melnick M, Scott P, Oakes A, McKenzie A. Sensory dysfunction associated with repetitive strain injuries of tendinitis and focal hand dystonia: a comparative study. *J Orthop Sports Phys Ther* 1996; 23: 234-244.
29. Melchior H, Vatine JJ, Weiss PL. Is there a relationship between light touch-pressure sensation and functional hand ability?. *Disabil Rehabil* 2007; 29(7): 567-575.
30. Byl N, Leano J, Cheney, L. The Byl-Cheney-Boccai sensory discriminator: reliability, validity, and responsiveness for testing stereognosis. *J Hand Ther* 2002; 15: 315-330.
31. Wilson F, Wagner C, Homberg V, Noth L. Interaction of biomechanical and training factors in musicians with occupational cramp/focal dystonia. *Neurology* 1991; 4(3 suppl1): 292-297.
32. Bennell K, Wee E, Crossley K, Stillman B, Hodges P. Effects of experimentally-induced anterior knee pain on knee joint position sense in healthy individuals. *J Orthop Res* 2005; 23: 46-53.
33. Byl N, Wilson F. Sensory dysfunction associated with repetitive strain injuries of tendinitis and focal hand dystonia: a comparative study. *J Orthop Sports Phys Ther* 1996; 23(4): 234-244.
34. Elbert T, Candia V. Alteration of digital representations in somatosensory cortex in focal hand dystonia. *Neuroreport* 1998; 9(16): 3571-3575.
35. Fitzpatrick F, Badley EM. An overview of disability. *Brit J Rheumatol* 1996; 35: 184-87.
36. Bennell KL, Hinman RS, Metcalf BR, Crossley KM, Buchbinder R, Smith M, McColl G. Relationship of knee joint proprioception to pain and disability in individuals with knee osteoarthritis. *J Orthop Res* 2003; 21: 792-797.
37. Rix GD, Bagust J. Cervicocephalic kinesthetic sensibility in patients with chronic, nontraumatic cervical spine pain. *Arch Phys Med Rehabil* 2001; 82: 911-919.
38. Lund H, Juul-Kristensen B, Hansen K, Christensen R, Christensen H, Danneskiold-Samsoe B, Bliddal H. Movement detection impaired in patients with knee osteoarthritis compared to healthy controls: a cross-sectional case-control study. *J Musculoskeletal Neuronal Interact* 2008; 8(4): 391-400.

Corresponding Author

Zeliha Baskurt,
Suleyman Demirel University,
Health Sciences Faculty,
Physiotherapy and Rehabilitation Department,
East Campus,
Cumur-Isparta,
Turkey,
E-mail: zelihabaskurt@sdu.edu.tr

Burnout syndrome among special education professionals

Nikola Petkovic¹, Dragana Macesic Petrovic¹, Vasilije Balos¹, Miroslav Misic², Milos Djordjevic¹

¹ Faculty for special education and rehabilitation, University of Belgrade, Serbia,

² Medical College of Professional Studies in Belgrade, Serbia.

Abstract

The objective of this study was to assess the level of Burnout syndrome (BOS) among special educators in Serbia and to investigate the relationship between demographic characteristics (gender, age, years of working experience, parental status etc.) and syndromic burden. The complexity of problems in working with persons with developmental disabilities, slow rehabilitation process, and frequent discrepancy between the achievable results and parental expectations of children with disabilities, are some of the factors that additionally burden professionals who deal with this delicate population. Data were collected by surveying 129 professionals in six institutions in five cities in Serbia. Each participant filled the questionnaire in voluntarily, anonymous fashion. Data were collected by Maslach Burnout Inventory (adjusted Croatian translation) which measures BOS level presence and with a series of survey questions, which enquired the main demographic information (age, gender, marital status, years of practice, parental status etc.) Respondents gave answers to Maslach Burnout Inventory – Human service survey. According to our findings, a high level of emotional exhaustion was present among 35.7% of examinees, a high level of reduced professional accomplishment was present in 11.6% of examinees, while 1.6% of examinees exhibited elements of depersonalisation. Examinees financial situation proved to be a particularly important factor for Burnout syndrome manifestation.

Even though clearly confirmed amongst special educators in Serbia, the Burnout syndrome represents a phenomenon. Possible reflections of such phenomenon are not acknowledged on a wider scale. Even though 92% of the respondents in the conducted study believe that there should be some sort of support program and stress management program for employees, these programs do

not exist in any institution for persons with developmental disabilities in Serbia.

Key words: Burnout syndrome, special educators, demographic characteristics.

Introduction

The topic of Burnout syndrome (BOS) and its consequential effects has been a subject of numerous studies over the past few decades worldwide. Such studies attempted to describe the psychological state of human services workers under severe and prolonged stress (Rose, 1991, Soderfeldt, 1995, Shaddock, 1998, Hastings, 2004). Characterising the employees in social services as professionals with high demands of long-term professional and emotional investments, has further directed the researchers to the field of special education and rehabilitation of people with developmental disabilities (Bradfield, 1986; Aitken, 1994; Wisniewski, 1997; Lloyd, 2002; White, 2006; Devereux, 2009; Hastings et al., 2009; Grey- Stanley, 2011).

The complexity of problems in working with persons with developmental disabilities, slow rehabilitation process, and frequent discrepancy between the achievable results and parental expectations of children with disabilities, are some of the factors that additionally burden professionals who deal with this delicate population. The Republic of Serbia was affected by war and economic crisis over the last twenty years and was not capable of making necessary investments in maintenance and improvement of social protection programs. In addition to that, the conditions, in which persons with disabilities reside, are often inadequate or even inhumane. The effects of all these stressors are cumulative and lead to a job related stress. Cross-cultural research can make contributions to theory development by identifying groups of people who seem not to behave according to established theories and by increasing the range of independent

variables available for study in any one culture (Brislin, 1976).

In a historical perspective, the burnout syndrome is not a recent concept. In the mid 70's of the 20th century, Freudenberger (1974) observed gradual changes of motivation and commitment of volunteers in psychiatric care. He was the first to define this syndrome as a state of physical, emotional or mental exhaustion, caused by long-term engagement in emotionally demanding situations.

A decade later, Maslach and Jackson (1981, 1986) proposed a more comprehensive definition according to which the BOS includes three dimensions. The burnout syndrome is defined as a sustained response to chronic work stress that includes three dimensions: a sense of emotional exhaustion, negative attitudes and feelings toward the recipients of the service (depersonalisation) and the sense of low personal accomplishment (professional failure), with emotional exhaustion as the key aspect of the syndrome. According to these authors, the feeling of "being unable to give oneself psychologically", is followed by depersonalization which results in cynical, uncaring and excessively detached responses toward clients, accompanied with symptoms of reduced personal accomplishment, resulting in a decline in one's competence, productivity and self-evaluated professional dissatisfaction (Lesic, 2009, Petkovic, 2010, Dedic, 2005). Significance of the contribution of these authors was in constructing of several versions of BOS assessment instruments, which improved further empirical research to a great extent.

Looking further into the field of special education and rehabilitation, one can see results that clearly indicate a high syndrome burden of professionals who work with persons with disabilities. It is, however, interesting to mention that, although the obtained data from these studies (conducted with professionals who work with persons with developmental disabilities, learning disabilities and similar developmental characteristics as in this study) suggest high levels of emotional exhaustion and reduction of personal accomplishment, the level of registered cynicism in relations with residents remained rather low (i.e. depersonalisation) (Male, 1997).

Except for several studies dealing with BOS prevalence among professionals employed in orthopaedic, oncologic and psychiatry departments, as well as in institutions for correction of juvenile

delinquents, serious local or international empirical studies that include professionals who work with persons with developmental disabilities, have not been carried out neither in our region, nor in other regions. (Lesic; 2009, Curcic, 2009; Rose, 1991; Male, May, 1997; Gray-Stanley, 2011).

The objective of this study was verifying the prevalence of the burnout syndrome among special educators in Serbia, as well as discovering the relationships between demographic characteristics (gender, age, years of working experience, parental status, socioeconomic status etc.) and BOS level.

Even though most authors concur that special educators and rehabilitators are particularly at risk in developing the Burnout syndrome (Bradfield, 1986), literature review showed that there appears to be a disagreement whether BOS is primarily determined by the specific nature of the work and work environment, or by the characteristics of the employees themselves (Petkovic, 2010). Furthermore, if we focus just on one of these aspects, the diversity of the scientific results leads to further confusion. (Perlman & Hartman, 1982).

Within the same context, Mearns & Cain (2003) stress the relative consistency of the results according to which young professionals show a higher level of BOS in comparison with their older colleagues. However, Friedman (1992), who presented results of a survey covering 1597 elementary school teachers, founded that the BOS level directly correlates to age.

Intercorrelation between work experience and BOS level showed results without significant statistical difference in several studies (Platsidou et al. 2008; Greem Resse et al, 2001), while Friedman (1992) in his study restated that professionals with a higher BOS level have more years of working experience.

Analysis of the influence of gender in relation to BOS in conducted studies also showed disparity in results. The impression that dominates the literature is the view, according to which women show higher level of emotional exhaustion, while men show higher level of depersonalisation. This could be explained by the significant emotional investment of women and higher commitment within helping professions (Byrne, 1998; Eichinger, 2000).

According to Maslach and Jackson (1985) the matter of marital status showed to have a stable

pattern of a lower BOS level in experts who are married, with respect to those who are single. However, these differences are frequently only of marginal statistical significance. Among the explanations of the possible protective effects of marriage, primarily, Petkovic (2010) lists the family support and understanding married persons have.

Within the same context, the previous statements gain in importance with the fact that parental status poses a significant predisposing factor for BOS. Hence, employees with no children show significantly higher values of medium scores in all aspects of BOS (Maslach and Jackson, 1985).

Finally, the specific socio-economic situation in Serbia has led to the fact that the financial status of employees working in social services significantly correlates to the Burnout Syndrome. In the study conducted by Petkovic et al (2010) it is stated that professionals with no home ownership show a higher level of emotional exhaustion (62%).

Method

Study sample

This study included 129 special educators from six institutions for permanent care and rehabilitation for children with disabilities in five cities in Serbia. Although various professional profiles were included among respondents (special educators - high educated professionals, medical stuff, social workers etc.), the fact that these professionals often work with multiply disabled children, led the authors to observe the sample as a whole, without further specific differentiation. Each participant filled the questionnaire in voluntarily, anonymous fashion. Incomplete questionnaires (16) were not included in the study. Despite the attempts to have a gender-equal sample, 86.8% of surveyed experts were female, and only 13.2% were male (Table 1). The average age of respondents was 42.1 years, with only 15.5% under the age of 30.

Analysis of marital status showed that 53.5% of the respondents were married, 3.2% were single, and 9.3% were divorced. Within the same context, 58% of them have children, and 41.9% gave a negative answer to the question regarding parenthood.

According to the years of working experience, the sample is quite uniform, 31% of surveyed persons had over 16 years of working experience,

27.1% between eleven and fifteen, 20.9% between five and eleven, and finally 20.9% had with five years and less of experience (Figure 1).

Among the important data, the fact that 67.4% of the respondents had a permanent contract, whereas 32.6% had temporary contracts, should be mentioned. At the same time, only 7% of the respondents observed their financial status as "favourable", 76% as "average" and a striking 17% as "unfavourable". Finally 15.5% of the respondents reported having a chronic organic disease, while 84.55% reported having a normal health status.

Instrument and statistical analysis

Data were collected by Maslach Burnout Inventory (adjusted Croatian translation) which measures BOS level presence and with a series of survey questions, which enquired the main demographic information (age, gender, marital status, years of practice, parental status etc.) (Jelec, 2009; Maslach, Jackson 1986).

Table 1. The distribution of gender and marital status among investigated professionals

Gender Marital status									
Male		Female		Single		Married		Divorced	
n	%	n	%	n	%	n	%	n	%
17	13.2	112	86.8	48	37.2	69	53.5	12	9.3

Maslach Burnout Inventory (MBI) consists of 22 statements on three subscales, with a respondent score from 0 to 6, which presents how often the respondent felt that way (0-never, 6- every day). Emotional exhaustion (EE) subscale consists of 9 items, a depersonalization subscale (DP) consists of 5 items, and a personal accomplishment subscale (PA) of 8 items. The results on MBI could be categorised as low, medium or high, depending on the presented scores (Table 2). It is important to mention that the emotional exhaustion and depersonalisation scores positively correlate with the BOS, while the personal accomplishment score is inversely proportional.

Internal consistencies for MBI were estimated by Cronbach's coefficient alpha. The reliability coefficients for the subscales were the following: .84 for Emotional Exhaustion, .58 for Depersonalisation, and .73 for Personal Accomplishment. Although EE and PA subscales showed good in-

ternal consistencies, occasional low level for DP subscale is due to the small number of items integrated into this subscale.

Statistical analyses of the results obtained by surveying participants, were performed using the software package SPSS-16. It includes descriptive statistical method, ANOVA, Kruskal-Wallis one way analysis of variance, and Pearson's correlation test.

Results

The distribution of scores on three MBI subscales showed that 46 (35.7%) of the respondents exhibited a low level of emotional exhaustion, 51 (39.5%) a moderate level and 32 (24.8%) of the respondents showed a high level. Viewed in the perspective of the overall sample, the average score on the EI subscale is 19.61. That corresponds to a moderate level of emotional exhaustion. Results on the depersonalisation subscale showed that 113 (87.6%) of respondents exhibited a low level of depersonalisation, 14 (10.9%) a moderate level, and only 2 (1.6 %) of respondents showed a high level of depersonalisation, with the average summary score of 2.65. *Table 2. Scores on MBI subscales according to Lesic, 2009*

	Low	Moderate	High
Emotional exhaustion EE	<17	17-26	>26
Depersonalisation DP	<7	7-13	>13
Personal accomplishment PA	>38	31-38	<31

Finally the results on personal accomplishment subscale showed that 78 (60.5%) of the respondents had a low level of reduced personal accomplishment, 36 (27.9%) a moderate level and 15 (11.6%)

of the respondents had a high level, with the average summary score of 39.13. (Figure 1, Table 3)

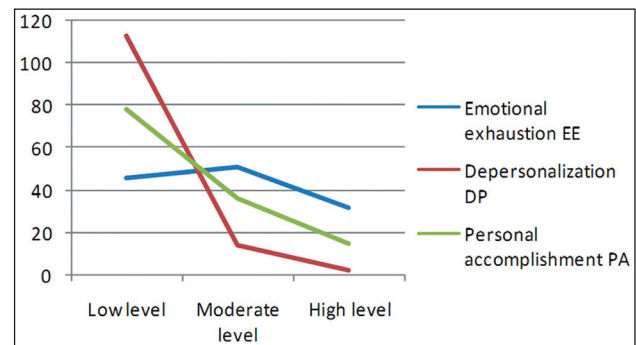


Figure 1. MBI subscales on total sample

Determining the level of burnout syndrome in regard to independent variables showed relative uniformity of the results by gender, without statistically determined significant differences between mean values for all three subscales. However, it is interesting to note that male respondents exhibited greater emotional exhaustion in comparison to female respondents, and a slightly higher depersonalisation score, while females exhibited greater personal accomplishment in comparison to male respondents. Final analysis of mean values showed that both men and women showed a moderate level of emotional exhaustion; low level of depersonalisation; women showed low, while men showed moderate level of reduced personal accomplishment (Table 4). In addition, Pearson correlation showed no significant correlation on any of the subscales ($r = -.162$; $p > 0.05$, Pearson correlation $-.033$; $p > 0.05$, $r = .137$, $p > 0.05$).

Result analysis by age, indicated statistically significant differences in mean values of the EE subscale between groups of respondents under the

Table 3. Scores on MBI subscales for total sample

	n	Min	Max	Med.	St.dev
Emotional exhaustion EE	129	0	43	19.6124	10.0142
Depersonalization DP	129	0	18	2.6589	3.3575
Personal accomplishment PA	129	19	48	39.1395	6.4550

Table 4. Scores on MBI subscales for gender subgroups

Gender	Female (112)		Male (17)		F	Sig.
Subscale	M	SD	M	SD		
EE	18.9826	9.7055	23.7647	11.3005	3, 430	.066
DP	2.6161	3.3510	2.9412	3.4905	0.137	.771
PA	39.4821	6.4486	36.8824	6.2137	2, 421	.122

age of 30 and those aged 31-40 years, while statistical significance was not confirmed in the following cross group – comparison in the sample (aged 40-50 and over the age of 50). However, comparison of registered levels of emotional exhaustion testifies that respondents under the age of 30 showed a low level of EE, while respondents in all three comparative groups showed a moderate level.

Finally, on the PA subscale, statistically significant difference between mean values was confirmed only in the comparison group of patients 30 years of age and those over the age of 50, with relative increasing trend of influence on personal accomplishment. All respondents under the age of 50 showed a low level on the PA subscale, and those over the age of 50 showed a moderate level. Pearson correlation showed no significant correlation on EE ($r=.045$; $p>0.05$), and DP subscale ($r=.097$; $p>0.05$), but it showed correlation on PA subscale ($r=-.210$; $p<0.05$)

Analysis of results, according to years of service, on the EE subscale showed statistical significance of differences between average values in the compared results of respondents with 0-5 years of service in relation to those with 11-15 years, as well as between those with 11-15 years of service and those with more than 15 years. The average values within the specified interval of 5 years showed a low level of emotional exhaustion at the beginning of working careers and a moderate level after 5 years. However the significant increasing trend was not observed. In addition, Pearson correlations analysis showed that there were no significance relation on EE subscale ($r = .078$, $p> 0.05$).

Looking at the DP subscale, statistically significant difference between mean values was found only between groups of respondents with work experience of 6-10 years and those with experience of 11-15 years of service. Results in other groups showed variation levels of DP with no clear correlation and statistical significance, with general trend of low DP. Pearson correlation analysis showed no significance relation on DP subscale ($r=.070$, $p>0.05$).

Results of the PA subscale showed no statistically significant difference between average values of compared groups. Still, the minimal increasing trend of reduced personal accomplishment was observed, noting that groups up to 15 years of service show low and those with over 15 moderate levels. Pearson correlation analysis showed no significance relation on PA subscale ($r = -.155$, $p> 0.05$).

Analysis of results by marital status on the EE subscale showed a statistically significant difference between the average values of the groups of respondents who are married and those who are single. These differences were not observed between respondents who are married and divorced. Statistical significance of difference was also found between respondents who were not married and those that were divorced. It is important to emphasise that on the EE subscale respondents who were married exhibited a low level of emotional exhaustion. Meanwhile, those married and divorced, had a moderate level of emotional exhaustion, higher emotional exhaustion was exhibited by married respondents (4.54 points) and by divorced respondents (7.61 points) compared to an average value of single respondents. Pearson

Table 5. Results on MBI subscales according to the chronological distribution of the sample

Gender	20-30		31-40		41-50		>50.		F	Sig.
Subscale	M	SD	M	SD	M	SD	M	SD		
EE	13.8500	10.7227	22.0508	9.1433	19.6190	11.3246	18.6207	8.8536	3, 687	.014
DP	.9500	1.2343	3.3051	3.8428	1.9048	2.3854	3.0690	3.5044	3.098	.029
PA	41.7000	4.7694	39.2034	6.3565	39.8095	4.8437	36.7586	7.9805	2, 529	.060

Table 6. Results on MBI subscales according to years of working experience

Years of practice	0-5		>5-10		>10-15		>15		F	Sig.
Subscale	M	SD	M	SD	M	SD	M	SD		
EE	16.2222	10.5441	20.2593	9.2843	23.2286	11.0775	18.3000	8.2964	2.948	.035
DP	2.5185	2.9400	1.5926	2.1169	3.6571	4.2905	2.6000	3.2407	2.005	.117
PA	40.4815	4.7585	40.0370	5.9192	38.7714	7.1170	37.9500	7.1250	1.055	.371

correlation showed no significance on EE subscale correlation ($r = -.051, p > 0.05$).

Group Analysis on the DP subscale was not statistically significant. All three categories, showed low levels of depersonalisation. Pearson correlation showed no significance on DP subscale correlation ($r = -.153, p > 0.05$). Finally, the comparison of group results on the PA subscale showed statistical significance of average values between married and unmarried, while further comparison did not show previously mentioned statistical significance. Registered high values correspond to low level of personal accomplishment. Pearson correlation showed significance on PA subscale correlation ($r = .214, p < 0.05$).

In regards to parental status, results showed a statistically significant difference between average values only on the EE subscale. Respondents, who have children, had an average score of 3.95 higher than those with no children. Respondents with no children had low levels of emotional exhaustion, while those who have children showed a moderate level of emotional exhaustion. Both groups showed low levels of load on DP and PA subscale. Pearson correlation showed significance on EE subscale correlation ($r = -.195, p < 0.05$) but no significance correlation on DP ($r = -.040, p > 0.05$) and PA subscales ($r = .118, p > 0.05$).

Employment status was found statistically significant as a variable. The results proved that difference between the average values of the EE subscale is statistically significant, indicating that people with steady employment exhibited lesser emotional exhaustion in comparison to people who have time-bound contracts. However both categories belong to a moderate level of emotional exhaustion. Pearson correlation showed significance on EE subscale ($r = -.221, p < 0.05$).

Although the results of the DP subscale showed statistically significant difference between mean values, both groups showed low load results for this scale. Pearson correlate showed significance correlation on DP subscale ($r = .191; p < 0.05$).

Finally, groups considered, showed no significant differences on PA subscale upstrokes. Pearson correlate showed no significance correlation on PA subscale ($r = -.049; p > 0.05$).

The most significant differences in results were found in relation to variable financial situation, according to which the respondents evaluated their financial status as good, average, or unfavourable. Kruskal-Wallis's one-way analysis of variance on the EE subscale showed significant statistical differences between all three subgroups with a clear correlation between higher levels of emotional exhaustion and declining quality of financial status.

Table 7. Results on MBI subscales according to marital status

Marital status	Married		Single		Divorced		F	Sig.
Subscale	M	SD	M	SD	M	SD		
eE	21.0145	9.5463	16.4792	9.8326	24.0833	10.6554	4.449	.014
DP	3.2029	3.9503	2.0000	2.4407	2.1667	2.2896	1.989	.141
PA	37.8261	6.39843	40.4792	6.60106	41.3333	4.65800	3.267	.041

Table 8. Scores on MBI subscale according to parental status

	Have children		Do not have children		F	Sig.
Subscale	M	SD	M	SD		
EE	21.2667	9.8053	17.3148	9.8053	5.004	.026
DP	2.7733	3.6965	2.5000	2.8467	0.207	.650
PA	38.4933	6.1652	40.0370	6.7933	1.807	.181

Table 9. Results on MBI subscales according to working status

	Time-bound contracts		Steady employment		F	Sig.
Subscale	M	SD	M	SD		
EE	22.7857	9.7843	18.0805	9.8148	6.523	.012
DP	1.7381	2.1646	3.1034	3.7324	4.824	.030
PA	39.5952	4.7424	38.9195	7.1515	.309	.579

Table 10. Results on MBI subscales according to financial status

Financial status	Good		Average		Not good		Chi-square	Sig.
Subscale	M	SD	M	SD	M	SD		
EE	11.4444	12.1563	19.1939	8.9749	24.8182	11.1851	11.903	.003
DP	2.3333	2.0000	2.5510	3.6044	3.2727	2.5853	3.515	.172
PA	43.2222	3.5978	39.5000	5.9453	35.8636	8.1725	7.959	.019

Thus, differences in average values among professionals who assessed their financial situation as a “convenient” and professionals who rated their financial situation as “unfavourable”, is 13.37 points. Pearson correlation showed significance on EE subscale correlation ($r = -.305$, $p < 0.01$).

Similarly, as in previously conducted comparisons, DP subscale showed no statistically significant results, with an average score that corresponds to a low level of burnout. Pearson correlation showed no significance on DP subscale correlation ($r = .079$, $p > 0.05$).

Results obtained on PA subscale from respondents with “favourable” and “unfavourable” financial position, or “the average” and “adverse” showed a statistically significant difference between average values. Respondents who marked their material situation as “unfavourable” exhibited a moderate level of reduced personal accomplishment, compared to those with “favourable” financial situation. Examinees with “favourable” financial situation exhibited a low level of reduced personal accomplishment. Pearson correlation showed significance on PA subscale correlation ($r = -.273$, $p < 0.01$).

The final variable we compared the results against, was the health of respondents. Kruskal-Wallis’s one-way analysis of variance showed no statistically significant difference between groups on the EE subscale ($\chi^2 1.113$, $p > 0.05$) and the DP subscale ($\chi^2 0.012$, $p > 0.05$), while the difference was confirmed on the PA subscale ($\chi^2 15.746$, $p < 0.05$). The scores of professionals with organic or chronic diseases were lower by an average of 4.36 points, than the scores of professionals in good health.

In summary, examinees on the EE subscale showed a moderate level of emotional exhaustion, low depersonalisation. On the PA subscale professionals with normal health status had a low level of PA reduction, while those with health problems had a moderate level of reduced personal accomplishment. Pearson correlation showed no signifi-

cance correlation on EE ($r = .098$; $p > 0.05$) and DP subscales ($r = .005$; $p > 0.05$) but it showed significance correlation on PA subscale ($r = -.246$; $p < 0.01$).

Discussion

Summary analysis of the results showed that 35, 7% of special educators and rehabilitators in Serbia have a low level of emotional exhaustion, 39, 5% a moderate level and 24, 8% a high level of emotional exhaustion. Even though the average score on the EE subscale is only 19.61, which corresponds to lower partitions of the moderate level of emotional exhaustion, results showed a significant presence of emotional exhaustion among professionals working with disabled children. Finally, these results correspond to previously registered regional and world tendencies, according to which close to 30% of experts employed in caring professions, show a high level of emotional exhaustion (Petkovic, 2010, Jelec, 2008).

Results on the DP subscale showed a similar trend, as the majority of previously mentioned studies estimated. 87.6% of the respondents exhibited a low level of depersonalisation, 10.9% a moderate level, while only 1.6 % a high level of depersonalisation, with the average summary score of 2.65 on the DP subscale.

However, paying more attention to detailed analysis of the results on this subscale, we observed an interesting discrepancy. A rather large number of respondents score highly on the EE and PA subscale, and strikingly low on the DP subscale. Even though there are no explicit data which could explain this situation, the author believes that given results correlate primarily to the design of the items which, due to the importance of their implications, attract socially desirable answers, with a striking trend in absolute denial of statements which testify on change in attitudes toward the recipients of the service.

Finally, results on the PA subscale showed that 60.5 % of the respondents had a low level of reduced personal accomplishment, 27.9% a moderate level and 11.6% a high level,

with the average summary score of 39.13. Taking this into account, previous results need additional explanation. Even though 11.6 of the professionals, who showed a high level of reduced personal accomplishment, do not present an alarming result, one must bear in mind the fact that the broader social context has had a significant influence on the situation. Namely, having informal conversations with the respondents revealed that the on-going harsh socio-economic situation and significant deficits in didactic, methodical and contemporary rehabilitation means, even besides the frustration, have brought a subjective feeling of satisfaction because of the proven abilities and care shown for persons with disabilities.

Further analyses were conducted in the context of intercorrelation between dependent and independent variables, i.e. BOS and demographic data. Hence, besides the fact that the hypothesis that women show a higher tendency for BOS exists (Byrne, 1998; Eichinger, 2000), gender significance was not established on any of the subscales. Of course, this kind of conclusion is disputable from the methodological aspect, since only a small percentage of respondents were male. However, the fact that more women are employed in caring professions has dictated the very structure of the sample.

Even though the interpretation of data, related to the correlation of age and BOS, has not confirmed the statistical importance of medium values in all comparisons of the subgroups, it has pointed out the tendency. Respondents aged 30 and under the age of 30 exhibited the lowest level of burden on all three subscales, which corresponds to earlier elaborated quotes of Friedman (1992). Hence, comparing respondents aged 30 to 50 years old, we observed that older respondents scored 5 units higher on the average on the EE subscale, 2.55 on the DP subscale and 4.95 on the PA subscale.

Researching the importance of working experience in relation to BOS carried the most methodology problems for the authors of this study. Due to previously mentioned turbulent social situation in Serbia, which was affected by war and economic crisis over the past two decades and the lack of ne-

cessary investments in maintenance and improvement of social protection programs, employment of special educators and rehabilitators has suffered a great deal. Therefore, it is quite frequent that years of working experience do not correspond to years of age, and that the previously mentioned experience often comes with pauses of several years. Bearing these facts in mind, authors of this study have opted for less comparative ranges of working experience, which cumulatively lead to taking the results with a pinch of salt.

Interesting results can also be observed when analysing the importance of marital status, where single respondents showed statistically significant results of medium values on the EE and PA subscale, in relation to those who are married, and to those who are divorced. This is especially important while taking into consideration the theoretical hypothesis that married persons have more support from the family, which leads to lower manifestation of BOS (Maslach and Jackson, 1985).

Analysis of the importance of parental status showed that respondents, who have children, scored approximately 4 units higher on the EE scale, than the respondents with no children. However, it would be interesting to see these data in a further intercorrelation with other independent variables, primarily with the financial status, which, unfortunately, the rational framework of this study did not allow.

The importance of working status, pointed out that persons who have temporary contracts scored higher on the measured subscales than the ones with permanent contracts. However these results become more interesting when viewed in the context of the importance of financial status of the surveyed professionals. Namely, the fact that only 7% of the respondents see their financial status as "favourable", and even 17% as "unfavourable", speaks about the specific, additional burden of special educators and rehabilitators in Serbia. Finally, clear progressive syndrome burden can be monitored on the level of medium values on the EE and PA subscale, which correlates with the decrease of the financial status.

Finally, the last variable we monitored BOS against was the health status of the respondent. However, even though there were expectations that people with chronic or organic diseases would show a higher level of BOS, this thesis was only confirmed on the PA subscale.

Conclusion

Even though clearly confirmed amongst special educators in Serbia, the Burnout syndrome represents a phenomenon whose possible reflections are not acknowledged on a wider scale. Psychological, medical and social consequences for the employees and users of the programs conducted by the special educators are often being ignored or rationalised. In that context, it is interesting to emphasise that, even though 92% of the respondents in the conducted study believe that there should be some sort of a support program and stress management program for employees, these programs do not exist in any institution in Serbia. Neither do in many countries all over the world.

References

1. Aitken C, Schloss J. Occupational stress and burnout amongst staff working with people with an intellectual disability, *Behavioral Interventions* 1994; 9(4): 225-234
2. Bradfield RH, Fones DM. Stress and the special teacher: How bad is it?, *Academic Therapy* 1985; 20(5): 571-577.
3. Brislin RW. Comparative Research Methodology: Cross-Cultural Studies. *International Journal of Psychology* 1976; 11(3): 215-229.
4. Byrne JJ. Teacher as hunger artist: Burnout: its causes, effects and remedies. *Contemporary Education* 1998; 69(2): 86-91.
5. Curcic Dj, Curcic M. Burnout syndrom in medical staff at the special hospital for psychiatric disorders "Dr Laza Lazarevic", *Engrami - časopis za kliničku psihijatriju, psihologiju i granične discipline* 2009; 31(3-4): 19-28
6. Dedic G. Professional burnout, *Vojnosanitetski preglod* 2005; 62(11): 851-855
7. Devereux J, Hastings R, & Noone S. Staff Stress and Burnout in Intellectual Disability Services: Work Stress Theory and Its Application, *Journal of Applied Research in Intellectual Disabilities* 2009; 22(6): 561-573
8. Eichinger J. Job stress and satisfaction among special education teachers: Effects of gender and social role orientation. *International Journal of Disability, Development and Education* 2000; 47: 397-412.
9. Freudenberg HJ. Staff burnout. *Journal of Social Issues* 1974; 30: 159-165.
10. Friedman I. High and low burnout schools: school culture aspects of teacher burnout, *Journal of Educational Research* 1992; 84: 325-333.
11. Gray-Stanley JA, Muramatsu N. Work stress, burnout, and social and personal resources among direct care workers, *Research in Developmental Disabilities* 2011; 32: 1065-1074
12. Green-Reese S, Johnson DJ, & Campbell WA. Teacher job satisfaction and teacher job stress: school size, age and teaching experience, *Education* 2001; 112(2): 247-252.
13. Hastings RP, Horne S, Mitchell G. Burnout in direct care staff in intellectual disability services: a factor analytic study of the Maslach Burnout Inventory, *Journal of Intellectual Disability Research* 2004; 48(3): 268-273
14. Jelec D. Sources of professional stress and burnout syndrome among health care social workers in the Republic of Slovenia. *Ljetopis socijalnog rada* 2009; 16(1): 133-151
15. Lesic ARA, Petrovic-Stefanovic N, Perunicic I, Milenkovic P, Lecic-Tosevski D, & Bumbasirevic MZ. Burnout in Belgrade orthopaedic surgeons and general practitioners: A preliminary report. *Acta chirurgica iugoslavica* 2009; 56(2): 53-59
16. Lloyd C, King R, & Chenoweth L. Social work, stress and burnout: A review. *Journal of Mental Health* 2009; 11: 255-265
17. Maslach C. & Jackson SE. The measurement of experienced burnout. *Journal of Occupational Behavior* 1981; 2: 99-113.
18. Maslach C, Jackson SE, the Role of Sex and Family Variables in Burnout, *Sex Roles* 1985; 12(7-8): 837-851
19. Maslach C. & Jackson SE. *Maslach Burnout Inventory* (2nd ed.). Palo Alto, CA: Consulting Psychologists Press 1986.
20. Male DB, May DS. Burnout and Workload in Teachers of Children with Severe Learning Difficulties, *British Journal of Learning Disabilities* 1997; 25(3): 117-121
21. Mearns J, & Cain JE. Relationships between teachers' occupational stress and their burnout and distress: Roles of coping and negative mood regulation expectancies. *Anxiety, Stress and Coping* 2003; 16: 71-82.
22. Perlman B, & Hartman EA. Burnout: Summary and future research. *Human Relations* 1982; 35: 283-305.

23. *Petkovic N, Macesic-Petrovic D. & Djordjevic M. Institutional treatment of juvenile delinquents, Socijalna misao 2010; 17(2): 49-69*
24. *Platsidou M, Agaliotis A, Burnout, Job Satisfaction and Instructional Assignment-related Sources of Stress in Greek Special Education Teachers, International Journal of Disability, Development and Education 2008; 55(1): 61-76.*
25. *Rose J. Work Stress in group homes for people with learning difficulties, Nursing Times 1991; 42-4*
26. *Shaddock AJ, Hill M, van Limbeek CAH. Factors associated with burnout in workers in residential facilities for people with an intellectual disability. Journal of Intellectual and Developmental Disability 1998; 23(4): 309-318*
27. *Söderfeldt M, Söderfeldt B. & Warg L. Burnout in Social Work, Social Work 1995; 40(5): 638-646.*
28. *White P, Edwards N, Townsend-White C. Stress and burnout amongst professional carers of people with intellectual disability: another health inequity, Current Opinion in Psychiatry 2006; 19(5): 502-507*
29. *Wisniewski L, Gargiulo RM. Occupational stress and burnout among special educators: A review of the literature. The Journal of Special Education 1997; 31: 325-346.*

Corresponding Author

Nikola Petkovic,

Faculty for special education and rehabilitation,

University of Belgrade,

Serbia,

E-mail: nikola82petkovic@yahoo.com

The level of awareness regarding conflict and violence in university students and the affective factors in Turkey

Seyda Dulgerler¹, Oguz Polat², Serap Yildirim¹, Serap Ozer³

¹ Ege University Faculty of Nursing, Psychiatric Nursing Department, Izmir, Turkey,

² Marmara University Faculty of Medicine, Forensic Medicine, Retired Faculty Member, Istanbul, Turkey,

³ Ege University Faculty of Nursing, Medical Nursing Department, Izmir, Turkey.

Abstract

Objective: The study was to investigate the awareness level regarding conflict and violence in nursing and medical faculty students, whom in the future will be providing health care, and thus be in direct contact with human beings.

Designs: This study was conducted during 2010-2011 educational year, upon 584 students from Ege University, Nursing and Medical Faculties. Any other sampling method was not used. Students who were at the faculties during the school period and voluntarily accepted to participate in the study constituted the sample group (584).

Results: A total of 584 students, 362 (62%) from Nursing Faculty, and 222 (38%) from Medical Faculty, participated in the study. 390 (66.8%), were female, and 194 (33.2%) were male. The age of the participants ranged between 19-30 years old, and the mean age was 22.2. The lowest score in the ACVS was 27, and the highest 135, with a mean of 102.81, which shows that the level of awareness of conflict and violence in nursing and medical faculty students was quite high. The difference in the level of awareness of conflict and violence between female and male students was not statistically significant ($t=-0.36$; $p=.71$). The level of awareness of conflict and violence was found to be quite high in both groups.

Conclusions: According to the results, it was established that the level of awareness of conflict and violence was higher in nursing faculty students compared to medical faculty students, and in the 22-30 age group compared to 19-21 age group. There was no significant difference in the level of awareness of conflict and violence when compared according to gender. In order to solve conflicts by constructive methods and also prevent violence,

it is of utmost importance to establish the level of awareness of conflict and violence in individuals.

Key words: Conflict, violence, university students

Introduction

Conflict is a concept that is used in relation to drawbacks, suffering, hostilities, and even battles that occupy our memories (Karip, 2000). Conflict is a part of life, and it is not a new phenomenon, but lately it has attracted quite a lot of attention, due to the increase seen in every level, and due to its easy conversion to violence. When defined in a large perspective, it can be said that conflict is a state of tension created by the distress that prevents the satisfaction of physiological, and/or psychosocial needs (Eren, 2000) or else as the challenging expressions and conducts an individual exerts to some other person, due to conflicting interests between individuals or groups (Longaretti ve Wilson, 2006).

Most of the problems encountered in daily activities comprise interpersonal conflicts. This conflict can be seen among children, between parents and children, teachers and students, health personnel and managers, and among adults etc. (Öğülmüş, 2001). Change is an invariable feature of this era of rapid evolution and variety, which results in the development of heterogeneous social groups from different backgrounds, and differentiation becomes inevitable (Karip, 2000). Differences are the most important sources of conflict (Karataş, 2007). In other words, differences bring conflicts. And conflicts, that are not resolved by positive and constructive methods, can easily result in violence.

Nowadays violence is a primary problem in societies. WHO (2002) has defined violence as deliberate threat or the use of physical power aga-

inst oneself, another person, or group or society, resulting in injury, death, psychological damage, prevention of evolution, or deprivation. The word violence, in general, defines an exaggerated state of mood, the intensity and severity of an event, and rough and harsh behaviour. In particular, it defines aggressive behaviour, brute force, the misuse of physical power, destructive behaviour, armed assault, and maleficent activities. Aggressive behaviour in humans are stereotyped, and comprise a wide spectrum, starting from a facial mimic or word, expressing the anger and rage, to destructive and violent activities (Köknel, 2000).

Perception is the process of organizing, interpreting, and giving a meaning to data that arrive to the brain through sensory organs (Dökmen, 2001). The interpersonal differences in the perception of the same stimulants can create interpersonal conflicts that can evolve to violence. In other words disparities in perception can cause conflicts, leading to violence. In daily life, instead of drifting to negative perceptions and trying to control the situation, one can use the approach of acknowledging the constructive and destructive results of conflict, through personal awareness and apprehension of the alternatives (Schrumph, Crawford and Bodine, 2007).

Being aware of a problem is accepted to be the first stage in solving the problem. Conflict and violence can also be encountered intensely at work. One of the most common examples are the institutes that educate health personnel. Factors such as crowded schools, interpersonal differences, and the developmental status of the students lead to conflicts and thus violence. In order to prevent the social problem of violence, as an occupational group that can be prone to, or else most likely experience violence, it is important for health personnel to have the sufficient knowledge, and with this purpose, increasing the education regarding violence during their occupational education, will most certainly create a better awareness. The aim of this study was to investigate the awareness level regarding conflict and violence in nursing and medical faculty students, whom in the future will be providing health care, and thus be in direct contact with human beings.

Materials and method

Sample

This study is a descriptive study aiming to establish the awareness level regarding conflict and violence in nursing and medical faculty students.

This study was conducted during 2010-2011 educational year, upon 584 students from Ege University, Nursing and Medical Faculties. Any other sampling method was not used. Students who were at the faculties during the school period and voluntarily accepted to participate in the study constituted the sample group (584).

Procedure and data Setting

The study was approved by the local Ethical Committee. Written approval was obtained from the Deans of the Medical and Nursing Faculties of Ege University. Informed consent was taken from the students participating and data were gathered by interview technique. As tools for gathering data: personal information form and Awareness Regarding Conflict and Violence Scale (ARCVS), developed by Ohio Educational Commission (2002) were used, the scale's validity and reliability studies were performed by Sargin (2010). The scale is a likert type scale with five gradings (1. I do not agree at all, 2. I do not agree, 3. I partially agree, 4. I agree, 5. I totally agree). There are no reversed items. The scale consists of 27 items. The ARCVS that can be applied to adolescents and adults, is a scale comprising 27 categorical symptom items, with five grades. The high scores obtained from the scale are interpreted as a high level of awareness regarding conflict and violence.

Data Analysis

The number and percent distributions of the demographic characteristics of the medical and nursing faculty students were calculated. The mean level of awareness of conflict and violence scores were also calculated and t-test was used for establishing their relationship to gender, age, and educational field.

Results

A total of 584 students, 362 (62%) from Nursing Faculty, and 222 (38%) from Medical Faculty, participated in the study. 390 (66.8%), were female,

and 194 (33.2%) were male. The age of the participants ranged between 19-30 years old, and the mean age was 22.2. (Table 1). The lowest score in the ACVS was 27, and the highest 135, with a mean of 102.81, which shows that the level of awareness of conflict and violence in nursing and medical faculty students was quite high. It can be seen in Table 2 that the difference in the level of awareness of conflict and violence between female and male students was not statistically significant ($t=-0.36$; $p=.71$). The level of awareness of conflict and violence was found to be quite high in both groups.

In Table 3 the awareness level of conflict and violence according to the educational field of students from medical and nursing faculty are shown.

The table shows that there is a significant difference of .05 in the level of awareness of conflict and violence between the students of medical and nursing faculty according to the field of education ($t=2.57$; $p=.00$). It has been established that the level of awareness of conflict and violence was higher in nursing faculty students compared to medical faculty students.

The table below shows the level of awareness of conflict and violence in students from nursing and medical faculty according to age.

It is seen in the table that the level of awareness of conflict and violence in the university students showed a .05 significant difference when compared by age variable ($t=3.52$, $p=.03$). It has been established that the level of awareness of conflict and violence in the students in the 19–21 age group is much lower compared to the 22–30 age group.

Discussion, conclusion and suggestions

In this study the level of awareness of conflict and violence in students from Ege University, Medical and Nursing Faculties was investigated. According to the study results, there was no significant difference in the level of awareness of conflict and violence according to gender in students from the medical and nursing faculty. This result, was parallel to the results obtained by Champion (1979), Revilla (1984), Paglia (2003) and Bozoğlan (2010). Generally speaking the mean score in these

Table 1. Demographic characteristics of the university students

Age groups	Female(%)	Male(%)	Total
19-21	156(40)	68(35.1)	224(38.4)
22-30	234(60)	126(64.9)	360(61.6)
Faculty			
Medical faculty	98(25.1)	124(63.9)	222(38)
Nursing	292(74.9)	70(36.1)	362(62)

Table 2. The distribution of the level of awareness of conflict and violence according to gender in university students

Gender	n	X	S	t	p
Female	390	102.65	13.30	-.36	.71
Male	194	103.12	14.05		

Table 3. The awareness level of conflict and violence according to the educational field of students

Field	n	X	S	t	p
Medical Faculty	222	99.24	14.14	2.57	.00
Nursing Faculty	362	105.71	12.89		

(*) $p<.05$

Table 4. The distribution of the level of awareness in nursing and medical faculty students according to age

Age group	n	X	S	t	p
19-21	156	97.40	14.56	3.52	.03
22-30	234	103.87	13.14		

(*) $p<.05$

studies was 67.5. The mean score of the participants in our study was 102.65 in females and 103.12 in males. It is seen that the participants' mean scores in the level of awareness of conflict and violence were much higher compared to the other mean scores. The reason for this can be that the participants' educational level was university level, and that programs educating health professionals comprise lessons such as communication, interaction, counselling, educational psychology, and developmental psychology. Significant difference was found in the level of awareness of conflict and violence according to the field of education. The awareness level of conflict and violence was found to be higher in nursing faculty students compared to medical faculty students. This result is parallel to the result of the study from Bozoğlu (2010). Entrance to the nursing and medical faculties is different, nursing students are chosen according to their verbal and social field success, whereas medical students are chosen according to their science field success. The education of students in the social and verbal field is based on understanding verbal and written expression, persuasion, impression, memory and analytic questioning and communication. Students from scientific field background are mostly educated to recognize abstract structures, develop rational thinking, to analyse connections and relationships, perform complicated calculations and use scientific methods. Also during faculty education, communication, interaction are more prominent in the nursing faculty. This can be the reason for the higher level of awareness of conflict and violence in nursing faculty students compared to medical faculty students. When evaluated according to age, there was significant difference in the level of awareness of conflict and violence among students. There was significant difference in the level of awareness of conflict and violence between the 19-21 and 22-30 age group. The level of awareness of conflict and violence in the 19-21 age group was lower compared to the 22-30 age group. Age is an important factor in achieving maturity and experience. Also, as one gets older, higher status brings more personal relationships, experience, and richness in educational life. This can cause an increase in the level of awareness of conflict and violence. Recently, conflict and violence has increased in Turkey, as has worldwide. Parallel to this increase,

studies on this topic have also increased (Tor ve Sargin, 2007; Sargin, Tor, Bozoğlu ve Köroğlu, 2007; Karip, 2000; Taştan, 2006; Tümnüklü, 2006; Ögülmüş, 2001; Gümüşeli, 1994; Kapıcıoğlu, 2008; Bozoğlu, 2010).

In this study the level of awareness of conflict and violence in university students has been evaluated. According to the results, it was established that the level of awareness of conflict and violence was higher in nursing faculty students compared to medical faculty students, and in the 22-30 age group compared to 19-21 age group. There was no significant difference in the level of awareness of conflict and violence when compared according to gender. In order to solve conflicts by constructive methods and also prevent violence, it is of utmost importance to establish the level of awareness of conflict and violence in individuals. Unnoticed, or else wrongly interpreted conflicts and violence can lead to negative consequences, increase in conflict, violent behaviour, and unpleasant situations. The fact that the level of awareness of conflict and violence was lower in the students from medical faculty compared to those from the nursing faculty, indicates that more should be done, with an effort to raise awareness regarding conflict and violence in medical faculty students.

Referencess

1. Acar NV. *Ne kadar farkındayım: Gestalt terapi (2. Baskı)*. Ankara: Babil Yayınevi 2004.
2. Bozoğlu B. *Balkan ülkeleri üniversite öğrencilerinin çatışma ve şiddete ilişkin farkındalık düzeyleri ve çatışma çözme stilleri*. Yayınlanmamış Doktora Tezi, Selçuk Üniversitesi 2010.
3. Champion D. *Comparison of men and women managers of preferences for organizational conflict management.. Unpublished Doctoral Dissertation, Florida State University 1979.*
4. Dökmen Ü. *İletişim çatışmaları ve empati*. İstanbul: Sistem Yayınları 2001.
5. Eren E. *Örgütsel davranış ve yönetim psikolojisi*. İstanbul: Beta Basım Yayım Dağıtım A.Ş. 2000.
6. Gümüşeli Aİ. *İzmir ili ortaöğretim okulları yöneticilerinin çatışmayı yönetme biçimleri*. Yayınlanmamış Doktora Tezi, Ankara Üniversitesi 1994.

7. Kapicioğlu, İ. Üniversite öğrencilerinin şiddet algısı. Yayınlanmamış Yüksek Lisans Tezi, Selçuk Üniversitesi 2008.
8. Karataş S. Afyonkarahisar ili merkez ilköğretim okullarında görev yapan sınıf ve branş öğretmenlerinin kurum içi çatışmaları yönetim biçimine ilişkin görüşleri. *Bilim Eğitim Düşünce Dergisi* 2007; 7(2).
9. Karip E. Çatışma yönetimi. Ankara: Pegem A Yayıncılık 2000.
10. Kline P. *An easy guide to factor analysis*. New York: Routledge 1994.
11. Köknel Ö. Bireysel ve toplumsal şiddet. İstanbul 2000.
12. Altin KY, Longretti L, Wilson J. The impact of perception on conflict management. *Educational Research Quarterly* 2006; 29(4): 3.
13. Ohio Department of Education and the Ohio Commission on Dispute Resolution and Conflict Management *School conflict management resource guide for grades* 2002; 7-12. Ohio: State Board of Education.
14. Opatow SV. Adolescent peer conflict: Implications for students and for schools. *Educational and Urban Society* 1991; 23(4): 16-441.
15. Öğülmüş S. Kişiler arası sorun çözme becerileri eğitimi. Ankara: Nobel Yayınları 2001.
16. Ömür S. Çatışma yönetiminde uluslar arası kültürel farklılıkların etkisi ve bir anket çalışması. Yayınlanmamış Yüksek Lisans Tezi, Anadolu Üniversitesi 1998.
17. Paglia A, Adlaf EM. Secular trends in self-reported violent activity among ontario students. *Canadian Journal of Public Health (ProQuest Health and Medical Complete)* 1983-2001; 94, 3.
18. Revilla VM. Conflict management styles of men and women administrators in higher education. Unpublished Doctoral Dissertation. USA: University of Pittsburgh 1984.
19. Sargin N, Tor H, Bozoğlu B, Köroğlu M. A study related to teacher candidates' conflict resolution methods. *Bulletin, Educational* 2008.
20. Sargin N. Öğretmen Adaylarının Çatışma ve Şiddete İlişkin Farkındalık Düzeylerinin Çeşitli Değişkenlere Göre İncelenmesi 2010. *Educational Administration: Theory and Practice* Vol. 16, Issue 4, pp: 601-616 Sciences Series. Petroleum-Gas university of Ploiești, Vol. LX, 2, 76-82. Çatışma ve Şiddete İlişkin Farkındalık
21. Schruppf F, Crawford DK, Bodine RJ. *Peer mediation, conflict resolution in schools, program guide*. (Çeviren Akbalık, G. F., 2007). *Okulda Çatışma Çözme ve Akran Arabuluculuk*. İstanbul: İmge Kitabevi 1991.
22. Stevahn L, Munger L, Kealey K. Conflict resolution in a French immersion elementary school. *Journal of Educational Research* 2005; 99(1): 3-18.
23. Taştan N. Çatışma çözme eğitimi ve akran arabuluculuğu. In Uğur Öner (Ed.). Ankara: Nobel Yayınları 2006.
24. Tor H, Sargin N. İlköğretim okullarının II. kademesinde okuyan öğrencilerin şiddetle karşı karşıya kalma durumları ve şiddete ilişkin görüşleri. *Selçuk Üniversitesi Eğitim Fakültesi Dergisi* 2007; 24: 305-328.
25. Türnüklü A. Sınıf ve okul disiplinine çağdaş bir yaklaşım onarici disiplin: okullarda yaşanan kişiler arası çatışmaları yapıcı ve barışçıl olarak yönetmek için çağdaş bir yaklaşım. Ankara: Ekinoks 2006.
26. Welt ES. Conflict management styles of middle school principals compared to comprehensive high school principal.. Unpublished Dissertation of Doctorate, University of La Verne 2000.
27. WHO. *Injuries and violence prevention, Youth Violence* 2002.

Corresponding Author
Seyda Dulgerler,
Ege University,
Faculty of Nursing Psychiatric,
Nursing Department,
İzmir,
Turkey,
E-mail: seydanurmetin71@hotmail.com,
seydadulgerler@yahoo.com

Subtypes of Interstitial cells of Cajal in normal and inflamed appendix in children

Dragoljub V Zivanovic¹, Mirjana Abramovic², Goran Radenkovic³, Andjelka Slavkovic¹, Zoran Marjanovic¹, Verica Avramovic³, Zlatko Djuric⁴

¹ Paediatric Surgery and Orthopaedic Clinic, Clinical Centre Nis, University in Nis, School of Medicine, Nis, Serbia,

² Institute of Chemistry, University in Nis, School of Medicine, Nis, Serbia,

³ Institute of Histology and Embryology, University in Nis, School of Medicine, Nis, Serbia,

⁴ Clinic for Pedaitrics, Clinical Centre Nis, University in Nis, School of Medicine, Nis, Serbia.

Abstract

Introduction: Repeated episodes of acute inflammation or a chronic inflammatory process may underlie the etiology of acute appendicitis and exacerbations could be triggered by coprostasis. Several subtypes of interstitial cells of Cajal (ICC) form networks that play a role in gastrointestinal motor control.

Aim of research: To investigate the presence of subtypes of ICC in the apex and base of normal appendix and in the appendix with various degrees of inflammation.

Material and method: The tissue for analysis was obtained after 67 appendectomies in patients with a mean age of 8 years. The specimens were exposed to anti-c-kit antibodies to investigate the ICC, enteric plexuses were immunohistochemically examined by using anti-neuron specific enolase (NSE), and smooth muscle cells (SMC) were studied with anti-desmin antibodies.

Results: In the normal and inflamed appendix, ICC were present within the circular (ICC-CM) and longitudinal muscle layer (ICC-LM), in the connective septa (ICC-SEP) and around the MP ganglia (ICC-MP), but not present at the submucosal border of the circular layer (ICC-SMP). However, ICC-MP never formed a network similar to that in other portions of the gut. There were no differences in ICC distribution between the base and apex of appendix. ICC were not present in most of the appendices whose walls were markedly thinned.

Conclusion: The absence of ICC network in the region of myenteric and submucous plexus constituted a significant difference compared to the colon. Inflammation does not lead to any significant reduction of ICC numbers, but increased intraluminal pressure can induce complete loss of ICC.

Key words: Interstitial cells of Cajal, appendix, C-kit, inflammation, human.

Introduction

Despite its high incidence and numerous studies, the etiology of appendicitis remains unclear. While the invasion of the appendiceal wall by micro-organisms is the ultimate pathologic event, the primary initiating condition is not known^{1,2}. Luminal obstruction is one of the most commonly proposed etiological factors, but Arnbjornsson and Bengmark³ could not record the increased intraluminal pressure in the majority of cases of acute appendicitis. Besides other possible etiological factors⁴⁻¹⁰, hypersensitive reaction¹¹ and inflammatory reaction on antigenic stimulation from some luminal source have been proposed recently^{12,13}. Repeated episodes of acute inflammation or a chronic inflammatory process may underlie the etiology of acute appendicitis¹⁴⁻¹⁶ and exacerbations could be triggered by coprostasis¹⁷.

Interstitial cells of Cajal (ICC) represent a distinct population of cells distributed in the muscular layer of gastrointestinal tract (GIT), from the upper esophagus to the inner anal sphincter^{18,19}. Several subtypes of ICC form networks that play a role in gastrointestinal motor control and overwhelming evidence has shown ICC to be the source of slow-wave pacemaker activity²⁰. Other subpopulations of ICC serve as mediators of enteric motor neurotransmission, play a role in afferent neural signaling and act as non-neuronal stretching receptors²¹⁻²³. According to topographic, morphologic, and functional criteria, ICC are classified into the following subtypes: ICC of the myenteric plexus (ICC-MP), ICC of the circular (ICC-CM) and longitudinal muscle layer (ICC-LM), ICC of the deep

muscular plexus (ICC-DMP), ICC of the submucosal plexus (ICC-SMP), and ICC along the connective tissue septa within circular layer (ICC-SEP)²⁴⁻³⁰. Electrophysiological studies of rat, dog and human colon have suggested that both ICC-MP and ICC-SMP are distinct pacemaker cells³¹⁻³³. Distribution of the ICC in normal and diabetic human appendix was described by Miller *et al.*³⁴. Interstitial cells of Cajal are important in the innervation and motility of gastrointestinal tract, so that alterations in their distribution have already been documented in various motility disorders of the gastrointestinal tract³⁵⁻³⁷. On the other hand, it was proven that inflammation leads to decreased ICC numbers and disruption of their networks, as well as the ischemia/reperfusion injury³⁸⁻⁴⁰.

Richter *et al.*⁴¹ could not find any statistical difference between the distributions of ICC in normal and inflamed appendices in children, but they investigated only the apex of appendix⁴¹. Therefore, our aim in the present study was to investigate the presence of subtypes of ICC in the apex and base of normal appendix and in the appendix with various degrees of inflammation. The specimens were exposed to anti-c-kit antibodies to investigate the ICC, enteric plexuses were immunohistochemically examined by using anti-neuron specific enolase (NSE), and SMC were studied with anti-desmin antibodies.

Material and methods

The tissue for analysis was obtained after 67 appendectomies in patients with a mean age of 8 years (range, 6 months -15 years; 37 boys and 30 girls). Twelve of them, without clinical signs of inflammation (incidental appendectomies), showed normal histology and served as controls (group I). Appendices with signs of inflammation were classified according to the degree of inflammation on histopathology into the following groups (Table 1): acute (group II), phlegmonous (group III), gangrenous and perforated (group IV), and chronic appendicitis (group V). Because of the lack of agreement between surgeons and pathologists in their description

of perforation, some of the clinically perforated appendices were classified as only gangrenous on histology, and we combined them into one group (IV). The study was approved by the ethics committee of the Faculty of Medicine of University of Nis.

Two pieces of each appendix were taken after appendectomy, immediately fixed in 10% formalin for 24h, and paraffin embedded. The first tissue sample, approximately 1 cm long, was taken from the appendiceal apex, always including the tip. The second sample was taken from the base, immediately distal to the tissue crushed during ligature and amputation during appendectomy. Each tissue block was sequentially sectioned at 4µm and stained. Immunohistochemical analysis was performed using the detection Kit-Polymer. The sections were deparaffinised in xylol and a descending series of alcohol rinses (<1 min each), and then rehydrated in distilled water. Endogenous peroxidase was blocked with 3% H₂O₂ for 10 min at room temperature. This was followed by the incubation with primary antibodies for 60 min at room temperature and rinses in a phosphate-buffered solution (0.1MPBS, pH 7.4). The primary antibodies were dissolved in Dako antibody diluent (catalogue no. S0809; Dako North America, Carpinteria, Calif., USA). The sections were incubated with streptavidin-horseradish-peroxidase conjugate for 30 min at room temperature. The complex was visualised with DAKO Liquid DAB + Substrate/Chromogen System (code no. K3468; Dako). All immunolabelled sections were counterstained with Mayer's haematoxylin. Immunoreactivity was absent in negative controls in which the primary antibody had been omitted. Sections were examined with an Olympus BX50 microscope.

The primary antibodies used, and their respective dilutions, are listed in Table 2.

Table 2. Antibodies

Antigen	Clone	Supplier	Dilution
C-kit	CD-117	Dako	1 : 300
NSE	BBS/NS VI-H14	Dako	1 : 100
Desmin	DE-R-11	Dako	1 : 100

Table 1. Number of patients in histopathology groups of appendicitis

Group	I	II	III	VI	V
Hystopathology	Normal	Acute	Phlegmonous	Gangrenous and perforated	Chronic
Number of patiens	12	14	15	14	12

Results

In normal appendix, c-kit IR cells were observed in the circular and longitudinal muscle layer and around the MP ganglia (Fig. 1A), but not at the submucosal border of the circular layer.

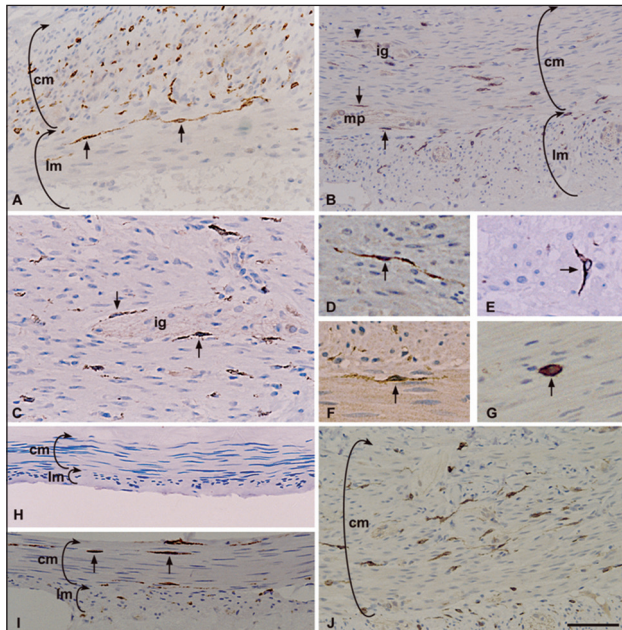


Figure 1. C-kit immunohistochemistry. **(A)** Normal appendix, base. C-kit IR cells were present in the circular and longitudinal muscle layer. Two spindle-shaped ICC-LM (arrows) appeared to be linearly interconnected at the inner margin of longitudinal muscle. **(B)** Phlegmonous appendicitis, apex. C-kit IR cells were present within the muscle layers, around the myenteric (arrows) and intramuscular ganglia (arrowhead). **(C)** Acute appendicitis, base. Two spindle-shaped c-kit IR cells (arrows) were located around the ganglion in the circular muscle layer. **(D)** Gangrenous appendicitis, apex. Cross section of the circular muscle layer with ICC-SEP (arrow), which was perpendicular to the adjacent SMC. **(E)** Phlegmonous appendicitis, base. One spindle-shaped ICC-SEP (arrow) was located within connective-tissue septa. **(F)** Chronic appendicitis, base. One spindle-shaped ICC-LM (arrow) lying in the inner part of the longitudinal muscle layer. **(G)** Gangrenous appendicitis, apex. In the circular muscle layer, a c-kit-IR mast cell (arrow) was seen. **(H)** Gangrenous appendicitis, base. C-kit IR cells were not present in both circular and longitudinal muscle layers, which were very thinned. **(I)** Acute appendicitis, base. ICC-CM (arrows) were very thin and

elongated in the appendix with thinned wall. **(J)** Gangrenous appendicitis, apex. Spindle-shaped and multipolar c-kit-IR cells form a network of interconnected cells in the circular muscle layer. mp, myenteric plexus; cm, circular muscle layer; lm, longitudinal muscle layer; ig, intramuscular ganglion. Bar: A, C - E, G - J = 30 - μ m; B = 60 - μ m; F = 20 - μ m.

In the circular layer, c-kit IR cells were spindle-shaped, with two long processes originating from the opposite ends. These cells were parallel to the longitudinal axis of the smooth muscle cells (SMC) and corresponding ICC-CM. Most commonly they were single, and cells connected in a linear way were very rarely seen. The c-kit-IR cells often layed perpendicular to the direction of the muscle bundles that they enveloped and corresponded to ICC-SEP. These cells were present in the inflamed appendices too (Fig. 1D, E). In the longitudinal layer, c-kit IR cells were similar by their shape and position to the cells described in the circular layer, but they were less numerous (Fig. 1A). These cells corresponded to ICC-LM. C-kit IR cells were detected around the MP ganglia, most commonly as single spindle-shaped cells, less frequently multipolar, lying with their body and processes at the border of the ganglia, and corresponded to ICC-MP. Very rarely, we were able to find two or three cells around the same ganglion, but these cells never completely enclosed the ganglion. In addition to the MP ganglia, commonly present in the appendix were also the ganglia in the muscle layers, especially in the longitudinal layer. C-kit IR cells were present at the border of the intramuscular ganglia, again as single cells.

All above described subtypes of ICC were present in the basis and apex of the appendix, without differences in their distribution. However, in normal and inflamed appendices, there was a small difference in the apex top, where somewhat denser network of ICC could be seen (Fig. 1J). Inside the circular layer at the apex top, a tridimensional network of interconnected cells was present in most of the studied cases. In addition to spindle-shaped cells, multipolar cells too were involved in the network (Fig. 1J).

In addition to ICC, we also found a large number of c-kit-IR mast cells, but they could be easily distinguished from ICC on the basis of their shape

and granular content. Mast cells were present in the submucosa, mucosa, serosa, and in some cases within muscle layers as well (Fig. 1G).

C-kit IR cells in the inflamed appendix

In groups II - V of inflamed appendices, all ICC subtypes described in normal appendices were present. ICC distribution in inflamed appendices was similar to that in normal ones (Fig 1B-F, J). The differences between the apexes and bases were related only to the ICC-CM network at the apex top, as already described in normal appendix.

In the observation of our results we found inflamed appendices whose whole wall, including the muscle layers, was very thinned, and SMC were very elongated, thinned, and compressed. There were 5 such cases, (two gangrenous, two phlegmonous and one acute), with content in the lumen of all these samples. These 5 samples were not included in the statistical processing of the ICC numbers in individual groups. In 4 described appendices ICC were not present in the wall – not one of the above described subtypes (Fig. 1J). At the same time, all samples contained large numbers of c-kit IR mast cells in their walls. In only one sample of appendix with a thinned wall (with acute inflammation type) ICC were present (Fig. 1I), which were very elongated and thinned, similar to the adjacent SMC.

Desmin immunoreactivity

In all the studied groups, DES-IR was intense in both circular and longitudinal muscle layer, although the longitudinal layer was thinner (Fig. 2A).

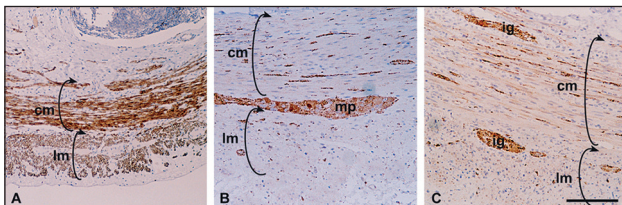


Figure 2. Desmin (A) and neuron specific enolase (B and C) immunohistochemistry. (A) Phlegmonous appendicitis, base. Both the circular and the longitudinal muscle layers are DES-IR. (B) Chronic appendicitis, apex. The myenteric ganglia were present between the muscle layers. (C) Phlegmonous appendicitis, base. The intramuscular ganglia (arrows) were present between

the muscle layers. mp, myenteric plexus; cm, circular muscle layer; lm, longitudinal muscle layer; ig, intramuscular ganglion. Bar: A = 120 – μ m; B - C = 60 – μ m.

NSE immunoreactivity

In all the studied groups, except in the group of appendicitis with thinned walls, immunostaining for NSE showed the presence of MP ganglia between the circular and longitudinal muscle layers, and numerous ganglia within both muscle layers (Fig. 2B,C). However, the MP of the appendix was very poorly developed, but submucosal and deep muscle plexuses were present neither in normal, nor in inflamed appendices. Intramuscular ganglia were more numerous in the longitudinal layer. In the group of appendicitis with thinned wall, nerve structures were compressed and hardly discernible, or they were missing altogether.

Discussion

In the present study we determined the distribution of subtypes of ICC in the normal and inflamed appendix in childhood. In normal appendix, ICC were proven within the circular and longitudinal muscle layer, in the connective septa, and around the MP ganglia, but we were unable to demonstrate them at the submucosal border of the circular layer. Our results differed from those obtained by Richter *et al*⁴¹ and Miller *et al*,³⁴ who had described only ICC-CM and ICC-LM in appendix. However, ICC-MP were present in the appendix as single cells at the ganglion border, rarely as two cells around the same ganglion, but they never formed a network between the muscle layers and around the MP ganglia, similar to that in other portions of the GIT^{24,25,30,42}. That has been the point of agreement of all the papers published so far. The absence of ICC network in the region of myenteric and submucous plexus was a significant difference compared to the situation in the colon^{30-33,42}, and could have been the reason for a different model of appendical contraction, in view of the fact that ICC-MP and ICC-SMP were the pacemakers in the colon³¹⁻³³.

It has been long known that ICC are neither distributed uniformly in the GIT nor distributed uniformly in a particular organ (oesophagus, gaster,

duodenum, colon)^{28,25,43,44}. We therefore observed the ICC distribution in the basis and apex of the appendix. All the above mentioned ICC subtypes were present in the basis and apex of the appendix, and we could not find significant differences in their distribution in the mentioned parts. ICC-CM and ICC-LM were mostly single – we rarely encountered cells connected in a linear way. This finding of ours is in accordance with the previous studies in view of the distribution of intramuscular ICC in appendix^{34,41}. The only difference was found in the circular layer at the tip of appendix, where we found dense tridimensional networks of interconnected cells in a large number of cases. These networks were localized in a confined area on the top, where ICC-CM from the opposite walls of appendix met. Such a network was not present in any of the other parts of the appendix, except on the apex top.

Suzuki *et al*³⁸ reported the muscular inflammation and the loss of ICC networks in endothelin receptor null rats as a model of Hirschsprung's disease. They concluded that the inflammation process may result in damage to ICC networks, leading to disordered intestinal rhythmic contractions. However, our results showed that the process of inflammation, regardless of the inflammation type, did not lead to any significant changes in the ICC distribution in the vermiform appendix. In all groups of inflamed appendices (acute, phlegmonous, perforative, chronic) all subtypes of ICC were found, as described in normal appendix. This finding indicated that inflammation did not lead to significant reduction or complete loss of ICC⁴¹, regardless of whether it was acute or chronic inflammation.

An important finding of our study was the absence of ICC in most of the appendices, whose walls were markedly thinned. Thinned walls and markedly elongated and flattened SMC indicated that thinning was induced by increased intraluminal pressure produced by the content accumulated in the lumen. The increased pressure can induce ischemia, and it has been found that ICC are easily damaged by ischemia⁴⁰. Shimojima *et al*⁴⁵ reported alterations in intestinal motility and ICC-MP networks during sudden damage to the intestines. The experiment showed the disruption of ICC-MP networks in ischemia/reperfusion injury. Our findings supported previous studies, investigating the

impact of increased pressure on ICC³⁹. However, in one case ICC were present in the appendix with thinned walls. Our assumption was that ICC loss was not found because the dilatation had lasted for a relatively short period, i.e. that ICC loss could have resulted if increased pressure had been present for a longer period of time.

In conclusion, we may assume that the ICC distribution in the appendix differs from that observed in the colon, especially regarding the ICC subpopulations creating electrical slow waves of ICC-MP and ICC-SMP. Therefore, there are no differences in the ICC distribution in the basis and apex of the appendix. Finally, the most important conclusion is perhaps that inflammation does not lead to any significant reduction of ICC numbers, but that increased intraluminal pressure is capable of inducing complete loss of ICC.

Acknowledgements

This work was supported by the Ministry of Science and Technological Development of the Republic of Serbia (Project 43012). We thank Mile Randjelovic for his technical assistance. We also thank Milkica Tosic Djordjevic for her precious help in immunohistochemical procedures.

References

1. Prystowsky JB, Pugh CM, Nagle AP. Current problems in surgery. Appendicitis. *Curr Probl Surg*. 2005; 42(10): 688–742.
2. Puri P, Mortel A. Appendicitis. In: Stringer M, Oldham K, Mouriquand PDE, editors. *Pediatric surgery and urology: long-term outcomes*. Cambridge: Cambridge University Press; 2006: 374–84.
3. Arnbjörnsson E, Bengmark S. Role of obstruction in the pathogenesis of acute appendicitis. *Am J Surg*. 1984; 147(3): 390–2.
4. Bickler SW, DeMaio A. Western diseases: current concepts and implications for pediatric surgery research and practice. *Pediatr Surg Int*. 2008; 24(3): 251–5.
5. Coggon D, Barker DJ, Cruddas M, Oliver RH. Housing and appendicitis in Anglesey. *J Epidemiol Community Health*. 1991; 45(3): 244–6.
6. Gardikis S, Giatromanolaki A, Kambouri K, Tripsianis G, Sivridis E, Vaos G. Acute appendicitis in preschoolers: a study of two different populations of children. *Ital J Pediatr*. 2011; 37: 35.

7. Gauderer MW, Crane MM, Green J a, DeCou JM, Abrams RS. Acute appendicitis in children: the importance of family history. *J Pediatr Surg.* 2001; 36(8): 1214–7.
8. Carr NJ. The Pathology of Acute Appendicitis. *Ann Diagn Pathol.* 2000; 4(1): 46–58.
9. Thanikachalam MP, Kasemsuk Y, Mak JW, Sharifah Emilia TS, Kandasamy P. A study of parasitic infections in the luminal contents and tissue sections of appendix specimens. *Trop Biomed.* 2008; 25(2): 166–72.
10. Toumi Z, Chan A, Hadfield MB, Hulton NR. Systematic review of blunt abdominal trauma as a cause of acute appendicitis. *Ann R Coll Surg Engl.* 2010; 92(6): 477–82.
11. Aravindan KP, Vijayaraghavan D, Manipadam MT. Acute eosinophilic appendicitis and the significance of eosinophil - Edema lesion. *Indian J Pathol Microbiol.* 2010; 53(2): 258–61.
12. Tsuji M, Puri P, Reen DJ. Characterisation of the local inflammatory response in appendicitis. *J Pediatr Gastroenterol Nutr.* 1993; 16(1): 43–8.
13. Wang Y, Reen D, Puri P. Is a histologically normal appendix following emergency appendectomy always normal? *Lancet.* 1996; 347(9008): 1076–9.
14. Nemeth L, Reen DJ, O'Briain DS, McDermott M, Puri P. Evidence of an inflammatory pathologic condition in “normal” appendices following emergency appendectomy. *Arch Pathol Lab Med.* 2001; 125(6): 759–64.
15. Xiong S, Puri P, Nemeth L, O'Briain DS, Reen DJ. Neuronal hypertrophy in acute appendicitis. *Arch Pathol Lab Med.* 2000; 124(10): 1429–33.
16. Nemeth L, Rolle U, Reen DJ, Puri P. Nitrergic Hyperinnervation in Appendicitis and in Appendices Histologically Classified as Normal. *Arch Pathol Lab Med.* 2003; 127(5): 573–8.
17. Sgourakis G. Are acute exacerbations of chronic inflammatory appendicitis triggered by coprostanis and/or coproliths? *World J Gastroenterol.* 2008; 14(20): 3179–82.
18. Torihashi S, Horisawa M, Watanabe Y. c-Kit immunoreactive interstitial cells in the human gastrointestinal tract. *J Auton Nerv Syst.* 1999; 75(1): 38–50.
19. Hagger R, Gharaie S, Finlayson C, Kumar D. Regional and transmural density of interstitial cells of Cajal in human colon and rectum. *Am J Physiol.* 1998; 275(6): G1309–16.
20. Huizinga JD, Lammers WJ. Gut peristalsis is governed by a multitude of cooperating mechanisms. *Am J Physiol Gastrointest Liver Physiol.* 2009; 296(1): G1–8.
21. Beckett EA, McGeough CA, Sanders KM, Ward SM. Pacing of interstitial cells of Cajal in the murine gastric antrum: neurally mediated and direct stimulation. *J Physiol.* 2003; 553(Pt 2): 545–59.
22. Thuneberg L, Peters S. Toward a concept of stretch-coupling in smooth muscle. I. Anatomy of intestinal segmentation and sleeve contractions. *Anat Rec.* 2001; 262(1): 110–24.
23. Suzuki H, Ward SM, Bayguinov YR, Edwards FR, Hirst GDS. Involvement of intramuscular interstitial cells in nitrergic inhibition in the mouse gastric antrum. *J Physiol.* 2003; 546(Pt 3): 751–63.
24. Hanani M, Farrugia G, Komuro T. Intercellular coupling of interstitial cells of Cajal in the digestive tract. *Int Rev Cytol.* 2005; 242: 249–82.
25. Komuro T. Structure and organization of interstitial cells of Cajal in the gastrointestinal tract. *J Physiol.* 2006; 576(Pt 3): 653–8.
26. Vanderwinden JM, Rumessen JJ. Interstitial cells of Cajal in human gut and gastrointestinal disease. *Microsc Res Tech.* 1999; 47(5): 344–60.
27. Radenković G, Nikolić I, Todorović V. Interstitial cells of Cajal – pacemakers of the intestinal musculature. *Facta Universitatis: Series Medicine and Biology* 2005; 12(1): 1–5
28. Radenkovic G, Ilic I, Zivanovic D, Vlajkovic S, Petrovic V, Mitrovic O. C-kit-immunopositive interstitial cells of Cajal in human embryonal and fetal oesophagus. *Cell Tissue Res* 2010; 340(3): 427–36
29. Faussonne-Pellegrini MS, Vannucchi MG, Alaggio R, Strojna A, Midrio P. Morphology of the interstitial cells of Cajal of the human ileum from foetal to neonatal life. *J Cell Mol Med.* 2007; 11(3): 482–94.
30. Rømer P, Mikkelsen HB. c-kit immunoreactive interstitial cells of Cajal in the human small and large intestine. *Histochem Cell Biol.* 1998; 109(3): 195–202.
31. Plujà L, Albertí E, Fernández E, Mikkelsen HB, Thuneberg L, Jiménez M. Evidence supporting presence of two pacemakers in rat colon. *Am J Physiol Gastrointest Liver Physiol.* 2001; 281(1): G255–66
32. Rumessen, JJ, Vanderwinden JM, Rasmussen H. Hansen A, Horn T. Ultrastructure of interstitial cells of Cajal in myenteric plexus of human colon. *Cell Tissue Res.* 2009; 337(2): 197–212
33. Tamada, H, Komuro T. Three-dimensional demonstration of the interstitial cells of Cajal associated with the submucosal plexus in guinea-pig caecum. *Cell Tissue Res* 2011; 344(1): 183–8
34. Miller SM, Narasimhan R a, Schmalz PF, Soffer EE, Walsh RM, Krishnamurthi V, et al. Distribution of interstitial cells of Cajal and nitrergic neurons in normal and diabetic human appendix. *Neurogastroenterol Motil.* 2008; 20(4): 349–57.

35. Rolle U, Piaseczna-Piotrowska A, Puri P. Interstitial cells of Cajal in the normal gut and in intestinal motility disorders of childhood. *Pediatr Surg Int.* 2007; 23(12): 1139–52.
36. Farrugia G. Interstitial cells of Cajal in health and disease. *Neurogastroenterol Moti.* 2008; 20 Suppl 1: 54–63.
37. Negreanu LM, Assor P, Mateescu B, Cirstoiu C. Interstitial cells of Cajal in the gut - a gastroenterologist's point of view. *World J Gastroenterol.* 2008; 14(41): 6285–8
38. Suzuki T, Won KJ, Horiguchi K, Kinoshita K, Hori M, Torihashi S, et al. Muscularis inflammation and the loss of interstitial cells of Cajal in the endothelin ETB receptor null rat. *Am J Physiol Gastrointest Liver Physiol* 2004 287(3): G638–46
39. Lou Z, Li JS. Interstitial cells of Cajal in abdominal sepsis and hypertension-induced ileus in rats. *Eur Surg Res.* 2009; 43(1): 47–52.
40. Suzuki M, Takahashi A, Toki F, Hatori R, Tomomasa T, Morikawa A, et al. The effects of intestinal ischemia on colonic motility in conscious rats. *J Gastroenterol.* 2008; 43(10): 767–73.
41. Richter A, Wit C, Vanderwinden J-M, Wit J, Barthlen W. Interstitial cells of Cajal in the vermiform appendix in childhood. *Eur J Pediatr Surg.* 2009; 19(1): 30–3.
42. Radenkovic G, Abramovic M. Differentiation of interstitial cells of Cajal in the human distal colon. *Cells Tissues Organs.* 2012; DOI: 10.1159/000336707
43. Radenkovic G, Savic V, Mitic D, Grahovac S, Bjelakovic M, Krstic M. Development of c-kit immunopositive interstitial cells of Cajal in the human stomach. *J Cell Mol Med.* 2010 14(5): 1125–34.
44. Radenkovic G. Two patterns of development of interstitial cells of Cajal in the human duodenum. *J Cell Mol Med.* 2012; 16(1): 185– 92
45. Shimojima N, Nakaki T, Morikawa Y, Hoshino K, Ozaki H, Hori M, Kitajima M. Interstitial cells of Cajal in dysmotility in intestinal ischemia and reperfusion injury in rats. *J Surg Res.* 2006; 135(2): 255–261.

Corresponding Author

Dragoljub Zivanovic,
Paediatric Surgery and Orthopaedic Clinic,
Clinical Centre Nis,
University in Nis,
School of Medicine,
Nis,
Serbia,
E-mail: dzivanovic.nis@gmail.com

The effect of intravenous pamidronate treatment for type i osteogenesis imperfecta patients have on their bone mineral density, fracture rate, and mobility

Zekeriya Oztemur¹, Hayati Ozturk¹, Esra Circi², Okay Bulut¹, Serdar Uner¹, Ahmet Altun³, Gunduz Tezeren¹

¹ Cumhuriyet University School of Medicine, Department of Orthopedic and Traumatology, Sivas, Turkey,

² Kayseri Numune Training and Research Hospital, Kayseri, Turkey,

³ Cumhuriyet University School of Medicine, Department of Pharmacology, Sivas, Turkey.

Abstract

Objective: Osteogenesis imperfecta (OI) is a genetic disorder caused by the mutation in encoding collagen type I, and characterised by fragile bone and reduced bone mineral density. The purpose of this study was to analyse the effects of intravenous pamidronate treatment has on the bone mineral density and the fracture rate and mobility.

Patients and Methods: The sample group of this study comprises of 7 patients (6 male (85.7%), 1 women (14.2%) with type I OI, who received intravenous pamidronate, between August 2004 and October 2010. The intravenous dose of pamidronate disodium (Aredia, Novartis) was 0.75 mg/kg of the body weight, administered as a single dose every 6 months, over 8 hours in a saline solution. Bone mineral density was measured before and after the treatment using a dual energy X-ray absorptiometer at vertebral bodies from L1 to L4. Bone mineral density (g/cm²), T scores and Z scores, number of fractures, and modified Bleck scores were recorded.

Results: The median age of patients at the time of treatment was 15 years (min: max=13: 18), the median BMI was 17.86 (min: max=14.29: 20.68) kg/m², the median follow-up period was 36 (min: max=12: 72), and the median number of doses received was 5 (min: max=1: 20). The median bone mineral content was increased from 0.368 (min: max=0.23-0.59) to 0.628 (min: max=0.53: 0.88) (p=0.02), the median T score was increased from -6.6 (min: max=-7.50: -1.90) to -4.2 (min: max=-5.10: -1.90) (p=0.043), the median Z score was increased from -4.91 (min: max=-7.7: -3.2) to -3.9 (p=0.144), and the median modified Bleck score was increased from 6 (min: max=2: 9) to 9 (min:

max=-7.7: -3.2) (p=0.043). The median numbers of fracture decreased from 0.40 (min: max=0.15: 0.76) to 0 (min: max: 0: 1) per year (p= 0.540).

Conclusion: Intravenous pamidronate in patients with OI increased bone mineral density and patient's mobility, and improved the fracture rate. Pamidronate is a safe and effective treatment method in patients with OI.

Key words: Osteogenesis imperfecta; pamidronate; bone density;

Introduction

Osteogenesis imperfecta (OI) is a genetic disorder of the connective tissue matrix caused by the mutation in COL1A1 or COL1A2, the genes encoding collagen type I. This collagen is the most plentiful protein of the bone and is also present in the tendon, ligament, dentin, skin, and sclera. A patient with osteogenesis imperfecta has less or poor quality type I collagen, causing bone deformation or fractures, and affect other connective tissue that contains type I collagen [1]. The clinical manifestations can present significant variations, ranging from a severe intrauterine lethal form to a mild symptom, which occurs in adulthood, manifesting as premature osteoporosis or severe postmenopausal bone mineral loss. Several clinical subtypes of OI have been revealed based on the molecular, biochemical, and clinical progress of the disorder [2]. The accurate incidence of OI is unknown, recent studies suggest a rate as high as 1 per 25000 live births [3].

The purpose of therapy is to reduce the fracture rate, prevent bone deformity and scoliosis, reduce chronic pain, and to improve mobility and functional capacity [4]. Treatment requires multidisci-

plinary studies and needs physical therapy, orthopaedic management is required for surgical interventions, or bracing, or both, and pharmacologic treatment, in some cases experimental studies [5].

Currently, the most used pharmacologic agent and the most hopeful therapy for OI is oral and intravenous bisphosphonates. Several clinical studies have revealed improved bone mineral density and reduced fracture rate for patient with OI [3].

The purpose of this study was to analyse the effects pamidronate treatment has on the bone mineral density and fracture rate of our cases, and exposed a number of issues regarding the clinical practice.

Material and Method

The Human Ethics Committee of our Institution approved this study in accordance with the declaration of Helsinki. The medical records of each OI patient were reviewed retrospectively, including the history of the fracture, family history, and physical manifestations. Verbal consent to participation in the study was obtained from parents and children.

Seven patients [6 male (87.5%), 1 women (12.5%)], between August 2004 and October 2010 were included in this study. One patient with a high fever during the intravenous drug infusion was not included in this study. According to the Sillence Classification², patients classified as type I OI had a blue sclera, minimal or absent limp deformity, more than one fracture caused by minimal trauma, and were fully ambulatory. All patients analysed in this study were classified as type I OI. Table 1 illustrates the demographic characteristics of patients.

We applied bisphosphonate treatment for patient with a history of three or more fractures, long bone deformities, and reduced bone mass. The intravenous dose of pamidronate disodium (Aredia, Novartis) was 0.75 mg/kg of the body weight, administered as a single dose every 6 months, over 8 hours in a saline solution. Diets were supplemented with 800-1200 mg of calcium and with a 400 IU of vitamin D per day.

Bone Mineral Density

Bone mineral density was measured before and after the treatment using a dual energy X-ray absorptiometer at vertebral bodies from L1 to L4.

Bone mineral density (g/cm²), T scores, Z scores, and the number of fractures were recorded.

Functional ability

The level of ambulation was scored according to the modified criteria of Bleck from 1 to 9 [6,7].

1. Non-walker older than 2 years of age
2. Therapy walker with the use of crutches or canes
3. Therapy walker without the use of crutches or canes
4. Household walker with the use of crutches or canes
5. Household walker without the use of crutches or canes
6. Neighbourhood walker with the use of crutches or canes
7. Neighbourhood walker without the use of crutches or canes
8. Community walker with the use of crutches or canes
9. Community walker without the use of crutches or canes

Statistical Analysis

Statistical analysis was performed using SPSS statistical software 13.0 for Windows (SPSS Inc, Chicaco, IL). Descriptive statistic, including frequencies, median, minimum and maximum values were calculated. The Wilcoxon signed-rank test was used to determine the differences in the bone density, Z score, T score, fracture, and modified Bleck score rate before and after the treatment. Results were considered statistically significant at P value <0.05.

Results

The median age of patients at the time of treatment was 15 years (min: max=13: 18), the median BMI was 17.86 kg/m² (min: max=14.29: 20.68) , the median follow-up period was 36 months (min: max= 12: 72), and the median number of doses received was 5 (min: max= 1: 20). The median bone mineral density was increased from 0.368 (min: max=0.23: 0.59) to 0.628 (min: max=0.53: 0.88) (p=0.02), the median T score was increased from -6.6 (min: max=-7.50: -1.90) to -4.2 (min: max= -5.10 - -1.90) (p=0.043), the median Z score

Table 1. The clinical features. Bone mineral density, Z score, T score, major fracture rate, and mobility before treatment, and during cyclic Intravenous Pamidronate treatment

Patient	Sex	Age	BMI	Follow-up (mo)	Number of received dose	Before treatment BMD	After treatment BMD	Before treatment Z score	After treatment Z score	Before treatment T score	After treatment T score	Major fracture rate before treatment (per/year)	Major fracture rate after treatment (per/year)	Bleck score before treatment	Bleck score after treatment
1	M	15	20.09	36	8	0.345	0.628	-5.58	-3.48	-6.8	-4.21	0.2	0	8	9
2	F	13	17.30	12	3	0.591	0.69	-3.20	-2.4	-5.4	-3.8	0.15	1	9	9
3	M	18	17.33	36	10	0.278	0.528	-7.70	-5.1	-7.4	-5.1	0.16	0	4	6
4	M	17	20.68	30	5	0.503	0.695	-4.91	-3.6	-5.4	-3.6	0.47	0	5	9
5	M	13	20.33	36	1	0.368	0.555	-4.90	-4.3	-6.6	-4.9	0.53	0	8	9
6	M	15	14.29	12	5	0.225	0.58	-5.90	-3.9	-7.5	-4.2	0.4	0	6	9
7	M	13	17.86	72	20	0.38	0.877	-4.83	-6.46	-1.9	-1.9	0.76	0.83	2	9
		Min=13 Max=18 Median =15	Min=14.29 Max=20.68 Median =17.86	Min=12 Max=72 Median =36	Min=1 Max=20 Median =5	Min=0.23 Max=0.59 Median =0.368	Min=0.53 Max=0.88 Median =0.628	Min=-7.70 Max=-3.2 Median =-4.91	Min=-6.46 Max=-2.40 Median =-3.9	Min=-7.50 Max=-1.90 Median =-6.6	Min=-5.10 Max=-1.90 Median =-4.2	Min=0.15 Max=0.76 Median =0.40	Min=0 Max=1 Median =0	Min=2 Max=9 Median =6	Min=6 Max=9 Median =9

was increased from -4.91 (min: max=-7.7: -3.2) to -3.9 (min: max=-6.46: -2.40) ($p=0.144$). The median number of major fracture decreased from 0.40 (min: max=0.15: 0.76) to 0 (min: max=0: 1) per year ($p=0.540$). The median modified Bleck score (1/9) was increased from 6 (min: max=2: 9) to 9 (min: max=6: 9) ($p=0.043$) (Table, Figure 1 and Figure 2).

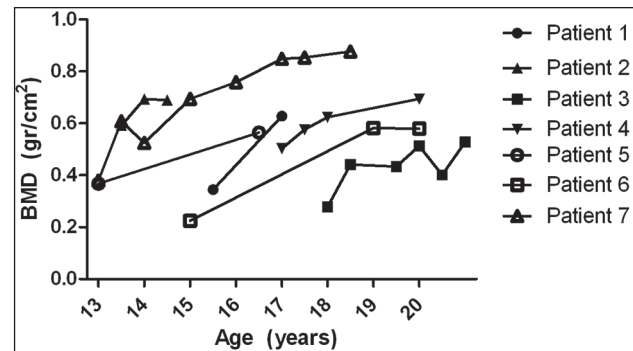


Figure 1. Changes in the bone mineral density between the first through to the fourth lumbar vertebrae in nine patients with osteogenesis imperfecta, treated with cyclic intravenous pamidronate

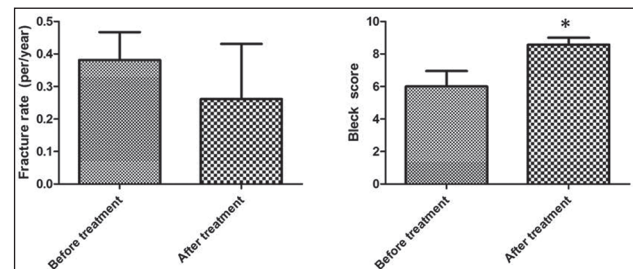


Figure 2. Fracture rate and modified Bleck score before and after treatment. Asterisk demonstrates statistically significance between before and after treatment ($p<0.05$)

Discussions

In this study, after a 36 (min: max=12: 72) month median follow up period, the median bone mineral content was increased from 0.368 (min: max=0.23: 0.59) to 0.628 (min: max=0.53: 0.88), the median T score was increased from -6.6 (min: max=-7.50: -1.90) to -4.2 (min: max=-5.10: -1.90) and the Z score was increased from -4.91 (min: max=-7.7: -3.2) to -3.9 (min: max=-6.46: -2.40) ($p=0.144$). While modified Bleck score among patients with pre-treatment level 9 in only patient, increased to level 9 in all cases after treatment. The fact that

number of fractures is less than the expected rates in spite of the improvement of the bone quality stems from the change in the life styles of patients and the increase in their mobility. pamidronate therapy, seems to support our hypothesis.

Recently, noticeable interest has been focused on treatment for patient with OI, attempting to reduce the incidence of fractures, and improving the deformities even though there is no cure for OI. However, questions remain regarding the drugs that are most effective, and reduce the fracture rate. Recent reports discuss treating OI with a growth hormone, calcitonin, parathyroid hormone, sodium fluoride, vitamin D, calcium, antiresorptive bisphosphonates including intravenous pamidronate, zoledronic acid and neridronate, and oral alendronate, olpadronate and risedronate [3,8].

Bisphosphonates are widely used in post-menopausal women to treat osteoporosis, as they are known to increase bone density, reduce fractures [9] and decrease bone turnover [10]. Bisphosphonates inactivate osteoclasts, nitrogenous bisphosphonates disrupt osteoclast formation, survival, cytoskeletal dynamic, and non-nitrogenous bisphosphonates initiate osteoclast apoptosis, thereby inhibit bone resorption [11]. Although, alteration in collagen type I molecules lead to structural change in the bone with OI to improve bone density and mechanical strength, oral and intravenous bisphosphonates are most commonly used treatment for OI.

The natural tendency in children increased bone density and growth, and decreased fractures with advancing age. As expected, we observed an improvement in the fracture rate after intravenous bisphosphonate treatment. The clinical study that compared intravenous bisphosphonates to no treatment groups reported that fracture incidences were significantly lower for intravenous bisphosphonates before therapy, and in comparison to the control group [12]. The other randomised controlled study indicated that there was no decrease in the lower extremity fracture rate after treatment [13]. The outcome of the fracture rate was not exactly presented. There was significant unpredictability in the individual response to treatment.

Akçay et al [14] reported a significant decrease in the fracture rate of the patient, and a significant increase in the Z scores of lumbar L2-L4 after daily oral alendronate treatment. They also indicated the

financial advantage of alendronate therapy. Ward et al [15] also reported alendronate treatment results for 131 OI patients. Oral alendronate therapy significantly decreased bone turnover and increased spine areal BMD, but was not associated with improved fracture outcomes after the two-year follow up. Glorieux et al [16] reported that the beneficial effect of using a daily dosage of oral alendronate could not be demonstrated.

Cyclic intravenous pamidronate is now the most widely used treatment for moderate to severe forms of OI. Oral bisphosphonates provide clinical benefit and convenience to patients with a mild form of OI. Some studies demonstrated that intravenous zoledronate in children with OI is safe in the short-term and similarly effective to pamidronate. There is no established guideline which states the most effective and safe treatment protocol for patients. Clinical studies assessing bone density reported increases after either oral or intravenous bisphosphonate treatment [12,14,17 -20]. Although alendronate therapy is effective, safe, and financially advantageous in comparison to pamidronate, long term daily oral medication has some disadvantages as the child may not be willing to take the pills. For this reason, using cyclic pamidronate treatment is thought to be a lot more appropriate.

The main limitations of our investigation are the small number of patients studied but all patient studied was Type I OI.

In conclusion, intravenous pamidronate increased bone mineral density, and improved the fracture rate and mobility in patient with OI. Pamidronate is a safe and effective treatment method for patient with OI. Further studies are required to determine the long-term safety of the drugs, the optimal dose, and the duration of the treatment to improve the bone strength, and to prevent the deformity while minimising its inappropriate effect on long bone growth and fracture healing.

References

1. Byers PH, Wallis GA, Willing MC. *Osteogenesis imperfecta: translation of mutation to phenotype. J Med Genet* 1991 Jul; 28(7): 433-42
2. Sillence DO, Senn A, Danks DM. *Genetic heterogeneity in osteogenesis imperfecta. J Med Genet* 1979 Apr; 16(2): 101-16.

3. Phillipi CA, Remington T, Steiner RD. 2008. Bisphosphonate therapy for osteogenesis imperfecta. *Cochrane Database Syst Rev*. 2008 Oct 8; (4): CD005088
4. Engelbert RH, Pruijs HE, Beemer FA, Helders PJ. Osteogenesis imperfecta in childhood: treatment strategies. *Arch Phys Med Rehabil* 1998 Dec; 79(12): 1590-4.
5. Zeitlin L, Fassier F, Glorieux FH.. Modern approach to children with osteogenesis imperfecta. *J Pediatr Orthop B* 2003 Mar; 12(2): 77-8
6. Bleck EE Nonoperative treatment of osteogenesis imperfecta: orthotic and mobility management. *Clin Orthop* 1981 Sep; (159): 111-22.
7. Tolboom N, Cats E. A., Helders P. J. M. Pruijs J. E. H Engelbert R. H. H. Osteogenesis imperfecta in childhood: effects of spondylodesis on functional ability, ambulation and perceived competence. *Eur Spine* 2004 Mar; 13(2): 108-13.
8. Shapiro JR, Sponsellor PD. Osteogenesis imperfecta: questions and answers. *Curr Opin Pediatr* 2009 Dec; 21(6): 709-16.
9. Black DM, Cummings SR, Karpf DB, Cauley JA, Thompson DE, Nevitt MC, et al.. Randomised trial of effect of alendronate on risk of fracture in women with existing vertebral fractures. *Fracture Intervention Trial Research Group*. 1996 Dec 7; 348(9041): 1535-41
10. Reid IR, Brown JP, Burckhardt P, Horowitz Z, Richardson P, Trechsel U, et al. Intravenous zoledronic acid in postmenopausal women with low bone mineral density. *N Engl J Med*. 2002 Feb 28; 346(9): 653-61.
11. Fisher JE, Rogers MJ, Halasy JM, Luckman SP, Hughes DE, Masarachia PJ, et al.. Alendronate mechanism of action: geranylgeraniol, an intermediate in the mevalonate pathway, prevents inhibition of osteoclast formation, bone resorption, and kinase activation in vitro. *Proc Natl Acad Sci U S A* 1999 Jan 5; 96(1): 133-8
12. Adami S, Gatti D, Colapietro F, Fracassi E, Braga V, Rossini M, et al.. Intravenous neridronate in adults with osteogenesis imperfecta. *J Bone Miner Res* 2003 Jan; 18(1): 126-30.
13. Letocha AD, Cintas HL, Troendle JF, Reynolds JC, Cann CE, Chernoff EJ et al.. Controlled trial of pamidronate in children with types III and IV osteogenesis imperfecta confirms vertebral gains but not short-term functional improvement. 2005 Jun; 20(6): 977-86.
14. Akcay T, Turan S, Guran T, Bereket A.. Alendronate treatment in children with osteogenesis imperfecta. *Indian Pediatr Indian Pediatr*. 2008 Feb; 45(2): 105-9
15. Ward LM, Rauch F, Whyte MP, D'Astous J, Gates PE, Grogan D, et al . Alendronate for the treatment of pediatric osteogenesis imperfecta: a randomized placebo-controlled study *J Clin Endocrinol Metab*. 2011 Feb; 96(2): 355-64.
16. Glorieux FH, Rach F, Ward LM. Alendronate in the treatment of pediatric osteogenesis imperfecta. *J Bone Miner Res*. 2004 Nov; 19(11): 1779-86.
17. Dimeglio LA, Ford L, McClintock C, Peacock M. A comparison of oral and intravenous bisphosphonate therapy for children with osteogenesis imperfecta. *J Pediatr Endocrinol Metab* 2005 Jan; 18(1): 43-53
18. Glorieux FH.. Treatment of osteogenesis imperfecta: who, why, what?; *Horm Res* 2007; 68 Suppl 5: 8-11.
19. Seikaly MG, Kopanati S, Salhab N, Waber P, Patterson D, Browne R, Herring JA. Impact of alendronate on quality of life in children with osteogenesis imperfecta.; *J Pediatr Orthop* 2005 Nov-Dec; 25(6): 786-91.
20. Gatti D, Antoniazzi F, Prizzi R, Braga V, Rossini M, Tato L, Viapiana O, Adami S. Intravenous neridronate in children with osteogenesis imperfecta: a randomized controlled study. 2005; 2005 May; 20(5): 758-63.

Corresponding Author

Zekeriya Oztemur;

Cumhuriyet University School of Medicine,
Department of Orthopedic and Traumatology,
Sivas,

Turkey,

E-mail: oztemur@cumhuriyet.edu.tr;

oztemurz@gmail.com

Quality of family interactions and mental development of preschool children

Radmila Milovanovic, Gordana Budimir-Ninkovic

Faculty of Pedagogy in Jagodina, Serbia

Abstract

The basic premise where this research starts is that the quality of interactions in a modern family is correlated with mental development of children, affecting the progress or delays in their mental development. The research sample is consisted of 148 mothers of children aged between two and six years from preschool institutions in Petrovac at the Mlava, Valjevo, Kruševac, Žagubica, Paraćin, Jagodina and Belgrade. To collect data on family interactions, modeled on the McMaster model, we used the shortened version of the Todosijević questionnaire that examines open communication, emotional warmth, joint solving of problems, hostility, disorder, and alienation in family interactions.

In collecting data on the status of mental development of children we used the questionnaires designed for this study and based on the norms of mental development of children by Ivić and collaborators, which examine dimensions of intellectual, emotional and social development. We assumed that all the dimensions of family interactions are associated with all mentioned dimensions of mental development of children. The results show a statistically significant correlation between the tested dimensions, confirming all of the initial assumptions. The results suggest that the family and family interactions strongly influence the overall mental development of preschool children and highlight the importance of education of parents in this sense in counsel bodies as well as in all other educational institutions.

Key words: Contemporary family, family interaction, cognitive, emotional and social development of children

Introduction

According to the interactional view, which is in line with modern genetics, the influence of biological and social factors is needed for the full devel-

opment of a person (Popper, Eccles, 2002:112). In other words, the ways of a personality's development depend both on its organic preconditions and on the social environment in which he or she develops. The prerequisites for organic mental development are primarily morphological and functional maturation of the cerebral cortex (Shaw, Greenstein, Lerch, Clasen, Lenroot, Gogtay, 2006:678). Social impacts are directly intertwined with the processes of growth, development and of organic maturation, and are consisted of all elements of the social environment in which a child lives, and this is above all, his or her family. The family and family interactions are directly involved in the ways of mental development (Marley, 2004:182). Family atmosphere, the quality of family interactions between parents and children, the level of sensitivity and stimulation in care of the child are the most important predictors of children's mental development and, ultimately, of his or her mental health. Sensitive parents or parents who are emotionally involving in interactions with children and provide them a stimulating family environment, have undoubtedly raised children who are cognitively, emotionally, socially and mentally healthier and more prosperous (Bjorklund & Pellegrini, 2000; Pancsofar, 2008:1702).

Given the importance of family, it is worth noting in this context that the large and rapid social and cultural changes are reflected on all the characteristics of modern families. Economic insecurity, uncontrolled flow of information, increased divorce and family abandonment, with increasing employment of parents (while the unemployment rate gets higher), then, division of roles in raising, upbringing and education of children between families and preschool institutions and schools, alternative forms of family and marital life, the collapse of traditional morality and the creation of new values of consumer society – all these factors certainly foster modelling of entirely new forms

of family functioning and new forms of family interactions. In a complex assessment of the impact of modern families in the mental development of children, one should take into account several factors, but most notably: family composition, family relationships, family function, parental personality, the pace of development of family relationships, the way children are brought up, the system of values and behavior norms in a family, social relations and the culture in which families exist, and many other important facts about the family. Of course, it is impossible to include all these factors in a study. In this paper we make an attempt to investigate in what way the quality of family interactions affect the mental development of children.

The theoretical framework of this paper is the McMaster model of family functioning (Epstein, 1978:23), which posits six dimensions of family interactions important for a family functioning. These are: 1) *solving problems*, defined as the ability of families to solve problems at a level that maintains effective family functioning, 2) *communications* relating to information exchange in a family, i.e. whether the communication is open or covert, direct or indirect, 3) the *role* dimension is related to established forms of behavior by which individuals fulfill their family functions, focusing on whether the roles are distributed appropriately, explicitly, through free discussion, and whether these are performed in a responsible manner; 4) *affective response* is defined as the ability to respond to various stimuli with the appropriate quality and quantity of emotion; 5) *affective involvement* is defined as the degree to which the family shows interest and evaluation of activities and interests of family members, with several possible degrees of involvement, from complete lack to symbiotic involvement, with medium levels to be understood as the healthy ones, and 6) *control of behavior*, defined as practices adopted by families in order to regulate behavior in specific situations - physically dangerous situations, situations involving satisfying and expressing psychobiological needs and instincts, and situations involving socializing within and outside the family. Also, the starting point for this research is the theoretical grounds based on the Development map by Ivić and collaborators (Ivić i sar., 2004) which purports the correlation of qualities of family interactions and of all aspects of a child's mental de-

velopment. In other words, the interactions guided above all by parents (and by educators), implying cooperation, emotional involvement and warmth, have stimulating effect on mental development, while interactions involving exclusion, coercion, threat, emotionally distanced interactions, have destructive influence on development of all aspects of a child's personality. One should keep in mind in this context that the family interactions are one of the two most important factors (the other is the constitutional type of a child) leading to occurrence of psychopathological phenomena in the age of child's development (Kondić, 1998:23).

Method

1. The subject and problem of research

The subject of the present research is to assess impact of interactions of family members on mental development of children. Given such a set of the subject, the problem of this research could also be posed as question whether family interactions, defined by harmony, hostility, disorder, and alienation in family interactions are associated with the degree of mental development of a child living at home, and attending a preschool institution within the appropriate age group, as defined by indicators of cognitive, emotional and social development.

2. The aim and objectives of research

In accordance with the subject matter and with the problem of this research, the following aim and objectives of research have been defined.

The aim of this research is to determine and explain whether there is a correlation between family interactions and the degree of mental development of a child living in the family.

To achieve such a specific goal of the research, it is mandatory to realize the following **research tasks**:

- To determine whether the open communication in family interactions is associated with cognitive, emotional and social development.
- To investigate whether the emotional warmth in family interactions is associated with cognitive, emotional and social development.
- To examine whether the joint solving of problems in family interactions is associated with cognitive, emotional and social development.

- To determine whether the hostility of family interactions is associated with cognitive, emotional and social development.
- To investigate whether the disorder in family interactions is associated with cognitive, emotional and social development.
- To examine whether the alienation of family interactions is associated with cognitive, emotional and social development.

3. Hypotheses of the research

Starting from the goals and objectives, we have posed the following hypotheses:

The general hypothesis

It is expected that there is an association of family interactions and mental development of a child living in the family.

Specific hypotheses

It is assumed that there is a correlation between an open communication in family interactions with cognitive, emotional and social development. Children living in families with open communication, display prominent cognitive, emotional and social aspects of their mental development.

It is expected that there is a correlation of emotional warmth in family interactions with the cognitive, emotional and social development. Children living in families with emotional warmth display prominent cognitive, emotional and social aspects of development.

It is considered that there is a correlation of common solving problems in family interactions with cognitive, emotional and social development. Children living in families in which members jointly solve problems, display more prominent aspects of cognitive, emotional and social development.

It is assumed that there is a correlation between hostility in family interactions with cognitive, emotional and social development. Children living in families in which there is hostility in family interactions, display less pronounced cognitive, emotional and social aspects of mental development or have difficulties in certain aspects of their development.

It is expected that there is a correlation between disorder in family interactions with cognitive, emotional and social development. Children living in families where there is disorder in family interactions, display less pronounced cognitive, emotional

and social aspects of mental development and have difficulties in certain aspects of their development.

It is considered that there is a correlation of alienation in family interactions with cognitive, emotional and social aspects of mental development. Children living in families where there is an alienation in family interactions, display less pronounced cognitive, emotional and social aspects of mental development and have difficulties in certain aspects of their development.

4. Research variables

Independent variable

Family interactions are operationalized by the instrument of family interactions measuring six dimensions: open communication, emotional warmth, joint solving of problems, hostility, disorder, and alienation.

Dependent variable

Degree of child's development is operationalized through three dimensions: cognitive, emotional and social development.

Control variables

Gender of child. The sample is divided into mothers of girls and mothers of boys.

Age of child - the child's age is treated, so to speak, as a control variable only in the sense that the mothers filled those questionnaires designed for the age of their children. However, questionnaires have the same number of questions and the same dimensions, so the data are processed as if it were one questionnaire, and therefore this variable will not be used in data processing in terms of testing the correlations or the differences.

5. Population and research sample

This research covers the population of mothers of children attending preschool institutions. In preschool institutions there are different groups divided by age of the children. These are mostly younger kindergarten, older kindergarten, medium and mixed or older age groups. The research was conducted in several preschool institutions in Petrovac at the Mlava, Valjevo, Kruševac, Žagubica, Paraćin, Jagodina and Belgrade.

The convenient research sample includes 148 mothers. The selected mothers are those with children under the age of 2, then of ages about 3 and 5, while questionnaires cover wider range of months

or years of children, because we took into account that some children may reach levels of development matching lower or perhaps even higher ages. In completing questionnaires on child development mothers had help from teachers and educators, because they like mothers spend lots of time with children.

The selected mothers are those whose families have more members and they were told that during answering questions take into account family interactions which their children are daily exposed to. The selected families are complete ones in order to avoid intervening effects of divorce and related traumatic experiences.

Table 1. The structure of the sample regarding gender of child

Gender of child	Frequencies	Percentage
Male	72	48%
Female	76	52%
Total	148	100%

Table 2. The structure of the sample regarding age of child

Age of child	Frequencies	Percentage
20-22 months	44	28%
72-76 months (ca 3 years)	47	31%
120-124 months (ca 5 years)	57	41%
Total	148	100%

Therefore, the sample consists of 148 mothers, 72 mothers of male children and 76 mothers of female children. Also, the sample consists of 44 mothers the children of whom are at the age 20-22 months, 47 mothers with children with the age of 72 to 76 months, and 57 mothers whose children are at the age between 129 to 124 months.

6. Methods, techniques and instruments of the research

The descriptive method is used in the paper, which is adequate for monitoring the biographical data in order to follow a child's development during early childhood, when parents constantly stand with the child and record all events and changes in a child's development. After the fifth-sixth year, the child's development is greatly expanded and rich, and the parents are no longer able to monitor and record everything needed despite their best intentions. The advantage of this method is in that the de-

velopment is followed by the one who is in constant contact with the child, while the lack is in that the observations of parents are not always systematic, and in that parents sometimes unconsciously modify their findings as a result of subjective attitude towards their own children. We tried to alleviate this deficiency by having involved teachers in responding to the questionnaire on child development.

The instruments used in the research are the questionnaires of the degree of the cognitive, emotional and social development: Questionnaire of the children development level under 2 years of age, Questionnaire of the children development from 2.5 to 4 years of age, and Questionnaire of the children development from 4.5 to 6 years of age; as well as the Questionnaire of family interactions.

There are three types of questionnaires on stage of development because distinct types were given to mothers with children of different ages (up to 2 years, from 2.5 to 4, and from 4.5 to 6 years). The questionnaires were designed for this research, based on the development standards by Ivić and collaborators (Ivić, 2004). Each of the questionnaire consists of three subscales:

- *Cognitive development* (related to level of speech development, perception and intellectual abilities),
- *Emotional development* (related to quality of attachment, emotional expression and emotional control), and
- *Social development* (related to quality of interaction and communication with adults and children, independence, behavior in the game).

Each subscale contains 7 statements which can be responded positively or negatively, and the total score is obtained simply by summing responses. Thus the scores can be obtained for each subscale, and for the scale as a whole.

The questionnaire of family interaction is constructed on the model of FAD questionnaire that was originally developed as an operationalization of the McMaster model of family functioning, and in relation to systemic family therapy (Todorović, 1996). The scale consists of 23 items (representing a shortened version of the original questionnaire). The scale is balanced, i.e. it contains items that express both positive and nega-

tive perceptions of the family. Both scales are of the Likert type with four possible degrees of disagreement (1-4), where a higher number indicates greater agreement with a given statement. Scores are obtained by summing the appropriate items (statements). In this paper six dimensions of family interactions are used:

- *Open communication* (items 19, 7, 18)
 - adequate sharing of information in the family, fostering tradition of honest discussion and communication about the usual, but also about taboos;
- *Emotional warmth* (items 17, 21, 9) - interest and evaluation of activities and interests of the family members;
- *Joint solving of problems* (items 1, 3, 8, 18, 23) - the ability of family to gather around solving family problems and problems of individual members;
- *Hostility* (items 2, 4, 5, 10, 22) - refers to negative emotional exchange between members, unfulfilling of the roles and responsibilities, criticism, etc.;
- *Disorder* (items 6, 14, 20) - relates to poor or non existing control of behavior in the family and the lack of commitment;
- *Alienation* (items 11, 12, 13, 15, 16) - refers to the lack of adequate interaction, manipulation, overall distance, coldness and indifference among the members.

7. Statistical analysis of research results

Having finished the research we performed data coding and made data as entries into raw matrix. For this a software package for statistical analysis of data (SPSS 17.0) was implemented. Since we were interested only whether there is an association of family interactions with the degree of mental development, i.e. dimensions of these variables, we used correlative techniques of research, that is, the partial correlation, since the gender was taken as a control variable. In doing so influence of gender

was reduced to minimum, discovering in what way family interactions of complete families affected the level of speech development of children. In order to show descriptive characteristics of the sample, frequencies and percentages were used.

Results and discussion

Research results will be presented according to the hypotheses (firstly according to the specific ones, and finally according to the general one) and the partial correlation will be used, indicating the degree and direction of the correlation among dimensions of independent and dependent variables, with the gender as a control variable.

1. Correlation of open communication with dimensions of mental development

The first of the specific hypotheses assumes that there is a correlation of open communication in family interactions with cognitive, emotional and social development. It is expected that children living in families with open communication display more prominent aspects of mental development.

Table 3 shows that open family communication is associated with cognitive development ($r=0,445$, $p<0,01$), emotional development ($r=0,435$, $p<0,01$) as well as with social development ($r=0,486$, $p<0,01$). Since the correlation is positive one, it can be concluded that children from families with open communication display more prominent aspects of cognitive, emotional and social development. This conclusion partly proves the specific hypothesis of this research. Families where clear and direct messages are used, and where the messages are being accepted, i.e. where there is knowledge on content of notification and the ways thereof, which is one of the most effective methods of verbal communication, are those that can bring up children who understand well other people's speech and speak well, have good perception, can learn without difficulties and can express interest in the world around them.

Table 3. Correlation of open communication in family interactions with cognitive, emotional and social development

Partial correlation (control variable: gender)		Cognitive development	Emotional development	Social development
Open communication	Correlation	,446	,435	,486
	Level of significance	,000	,000	,000

On the other hand, families where the messages are masked and/or indirect, and where the messages are being ignored or disqualified, i.e. the families with poor communication, are able to bring up children that can understand less, that make lesser use of verbal expressions, that are less interested in the world and can learn with difficulties.

2. Correlation between emotional warmth with dimensions of mental development

According to second hypothesis, it is expected that there is a correlation of emotional warmth in family interactions with the cognitive, emotional and social development. It is expected that children living in families with emotional warmth would display more prominent aspects of cognitive, emotional and social development.

Table 4 shows that emotional warmth in family interactions is positively and in statistic sense significantly correlated with all the dimensions of mental development of preschool children. Namely, the more increased emotional warmth is, the better are all of the indicators of cognitive, emotional and social development. This entirely proves the second specific hypothesis. The emotional warmth is dimension related to the pronounced emotional involvement in which family members are interested in each other, but without intrusion. This involvement is based on the needs of others and on constant evaluation of the emotional state of other members. Families where there is such a family atmosphere and where such a participation in the lives of its members is fostered, are able to facilitate the youngest members with an adequate mental development. Families

where there are cold emotional relationships, where members relate to each others as strangers and therefore barely talk, can bring up children with poor social interaction, activity and attention, children that can understand others' speech less and can talk less, learn and solve problems with difficulties, children that are emotionally and socially not adapted.

3. Correlation of joint solving of problems with the dimensions of mental development

The third hypothesis is the following: It is considered that there is a correlation of solving of common problems in family interactions with cognitive, emotional and social development. Children living in families in which members jointly solve problems, have more prominent aspects of mental development.

Table 5 displays the joint solving of problems in family interactions is positively and significantly associated with cognitive, emotional and social development. Thus, the families that are able to jointly solve problems can develop with their youngest members exactly attention, interaction, as well as emotional and social competence. In this way the third specific hypothesis is proven. Joint solving of problems involves the relationship of unity in dealing with both the practical and emotional problems. The most effective family functioning is the one including all seven stages in relation to a problem: identification of a problem, communication on a problem, alternative plans to solve a problem, decision on action based on selection of alternative possibilities of actions to implement a plan, direction of actions towards the

Table 4. Correlation between emotional warmth in family interactions with cognitive, emotional and social development

Partial correlation (control variable: gender)		Cognitive development	Emotional development	Social development
Emotional warmth	Correlation	,337	,450	,579
	Level of significance	,001	,000	,000

Table 5. Correlation of joint solving of problems in family interactions with cognitive, emotional and social development

Partial correlation (control variable: gender)		Cognitive development	Emotional development	Social development
Joint solving of problems	Correlation	,388	,494	,325
	Level of significance	,000	,000	,000

final solution, and finally, assessment of success of the action. Families that in this way meet their problems do talk a lot and work together a lot, interacting with each other, and promote development of interaction, activities and child care, as well as emotional and social competence.

On the other hand, families the members of which successfully or unsuccessfully but independently solve their problems without seeking help from others, and the families with common problems the individual members of which attempt or not to solve, can only hinder cognitive, emotional and social development of children.

4. Correlation of hostility with dimensions of mental development

The fourth specific hypothesis suggests that there is a correlation between hostility in family interactions with cognitive, emotional and social development. It is expected that children living in families with hostility in family interactions display less pronounced aspects of mental development.

Table 6 displays the hostility in family interactions is negatively and significantly associated with all the dimensions of mental development. This means that increased hostility in the family decreases level of cognitive, emotional and social development. Families with increased hostility in their relationships have children with less progress in all aspects of mental development. This *proves the fourth specific hypothesis*. Families where there is hostility, negative emotional exchange, rows, cold relationship, criticism, etc. show diminished interest and reduced the interaction between members, which also results in paying less attention on children and towards

providing appropriate incentives for their development. Moreover, the relationships with the prevailing enmity incite anxiety forming basis for development of neurotic symptoms.

5. Correlation of disorder with the dimensions of mental development

The fifth specific hypothesis is: It is expected that there is a correlation of disorder in family interactions with cognitive, emotional and social development. Children living in families with disorder in family interactions display less pronounced aspects of mental development.

Table 7 shows that disorder in family interactions is negatively and in statistic sense significantly correlated with all the dimensions of mental development. It is to be concluded that families with disordered family interactions bring up children with lower level of mental development. Thus the fifth specific hypothesis of this research is confirmed. Disorder in the family interactions is related to chaotic control of behavior. Control of behavior can be rigid, where there is no agreement and the rules are inflexible and are usually the same for all ages. In setting the rules of conduct the new circumstances and a flexible control are taken into account. *Laissez faire* is a form of educational freedom, where anything is permitted. The chaotic control includes all forms of control alternately or simultaneously, and is very confusing especially for children. Families with consistently established flexible control, of course, work better and have positive impact on child's overall development.

Table 6. Correlation between hostility in family interactions with cognitive, emotional and social development

Partial correlation (control variable: gender)		Cognitive development	Emotional development	Social development
Hostility	Correlation	-,380	-,485	-,257
	Level of significance	,000	,000	,010

Table 7. Correlation of disorder in family interactions with cognitive, emotional and social development

Partial correlation (control variable: gender)		Cognitive development	Emotional development	Social development
Disorder	Correlation	-,384	-,524	-,416
	Level of significance	,000	,000	,000

6. Correlation of alienation with the dimensions of mental development

The sixth and final specific hypothesis is: It is considered that there is a correlation of alienation in family interactions with cognitive, emotional and social development. It is assumed that children living in families with alienation in family interactions display less pronounced aspects of mental development.

On the basis of Table 8 it can be concluded that the alienation between family members is in a negative and statistically significant correlated to the dimensions of mental development: with cognitive, emotional and social development. Specifically, these dimensions are less pronounced in children from families with an increased alienation in family interactions. This *confirms the sixth specific hypothesis*.

Families where their members are alienated from each other, who know little about each other and do not attach themselves with the problems or the joyful moments of other family members, in a word families with estranged members, the ones who do not communicate, have children with lower levels of mental development in all tested dimensions. Such children poorly understand and express their own voice and poorly respond to orders, do not show need for interaction, have poor attention to all kinds of stimuli, have no interests, poorly learn, and are emotionally uncontrolled and socially excluded. In contrast, the families that make appropriate contacts, take part in the lives of each other, manage to positively influence the development of children.

7. Correlation of family interactions with mental development

The general hypothesis states that there is a correlation of family interactions with mental development. On the basis of specific hypotheses that are proven, we can conclude that the variables are interrelated, and this to be concluded from Table 9 which displays positive and statistically significant correlation of family interactions with mental development. The variable of family interactions occurred by recoding items of hostility, disorder and alienation, so that higher scores on this variable indicates the higher quality of family relationships.

Families where there is high quality in the family atmosphere and where an adequate communication is achieved, can foster warm emotional relationships and can have flexible control of behavior. In that way they can jointly solve their problems, in the family circle coping with losses and difficulties. Where family members are not in conflict, the conditions encouraging full development of child are created.

Conclusions

The basic premise on which this research started was that the family interactions may be correlated with mental development, i.e. that they affect progress or delay in a mental development. To investigate this hypothesis, we examined mothers and educators of preschool children in whose development we have been interested in. The selected mothers were ones of those children living in complete families and with no organic deficiencies that may have caused problems in mental development. We have controlled the variables of gender and age of children, in order to avoid

Table 8. Correlation of alienation in family interactions with cognitive, emotional and social development

Partial correlation (control variable: gender)		Cognitive development	Emotional development	Social development
Alienation	Correlation	-,319	-,426	-,341
	Level of significance	,001	,000	,000

Table 9. Correlation of family interactions with mental development

Partial correlation (control variable: gender)		Mental development
Family interactions	Correlation	,276
	Level of significance	,006

occurrence of differences in development due to gender and age distinctions.

The area of family interaction being very wide one, we tried not to expand it much further and have encompassed with this term (according to the McMaster model and the shortened version of the Todosijević questionnaire) open communication, emotional warmth, joint solving of problems, hostility, disorder, and alienation. We assumed that all these dimensions of family interactions significantly correlated in a statistic sense with the dimensions of mental development, as are cognitive, emotional and social aspects of development. These assumptions were confirmed. Described in such a way, we have investigated and found out that family interactions are correlated with the degree of mental development. Therefore, on the basis of these results we can conclude the following:

Families where there is open, clear and direct communication manage to influence preschool children to develop cognitively adequate (developing the ability to understand speech, abilities of expressive language, perceptual abilities, as well as skills of learning and thinking).

Families whose members are emotionally connected, participating in problems and joys of other family members, who can and want to share their affective states with other members, are families where children have harmonious mental development.

Those families where members jointly deal with the problems and try to solve of them with the effort of all the members, represent suitable framework of cognitive, emotional and social development.

On the other hand, families where emotions are not expressed and are not shared among family members, where quarrels are frequent, where for a long time there is no conversation between the members, are the families bringing up children with difficulties in cognitive, emotional and social development. Families with no order and rules, where there is no control of behavior, and where members are independent from each other and where there is no agreement nor exchange, have children with poorer ability of interaction, children who gesture less and have lesser motoric response to verbal orders, as well as children who speak less in general, that are insecure, distant,

frightened, dependent, indifferent to environment, uncooperative, with poor ability to delay satisfaction with neurotic manifestations, such are thumb sucking, hair picking, nail biting, rubbing of body parts, enuresis and the like. Such children are brought up in families the members of which are alienated, where there no discussions, interactions and communication.

Thus, we conclude that the family and behavior of the family members strongly influence the overall mental development of child. It is therefore important to encourage a constructive family interaction and communication in counseling bodies, as well as in all other educational institutions.

We are aware that we made a modest contribution to explaining the above issues and problems, and we expect that this research may be an incentive to other authors for more complete discussion of these contents.

References

1. Bjorklund DF, Pellegrini AD. *Child Development and Evolutionary Psychology*. *Child Development*, 2000; 71: 1687–1708.
2. Enfield NJ. *Without social context?* *Science*, 2010; 329: 1600–1601.
3. Epstein NB. et al. *The McMaster Model of Family Functioning*. *Journal of Marriage and Family Counseling*, 1978; 4: 21–26.
4. Goldstein MH, Schwade J. *Social feedback to infants babbling facilitates rapid phonological learning*. *Psychological science: a Journal of the American Psychological Society/ APS*, 2008; 19(5): 515–23
5. Hardy S. *Mothers and others. The evolutionary origins of mutual understanding*. Cambridge, MA and London: Belknap press of Harvard University Press. 2009
6. Ivić I. *I sar. Razvojna mapa*, Beograd: Kreativni centar. 2004
7. Kendler KS, Prescott CA. *Genes, environment and psychopathology: Understanding the causes of psychiatric and substance use disorders*. Boston: Guilford Press. 2006.
8. Knight C, Power C. *Social conditions for the evolutionary emergence of language*. Tallerman and Gibson (eds), *Handbook of language evolution*. Oxford: Oxford: University Press. 2011; 346–49

9. Kondić K, i sar. *Psihodinamska razvojna psihologija*. Beograd: Plato. 1998.
10. Lerner RM. *Concepts and theories of human development*. Mahwah, NJ: Erlbaum. 2002.
11. Marley JA. *Family involvement in treating Sch: Model, essential skills, and process*. The Haworth Clinical Practice Press. 2004; 43: 178-216
12. Pancsofar N. et al. *Family relationships during infancy and later mother and father vocabulary use with young children*. *Early Childhood Research Quarterly*, 2008;23: 493.
13. Popper K, Eccles J. *The Self and Its Brain*, Boston: Little, Brown & Company. 2002
14. Reid, V.; Striano, T. & Koops, W. *Social Cognition During infancy*. Psychology Press. 2007.
15. Shaw P, Greenstein D, Lerch J, Clasen L, Lenroot R, Gogtay N, et al. *Intellectual ability and cortical development in children and adolescents*. *Nature*, 2006; 440: 676 -79
16. Skinner H, Steinhauer P, Sitarenios G. *Family Assessment Measure (FAM) and Process Model of Family Functioning*. *Journal of Family Therapy*, 2000; 22(2): 190-210
17. Thompson-Schill S, Ramscar M, Chrysikou M. *Cognition without control: When a little frontal lobe goes a long way*. *Current Directions in Psychological Science*. 2009; 8(5): 259-263.
18. Tomasello M. *Origins of Human Communication*. MIT Press. 2008
19. Venar Č. *Razvojna psihopatologija i psihijatrija*, Zagreb: Naklada Slap, 2003.
20. Todosijević B. *Relacije između porodičnog funkcionisanja i autoritarnosti*. u Genc, L. i Ignjatović, I. (Ur.): *Ličnost u višekulturnom društvu*, Br. 3, Novi Sad: Univerzitet u Novom Sadu, Filozofski fakultet, Odsek za psihologiju, str: 1996: 138-153.

Corresponding Author

Radmila Milovanovic,

Faculty of Pedagogy in Jagodina,

Serbia,

E-mail: budimirninkovic@yahoo.com

The knowledge of teenagers about breast self-examination

Huriye Demet Cabar¹, Dilay Argun Acil², Birsen Altay³, Yelda Guler¹

¹ School of Nursing, Sinop University, Sinop, Turkey,

² Faculty of Nursing, Dokuz Eylül University, İzmir, Turkey,

³ School of Nursing, Ondokuz Mayıs University, Samsun, Turkey.

Abstract

Purpose: The purpose of this study is in order to determine the knowledge of teenagers about breast self- examination (BSE).

Methods: A descriptive study that was performed, were included 841 students in the centre of the Sinop. The data were collected via information form consisting 12 questions. The collected data were evaluated by SPSS statistical software version 14.0.

Results: Overall, 17.4 % of them were in 18-19 age group, whereas 61% of them were in 15-17 age group and 76.1% of the participant were mid school graduated. However, 37.1 % of the participants stated that they had never heard the term of BSE, where as 11.9 % of them stated that they had taken information from doctor, 14.6 % of them from nurse. Presents conditions related with BSE, 30.1 % of the participants know how to perform BSE and 86.6 % of participants believe the benefit of BSE on early diagnosis of breast cancer.

Conclusion: According to results of the study, the ratios of state of being heard about BSE, knowing how to do it, and believing the importance of BSE in early diagnosis of the participants were low.

Key words: Breast self-examination, teenagers, nurse, education

Introduction

Breast Cancer in Turkey and In The World

Breast cancer is the most common cancer and one of the most important cause of death among females around the world (1, 2, 3, 4, 5). Therefore, in every 3 minutes a female is diagnosed as breast cancer according to International Agency on Cancer for Research of WHO (IARC) (1,6,7,8). Breast cancer is seen in 10 of 100 females (9). Approximately 1 million women lost their life due to breast cancer in USA between 1950 and 1970

(10, 11). According to the data of 2008 in USA, 40480 women lost their life due to breast cancer, while 182.460 women was diagnosed as breast cancer and in Europe it is 320.000 (3, 10, 11, 12, 13). The frequency of breast cancer in North America and Europe is higher than the other continents (9). In every 11 minutes, a female loses her life because of breast cancer in the world. It happens frequently in low and middle income countries (approximately 221.000) (1, 4, 7, 10, 12, 14, 15).

According to data of Health Ministry and Globakan 2002, the most common type of cancer (36.47/100.000) and one of the most important factor of death (~10/100.000) among females in Turkey is breast cancer (1, 2, 3, 5, 8, 16, 17, 18, 19, 20, 21, 22). The incidence of breast cancer is variable in different parts of Turkey, due to personal, geographic, social and cultural factors (20, 23). At the east of Turkey, the incidence is 20/100.000, while it is 50/100.000 in west, because of early menarche, late menopause, first birth after 30 years old and inadequate breast feeding rates (4). According to these data, the number of women diagnosed as breast cancer is accounted approximately 10.000, in Turkey (4, 14).

The Definition of Breast Cancer and the Risk Factors

Breast cancer is a type of cancer that originates from the lobules formed by the glands that provide milk production, from the ductuli that provides milk secretions or connective tissues that fill the spaces among these structures. (7,8)

Although the etiology of the breast cancer has not been identified yet, some factors such as sex, age, presence of previous bening or maling tumor, genetics, race, age of menarche, age of menopause, age of pregnancy, history of lactation, use of diethylstilbestrole (a nonsteroidal synthetic estro-

gen), hormone replacement therapy, nutritional habits, body weight, alcohol intake, exercises and exposure to radiation, are known to have role in the progression of breast cancer (7,10,11,24).

In the adolescence period, that begins 10-12 ages and lasts up to 18-20 ages, physiological changes and diseases in breast are frequently seen (25,26). Infections, hormonal changes, injuries and tumors are frequently seen breast diseases of adolescence. Malignant breast tumors are very rare in childhood, and they are classified into three groups; primary breast cancer, metastatic tumors and secondary breast cancer. Only 0.2 % of primary breast cancers are seen before the 25 of age (27). Under the age of 20, almost no women die due to breast cancer, however, 1 % of patients die between the ages of 20 and 34 (8,26).

Breast Cancer and Early Detection

Breast cancer is a type of cancer both early diagnosis and screening programs are recommended (28). The cure of the patients varies from 80 % to 100 % with the early diagnosis methods (8,9,10,11,24). The overall five-year survival rates of patients with breast cancer are 73 % and 53% at developed and developing countries, respectively. This significant difference may be explained by opportunity of early diagnosis by screening mammographies and better treatment in developed countries. When it is performed at appropriate age range and intervals, community based breast cancer screening (Clinical breast examination + mammography), and may provide 30 % decrease in mortality of female breast cancer. (7,15,28,29). In addition, MRI and mammography are recommended for people with risk factors for breast cancer such as BRCA mutation (13).

In our country, the national standards of breast cancer screening has been defined as "Two X-ray images of each breast which is taken following clinical breast examination and is evaluated by double reading every 2 years for the women between 50-69 years old, and at ages and intervals that should be determined by physician for women below 50 years old at risk group" and the screening service is free for women 50-69 ages at KETEM (Cancer Early Diagnosis and Screening Centres)'s which are sub-organization of Health Ministry (30,31). However, there is no systematic

study (instructing, BSE education vs.) about breast cancer which covers adolescents. The most important independent risk factor for breast cancer is age (3). Hence, it is thought that the studies providing knowledge for early diagnostic methods at younger ages are important (27).

The Importance of BSE at Early Detection

BSE is a regularly and systematically performed self-examination method of breast and surrounding tissues for women in order to determine unusual masses and irregular contours which aim to provide the diagnosis of breast cancer as early as possible (16). It has been reported that decreased stage of breast cancer, increased awareness on breast cancer and longer life span may be provided by BSE (18). Up to few years ago, BSE had been considered as an essential practice for early diagnosis. Recently, it has been showed in randomized controlled trials that BSE is not effective in early diagnosis of breast cancer and it has limited effect on decreasing the mortality rates alone, however, it has also been noticed that it is important for increasing the awareness of breast cancer (13,16,32,33). Absence of health reassurance for all individuals, decreased application of mammography regularly due to economical insufficiencies and knowledge deficiencies in developing countries such as Turkey exhibits that BSE, which don't require any cost, is essential in early diagnosis of breast cancer and has to be generalized (16,33).

It is very important to inform the teenager as well as adolescents about the breast self examination especially for the early detection of breast tumors (benign and/or malignant) and increasing the awareness of breast cancer (27). The cure rates with early diagnosis reaches approximately 90% (8,28). BSE should be begun to be performed after the age of 20. However, it is thought that it will be very effective to have information about breast cancer and early diagnostic methods before the age of 20 in performing BSE as a habit. An educational programme about regular performing BSE should be given in school years (34,35).

Nurses, who have important role in health team, should carry out the BSE programmes towards adolescents in schools (school nurses), primary health care units, and health institutes. It is very important in generalizing the BSE. American Can-

cer Society states that nurses are responsible for the education of women about BSE (13,15,29).

In our country the breast cancer screening programme is carried out by “Breast Self Examination” educations which increase the awareness together with “Cancer Early Diagnosis and Screening Centres (KETEM)” which is present at 49 province and “National Standards for Breast Cancer Screening for Women” published by the Ministry of Health Cancer Control Department at 20th July 2004 (28). For this reason, this study may be thought to be integrated in school health services in order to increase the awareness of adolescents on breast cancer.

This study is a descriptive study that was done due to determine the knowledge and attitudes of adolescents between 12 and 19 ages about breast self examination.

Methods

Scope of the study

The universe of the study was composed of 841 students that attending to total of 7 schools containing first school, mid school and undergraduate education in the centre of Sinop which are the practice zones of Public Health Nursing of College of Health of Sinop University. It was aimed to reach all of the students between the ages 12 and 19, and the method of sample selection was not used. The necessary permissions were taken from related foundations and participants, and the aim of the study was explained.

Ethical Dimension of The Study

The purpose of the study was explained required permissions from departments of Sinop University, Office of Administrative Province National Education Director, office directors of schools and the. The importance of study and how it would be carried out was explained to both the students attending to primary and secondary schools and their parents; the students attending to university and the researchers got permission them too.

Questionnaire

Data were obtained by an information form that is composed of 12 questions. There are 4 independent variables such as age, school, educational state of mother, educational state of father; and

7 dependent variables such as state of previously being heard about BSE, source of information of BSE, presence of breast cancer in family, increase in the possibility of cancer in the presence of breast cancer in mother or sisters, state of knowledge of performing BSE, state of belief on benefits of BSE in the early diagnosis of cancer, age of beginning to BSE, in the question form.

Analysis of Data

The data were evaluated in SPSS 14.0 for Windows by using chi-square and percentage tests. Sociodemographic characteristics, being heard explanation of BSE, information sources of BSE, knowing how to perform BSE and other variables were analyzed by using descriptive statistical methods. In addition, the relationship between age groups with being heard explanation of BSE, knowing how to perform BSE and state of knowing that breast cancer has a genetic inheritance; mother-father's education situation with being heard explanation of BSE, believing BSE is useful and other comparisons were made using chi-square test.

Results

The data of the study were arranged in the tables that contains the personal informations, and knowledge and attitudes about BSE of the participants.

Overall, 17.4 % of them were in 18-19 age group, whereas 61% of them were in 15-17 age group and 76.1% of the participant were mid school graduated. (Table 1).

Table 1. Individual Features of Participants

Individual Features	N	%
Age		
12-14	182	21.6
15-17	513	61
18-19	146	17.4
Educational state		
First School Graduated	174	20.7
Middle School Graduated	640	76.1
High School Graduated	27	3.2

N:841

However, 37.1 % of the participants stated that they had never heard the term of BSE, whereas 11.9 % of them stated that they had taken informa-

tion from doctor, 14.6 % of them from nurse, 18.1 % of them from their mothers, 30.7 % of them from internet, 36.9 % of them from television, 11.9 % of them from their friends, 6.8% of them from their neighbours (Table 2).

Table 2. The state of being heard about bse of participants and source of information

TERM of BSE	N	%
Heard About The Term "BSE"	529	62.9
Not Heard About Term "BSE"	312	37.1
Source of information	N	%
TV/ radio	310	36.9
Internet/ newspaper	258	30.7
Mother/Elder sister	152	18.1
Nurse	123	14.6
Doctor	100	11.9
Friend	93	11.9
Teacher	60	7.1
Neighbour/ relative	57	6.8

*: Breast Self Examination

Only, 7 % of the participants noticed positive family history of breast cancer. 75.7 % of them believe that they would have increase risk of breast cancer in the presence of breast cancer in their mothers or sisters.

Table 3 presents conditions related with BSE, 30.1 % of the participants know how to perform BSE and 86.6 % of participants believe the benefit of BSE on early diagnosis of breast cancer (Table 3).

*Table 3. Conditions Related with BSE**

	N	%
Individuals with positive family history of Breast cancer	59	7
Individuals know that cancer has genetic inheritance	637	75.7
Individuals know how to perform BSE	253	30.1
Individuals believe the benefit of BSE in early diagnosis	728	86.6

*: Breast Self Examination

When the beginning age for BSE was asked, 60.2% of the participants stated that BSE have to begin by the age 13-14, 2.3% of them by marriage, 1.9 % of them by birth, 0.2% of them by the age 18, and 1% of them by puberty.

Only 26.2 % of the participants stated that BSE have to be performed by the age 20, where as 8.2 % of them do not know the beginning age of BSE (Table 4).

Table 4. Beginning age for breast self examination

	N	%
At the Ages of 13-14	506	60.2
By the Age of 20	220	26.2
By Marriage	19	2.3
By Giving Birth	16	1.9
By the age of 18	2	0.2
By Puberty	9	1
I don't know	69	8.2

N:841

Table 5. The comparison of participant's age and variables about breast cancer, BSE

Features	Groups of age				Total	
	12-15		16-19			
	n	%	n	%	n	%
Knowing That Cancer Has A Genetic Inheritance						
Yes	116	18.2	521	81.8	637	100.0
No	65	31.9	139	68.1	204	100.0
Total	181	21.5	660	78.5	841	100.0
		X2=17,051	P=,000			
Knowing How to Perform BSE						
Yes	22	8.7	231	91.3	253	100.0
No	160	27.1	428	72.9	587	100.0
Total	181	21.5	660	78.5	841	100.0
		X2=35,680	P=,000			
Believing The Benefit Of BSE						
Yes	128	17,6	600	82.4	728	100.0
No	53	46.9	60	53.1	113	100.0
Total	181	21.5	660	78.5	841	100.0
		X2=49,787	P=,000			

Table 6. The Comparison of Knowing Genetic Inheritance and Family History of Breast Cancer

	Family History Of Breast Cancer					
Knowing That Cancer Has A Genetic Inheritance	Yes		No		Total	
	n	%	n	%	n	%
Yes	47	7.4	590	92.6	637	100.0
No	12	5.9	192	94.1	204	100.0
Total	59	7.0	782	93.0	841	100.0
	X2=,530		P=,467			

Table 7. The comparison of knowing how to perform breast self examination and believing the benefit of BSE in the early diagnosis of cancer

	Knowing How To Perform BSE					
Believing The Benefit Of Bse In The Early Diagnosis Of Cancer	Yes		No		Total	
	n	%	n	%	n	%
Yes	245	33.7	483	66.3	728	100.0
No	9	8.0	104	92.0	113	100.0
Total	254	30.2	587	69.8	841	100.0
	X2=30.622		P= .000			

A statistically significant relationship between age groups and state of being heard about BSE, state of knowing how to perform BSE, state of knowing that cancer has a genetic inheritance, state of believing the benefit of BSE, state of knowing that BSE should begin by the age 20. A significant relationship between the state of being heard about BSE and state of how to perform BSE. ($p < 0.05$) (Table 5).

No statistically significant difference between presence of positive family history of breast cancer and state of knowing that cancer has genetic inheritance, state of knowing how to perform BSE, state of believing the benefit of BSE ($p > 0.05$) (Table 6).

There is a statistically significant relationship between the state of knowing how to perform breast self examination and state of believing the benefit of BSE in the early diagnosis of cancer ($p < 0.05$) (Table 7).

Discussion

It is very attention getting that 37.1 % of the participants have never heard about self breast examination. The ratio of state of being heard about BSE showed an increase by age ($p < 0.05$). In the study of Çevik et al., it was determined that 35.5% of women had never heard about BSE (36).

However, Milaat have found that 39.6% of 6380 girl students; whose average age was 18.1, were informed about BSE; this ratio was 37.9% in the study of Karayurt et al. (2008) (34,37). These results show parallellism with the findings of this study. Seçginli and Nahcivan (2006) determined in their study that people who are aware of breast cancer perform BSE 2 times more frequent, whereas people who are aware of BSE perform BSE 15 times more frequent (32).

One point eighth percent (1.8%) of the mothers and 0.8 % of the fathers of the participants were non literate; therefore, only 6.8 of the mothers and 13.6 % of the fathers were university graduated, and this result shows the perpetuation of problem of education and difference between sexes. According to data of TUIK in 2000, the ratio of the non-literate individuals in Turkey was 23%, and 6% of them were male and the rest of them were female (38). The literateness of families of participants were higher than the general community. Especially higher educational status of mothers has positive effect on knowledge and attitudes of their children about breast self examination. According to the results of the study, the ratio of being heard about BSE was 26.7% and 70.2% in the children of non-literate mothers and in the children of the mothers who were university graduated; respectively.

The most common source of information about BSE was television/radio, and the others were internet/newspaper, mother/elder sister, nurse; respectively. However, because the applicers of the questionnaire were nurses, it is supposed that the number of the participants that marks the "nurse" choice is high due to this reason. This is thought to be the limitation of this study. Therefore, there is a significant relationship between increase in age and showing the nurses as the source of information about BSE ($p < 0.05$). In the study of Karayurt et al., 44.4 % of the participants pointed that the source of information about BSE was health professionals. In the same study, media was determined as the main source of information about breast cancer and BSE by participants (37). In the study of Gerçek et al. (2008), media and books (%57), health professionals (%43) were pointed out as the source of information; however in another study (Kiliç et al. 2009) written and verbal media (%43.3), and health professionals (% 26.9) (18,19). By these datas supported by the results of the study, it was shown that media and health professionals have an important role in health protection and promotion.

There were positive family history of breast cancer in 7% of the participants. In the study of Karayurt et al., the same ratio was also found (7%) (37). 75.7 % of the participants stated that presence of family history of breast cancer affects the occurrence of breast cancer. Although it is known that there is a genetic inheritance, it is thought that the number of the people that believe opposite of this is not low. According to literature, it is certain that family history for breast cancer influences health beliefs and increases sensitiveness about breast cancer. Although no significant relationship was determined between the presence of positive family history and state of believing the benefit of BSE in this study, the χ^2 values were too close. Another notable finding of this study, 60.2 % of the participants stated that the beginning age to BSE was 13-14, whereas, only 26.2 % of participants said correctly that the beginning age of BSE was 20.

However, 69.8 % of the participants did not know how to perform BSE, whereas, 13.4 % of them did not believe the benefit of BSE on early diagnosis of cancer. These findings of this study was supported by the study of Karayurt et al. in which the 65.4 % of female students stated that

they did not know how to perform BSE. In the study which is performed on university students revealed that 66.5% of the students do not know how to perform BSE and this condition was the most important reason for not performing BSE (37). In another study performed on midwifery students revealed that 18.3 % of students do not know how to perform BSE. This condition suggests the coequal education that can be carried out by an appropriate programme. As the study of Aydin A. et al.(2008), there is a significant relationship between the participants know how to perform BSE and individuals believe the benefit of BSE in early diagnosis ($p < 0.05$) (2). This result shows that increase in information about BSE may affect improving the attitudes and changing behaviours.

Gök et al. pointed out the necessity of generalization of BSE which carries high importance for women health (33). When the data of the study are considered, it is clearly seen that teenagers have insufficient information about breast self examination and breast cancer. Not only the adults but also the teenagers should be educated about breast cancer and breast self examination. When it is considered that Turkish population is open to information sharing, the peer-education would be provided for breast self-education programmes. Appropriate early diagnosis and screening programs should be hold down periodically in order to control breast cancer and decrease the mortality rates. (14). In order to give effective education on clinical breast examination, mammography screening. Therefore, nurses have to carry out several programmes in order to provide effective education about BSE (33). For example, the health professionals who are working in the constitution of Health Directorate of Bursa carried out a consciousness raising programme about breast cancer and BSE for both womens and teenagers (39). This education programmes may be increased by integration among foundations (especially by KETEM). The targets of the education programmes have to be determined cognitively, affectively and behaviourly, and practices have to be performed by participants during education. Examples from the real life about examination may ease the practice period. The participants should learn how to do examination appropriately and in exact time. Some options have to be presented to participants in order to realize the behavioural changes.

Conclusion

According to results of the study, the ratios of state of being heard about BSE, knowing how to do it, and believing the importance of BSE in early diagnosis of the participants were low. Only 26.2 % of the participants stated that BSE would be performed by the age 20. The knowledge of participants about BSE and breast cancer is inadequate.

This study is recommended to plan as a prospective study. The individuals educated about BSE and breast cancer should be evaluated periodically about performing BSE and attitudes due to protecting against breast cancer.

References

- Altunkan H, Akin B, Emel E, 20-60 Yaş Arası Kadınların Kendi Kendine Meme Muayenesi (KKMM) Uygulama Davranışları ve Farkındalık Düzeyleri, *Meme Sağlığı Dergisi*, 2008, 4;2, 84-91
- Aydin AI, Altay B, Kocatiürk B, Ebe Öğrencilerin Kendi Kendine Meme Muayenesine Yönelik Sağlık İnançları, *Meme Sağlığı Dergisi*, 2008, 4;1, 25-28
- Eroğlu C, Eryılmaz MA, Cıvık S, Gürbüz Z, Meme Kanseri Risk Değerlendirmesi: 5000 Olgu, *Uluslararası hematoloji Onkoloji Dergisi*, 2010, 1;20, 27-33
- Özmen V, *Breast Cancer In the World and Turkey*, *The Journal of Breast Health*, 2008, 4;2, 7-11
- <http://www.turkkanser.org.tr> Türkiye'de Kanser İstatistikleri ET. 27.01.2011
- <http://globocan.iarc.fr/factsheets/populations/factsheet.asp?uno=900> ET. 12.08.2011
- <http://www.metam.org> ET. 23.06.2009
- <http://www.kanser.org> ET. 20.07.2009
- Haydaroglu A, Bölükbaşı Y, Özşaran Z, Ege Üniversitesinde Kanser Kayıt Analizleri: (34134 Olgunun Değerlendirilmesi), *Türk Onkoloji Dergisi* 2007, 22;1, 022-028
- <http://seer.cancer.gov/>, Surveillance Epidemiology and End Results, providing information on cancer statistics to help reduce the burden of this disease on the USA, 2008 ET. 14.07.2009
- <http://progressreport.cancer.gov/>, Cancer Trends Progress Report in 2004, based on methods described in Medical Care 2002 Aug, 40 Accessed July 12, 2009
- <http://annualreport.cancer.gov/> Annual Report to the Nation Finds Declines in Cancer Incidence and Death Rates on 1975-2005, 2007 Accessed July 12, 2009
- Smith RA, Cokkinides V, Brooks D, Saslow D, Shah M, Brawley OW, *Cancer Screening in the United States, 2011: A Review of Current American Cancer Society Guidelines and Issues in Cancer Screening*, *CA Cancer Journal of Clinicians*, 2011; 61; 8-30
- Özmen V, Fidaner C, Aksaz E, Bayol Ü, Dede İ, Göker E, Güllüoğlu BM, Işıkdoğan A, Topal U, Uhri M, Utkan Z, Zengin N, Tuncer M, *Türkiye'de Meme Kanseri Erken Tani ve Tarama Programlarının Hazırlanması*, *Meme Sağlığı Dergisi*, 2009, 5;3, 125-134
- <http://www.cancer.org> ET. 02.07.2009
- Akyolcu N ve Uğraş Altun G, Kendi Kendine Meme Muayenesi: Erken Tanıda Ne Kadar Önemli?, *Meme Sağlığı Dergisi*, 2011, 7;1, 10-14
- Eryılmaz MA, Karahan Ö, Sevinç B, Ay S, Cıvık S, *Meme Kanseri Taramalarının Etkinliği*, *Meme Sağlığı Dergisi*, 2010; 6; 4, 145-149
- Gerçek S, Duran Ö, Yildirim G, Karayel H, Demirliçakmak H, Kredi Yurtlar Kurumunda Kalan Kız Öğrencilerin Meme Kanseri Ve Kendi Kendine Meme Muayenesi Sağlık İnançları ve Bunu Etkileyen Faktörlerin Belirlenmesi, 2008; 4; 3, 157-161
- Kiliç D, Sağlam R, Kara Ö, Üniversite Öğrencilerinde Meme Kanseri Farkındalığını Etkileyen Faktörlerin İncelenmesi, 2009; 5; 4, 195-199
- Yılmaz HH, Yazihan N, Tunca D, Sevinç A, Olcayto EÖ, Özgül N, Tuncer M, *Cancer Trends and Incidence and Mortality Patterns in Turkey*, *Japanese Journal of Clinical Oncology*, 2010, 41; 1, 1-7
- "Kanser Yüğü 2006" Raporu, Ankara Ticaret Odası (ATO), Türk Kanser Araştırma ve Savaş Kurumu ve Hacettepe Üniversitesi Onkoloji Enstitüsü www.atonet.org.tr ET. 31.01.2011
- www.saglik.gov.tr ET. 21.08.2010
- Kavlak O, Yılmaz BH, Dülgerler Ş, Emzirme ve Kanser Araştırmalarının İncelenmesi, *Meme Sağlığı Dergisi*, 2010, 6; 4, 141-144
- Ries L, Melbert D, Krapcho M, Stinchcomb DG, Howlander N, Horner MJ, Mariotto A, Miller BA, Feuer EJ, Altekruse SF, Lewis DR, Clegg L, Eisner MP, Reichman M, Edwards BK (eds) *Source for Incidence And Mortality Data: Surveillance Epidemiology and End Results (SEER) Program and the National Center for Health Statistics*, 2008

25. Kinik E, Adölesan, Tunçbilek E (Ed): Çocuk Sağlığı-Propedötik, Öztürk Matbaası, 1990, Ankara, S; 275-289
26. Marshall WA, Taner JM, Variations in Pattern of Pubertal Changes in Girls, Arch Dis Child, 1969, 44: 291-303
27. Aslan A, Karagüzel G, Karagüzel G, Çocuk ve Ergenlerde Meme Hastalıkları, Klinik Çocuk Forumu, Temmuz- Ağustos 2005, İstanbul, S; 31-37
28. Hatipoğlu AA, Kanserde Erken Tani ve Tarama Problemleri, Tuncer M (ed), Ulusal Kanser Danışma Kurulu Türkiye’de Kanser Kontrolü, 33. Bölüm, 2007, Ankara www.ukdk.org ET.28.01.2011
29. Harper S, Lynch J. Methods for Measuring Cancer Disparities: Using Data Relevant to Healthy People 2010 Cancer-Related Objectives. NCI Cancer Surveillance Monograph Series, Number 6. Bethesda, MD: National Cancer Institute, 2005. NIH Publication No. 05-5777.
30. Ulusal Kanser Danışma Kurulu, Tuncer M (ed), Ulusal Kanser Programı (2009-2015), 2009, Ankara www.ukdk.org ET. 28.01.2011
31. Uluşu S, Özgül N, Yılmaz İ, Şalk İ, Kelkit Ş, Gültekin M, Demirkol MR, Çınar Z, Türkiye’de Toplum Tabanlı Meme Kanseri Taraması Programı: İlk Değerlendirme Raporu, Türk Jinekolojik Onkoloji Dergisi, Aralık 2007, 10;4, 85-90
32. Seçginli S ve Nahcivan ON, Factors Associated with Breast Cancer Screening Behaviours in a Sample of Turkish Women: A Questionnaire Survey, International Journal of Nursing Studies 43 (2006),161–171
33. Gök Özer F, Yavuz Karamanoğlu A, Meme Kanseriinde Erken Tani; Hemşirelik Forumu Dergisi; Mayıs- Haziran 2009; S: 55-59
34. Milaat WA. Knowledge of secondary-school female students on breast cancer and breast- self examination in Jeddah, Saudi Arabia, East Mediterr Health J 2000; 6; 338-344. [PubMed]
35. Güner Coşkun İ, Tetik A, Gönener HD, Kadınların Kendi Kendine Meme Muayenesi (KKMM) ile İlgili Bilgi, Tutum ve Davranışlarının Belirlenmesi, Gazi- antep Tıp Dergisi,2007, Cilt 13, Sayı 2, S: 55-60
36. Çevik C, Akbulut G, Erkal S; Kadınların Kendi Kendine Meme Muayenesi Hakkındaki Bilgi Düzeylerinin Kitlenin Fark Edilmesine Etkisi; Hemşirelik Forumu Dergisi 2005; Mart- Nisan; S: 44-49
37. Karayurt Ö, Özmen D, Çakmakçı ÇA, Awareness of breast cancer risk factors and practice of breast self examination among high school students in Turkey, BMC Public Health, 2008; 8: 359
38. <http://www.tuik.gov.tr> Türkiye İstatistik Kurumu, DİE, 2000, Ankara ET. 12.07.2009
39. Çelik İ, Pişkin E, Bursa Valiliği, İl sağlık Müdürlüğü, Meme Kanseri Bilinçlendirme Ayı etkinlik Raporu, Aralık 2007, Bursa

Corresponding Author
Huriye Demet Cabar,
Sinop University,
School of Nursing,
Ordu Koyu Mevkii,
Sinop,
Turkey,
E-mail: gonener@hotmail.com

Analysis of implementation of the strategic management concept in the healthcare system of Serbia

Marko M. Mihic, Vladimir Lj. Obradovic, Marija Lj. Todorovic, Dejan C. Petrovic

University of Belgrade, Faculty of Organizational Sciences, Department for Management and Specialized Management Disciplines, Serbia

Abstract

Background/Aim: Healthcare institutions in Serbia are facing both considerable external pressures, such as political, economic, demographic and epidemiologic volatility on the one hand, and the need to maximize the utilization of their capacities and enhance the functioning of the facilities in an effective and efficient manner. The purpose of this paper is to assess the current state of strategic management in healthcare organizations in Serbia and suggest an appropriate model to facilitate and improve this process.

Methods: The research conducted entailed collection of information by means of a survey. The survey consisted of 20 questions selected after conducting interviews with the focus groups and performing an analysis of the current trends in implementation of strategic management in the healthcare institutions across the world. A total of 43 institutions were surveyed.

Results: Statistical processing of the data confirmed the general hypothesis that healthcare organizations in Serbia do in fact use strategic analysis methods and use them to set objectives and identify initiatives, however, the monitoring and control of strategy implementation are not undertaken in a way that is founded in theory and empirically confirmed. This general hypothesis was confirmed by individual hypotheses which indicate the existence of a direct link between the strategic initiatives that are successfully implemented and the following: strategic alignment of the initiatives, systematic approach to priority setting; clear definition of plans for implementation of initiatives; systems of monitoring, control, and evaluation of strategies.

Conclusion. The results of research undertaken across healthcare organizations in Serbia, togeth-

er with the analysis of systems in other countries indicate that strategic management constitutes a critical factor of success of these institutions. The strategic management model presented herein encompasses methods and techniques used in healthcare organizations to a greater or smaller extent which, in a slightly modified form, has been confirmed in practice in Serbia in many ways. Thus, the model constitutes one of the ways forward towards a more efficient and effective provision of healthcare services to Serbian citizens.

Key words: Strategic management, healthcare institutions in Serbia, strategic management model.

Introduction

Healthcare institutions in Europe and elsewhere in the world are exposed to substantial external pressures. Countries in transition are inundated with changes of political systems and reform agendas, changes in ownership structure and macro level societal changes such as political, economic, demographic and epidemiological ones, as well as changes in expectations of citizens and patients. These pressures give rise to a number of measures (reforms, policies, etc.) relating to procurement, reporting, payment and other systems that hospitals need to implement in order to ensure the quality of healthcare services. [1] The focus of a number of researches in the field of healthcare policy is, in fact, the adoption of different policies and reforms by healthcare institutions within the national healthcare system [2-6].

The way an organization is set up (in terms of management, administration, organizational design, physical characteristics, organizational culture and management of information) is highly

relevant in the sense that it determines the way the organization embraces and implements different initiatives. [3] Beside those organizational factors management of the organization is also emphasized, to the extent that many experts attribute the success or failure of an organization to the difference in their management styles, managers' skills and knowledge. [7] Research results in [8] indicate that required skills of the managers in transition countries such as Serbia are similar to the required skills of managers in developed countries. This points to the fact that - prior to setting the long-term goals and identifying appropriate strategy for their achievement, it is critical to analyse the capabilities and capacities of an organization.

In recent years, improving the quality of healthcare services has become the focus of many scientific research papers. [9-12] The problems that healthcare organisations most frequently encounter in improving the quality of provision of healthcare are: identification of priorities, development of sustainable processes and identification of an appropriate framework for implementation of initiatives undertaken. [3]

Managers of healthcare institutions are responsible for making best possible decisions while faced with numerous constraints (mainly budgetary) and various external influences. Accordingly, they must be able to justify each proposed increase in costs, suggesting the best solution. Economic evaluation in health is comparative analysis of different (alternative) aims of actions regarding their expenses and consequences. [13] From the point of view of a manager, efficiency is often viewed through investments in particular services. On the other hand, effectiveness is reflected through quality and timelines of delivery of services to the end beneficiary (e.g. no long queues), but this is more a concern of external stakeholders, such as various donors, than the service beneficiaries. [14]

Effectiveness of healthcare organizations in the healthcare systems of the more developed countries such as United Kingdom, Canada, Australia and USA is demonstrated in the existence of effective links in organizational performances in delivery of services in terms of the following: delivery of evidence based desired results, availability of services, meeting the needs of beneficiaries, timeliness and high quality of services. In USA this

also entails avoiding the use of services below or above the optimum level. [11]

The main focus of strategic management in corporate environment is to ensure the organizations conduct their business in line with the principle of going concern. The core principles of strategic management have been derived from the need for the organization to constantly follow the trends in both its external and internal environment so as to ensure it develops and grows in an efficient and effective manner. [15] With regard to the growing trend of global competitions, hospitals have also approached business process reengineering for success and increase of their efficiency and effectiveness. [16]

Embracing of this approach to implementation of strategic management may help healthcare institutions in Serbia to become efficient and to institute appropriate mechanisms for reacting to external changes.

Implementation of Strategic Management in Healthcare Institutions

The development of strategic management in healthcare institutions in USA started in the late twentieth century by adjusting the model of strategic management to hospital operational strategies. [17]. The discipline of strategic management comprises a series of methods and techniques the implementation of which had yielded positive, quantitatively and qualitatively measurable results in many countries. Griffith et al. discuss the effects of the use of management models, including the strategic planning techniques, market analysis, stakeholder analysis and performance measurement. [18] (as presented in Table 1). Furthermore, Bart and Tabone suggest the existence of correlation between the organization's mission and results achieved. They have conducted a research of 103 healthcare organizations in Canada, which set out to prove that the achievement of the results largely depends on how the mission is defined, the elements it encompasses and the clarity and precision of its articulation. [19] Janssen emphasises the significance of use of SWOT analysis (as one of the most frequently used techniques in analysis of the environment) as a tool used for analysis of the entire healthcare system of Denmark, one of

Table 1. Implementation and impacts of use of strategic management methods and techniques

Country	Methods and Techniques	Impacts	References
USA	- Strategic planning - Market analysis - Stakeholder analysis - Focus on employees - Process management - Performance measurement - Balanced Scorecard	- Substantial reduction in length of stay, and 34 % decrease in cost of inpatient care - Heart-risk screenings are more than doubled in three years - Cardiology and orthopaedic market shares are Increased by one-third - Referrals from primary care physicians are Improved by one-third - Admitting-physician satisfaction is Improved by one-quarter - Mammogram turnaround - Four days to one day - Lab tests/adjusted discharge is “among the lowest in the nation” - Operating expense per adjusted patient day are declined - Special-effort recognition is increased by one-third	Analysis of five healthcare institutions recipients of national award for quality of delivery of healthcare services. [18]
Afghanistan	Balanced Scorecard	- Enables identification of problems and focusing on critical areas - Higher access to healthcare services in rural areas and increased number of healthcare service beneficiaries in rural areas - Setting the foundations for well-balanced healthcare sector from the point of view of the patients, employees, service delivery capacities, quality and financial indicators.	National healthcare system. [25]
Sweden	Balanced Scorecard	- Improved managerial work - Enhanced understanding among employees - Improved inter departmental coordination - Broader perspective of the significance of organizational leadership - Personal development - Increased interest for staff engagement - Increased participation of staff in developmental activities	Case studies in three healthcare institutions. [23]
Canada	Organization's mission statement	Establishing significant correlation between the performances of an institution with elements of a mission	Research conducted in 103 healthcare institutions. [19]
Denmark	SWOT analysis	- Analysing strengths, weaknesses, opportunities and threats in the healthcare system and identification of areas for potential improvement: - Improving co-operability between the subsystems - Investing in education programs	National Healthcare System. [20]
Germany	- Strategic maps, - Balanced Scorecard	- Easier implementation of acute care strategy - Breaking down of objectives into measurable elements	German-holding Immanuel Diakonie Group. [22]

the highest ranking countries in terms of international performances in delivery of healthcare services. [20] Vukašinović at al. evidences the need for implementation of strategic planning methods in alleviating the crisis, identifying the problems in management of healthcare organizations and suggesting appropriate recovery strategies in healthcare institutions in Serbia. [21]

Monitoring and control of results achieved plays a critical role in implementation of strategic management. The information about patients, staff, and internal core processes and potential innovations are of great significance for medium-term and long-term planning of operations of healthcare institutions. Balanced Scorecard Method (BSC) views the performances of an organization from the perspective of four critical success factors (business processes, finances, customers and learning and growth). Groene et. al., have dealt with development and implementation of this method in healthcare institutions in Germany, arriving at the conclusion that, with certain adjustments of the method to tailor it to the requirements of the health system, the BSC constitutes a very useful tool in development and implementation of strategy in health institutions. Using an example of a holding of 50 healthcare institutions, the authors have demonstrated the development and implementation of a strategy through the following phases: establishing the foundation for strategy development, development of a strategy map, preparation of a BSC and breaking down of the objectives into action plans. [22] Kollberg and Elg had been examining the use of the BSC method in public health organizations in Sweden, focusing on the manner of management, organizational roles and balancing of the four critical success factors of the method. [23] Grigoroudis et al. take this even further in their paper by elaborating in great detail the method for development of strategic performance measurement in healthcare institutions based on BSC method. [24] Afghanistan is one of the developing countries that had embraced the BSC method as a part of its national healthcare system and has thus improved the overall functioning of the system. [25] The table below provides a brief overview of the implementation and impacts of use of the aforementioned strategic management techniques.

Several studies on improvement of healthcare protection in developing countries address the topic of improvement of healthcare protection by implementation of adequate management systems. [10, 26-29]

The previous analysis leads to the conclusion that the use of methods and techniques of strategic management gives rise to considerable improvements of efficiency and effectiveness indicators in the organisations under review. In order to empirically verify the assumptions that strategic management concepts can in fact be successfully implemented in the healthcare institutions in Serbia, a research was conducted pertaining to present the current state of affairs in the healthcare system of Serbia. The research was conducted between June and September 2011 on a sample of 34 institutions.

On the basis of theoretical research the following hypotheses have been derived:

General hypothesis:

Strategic analysis methods are used in healthcare organisations in Serbia as a basis for formulation of goals and initiatives, whereas monitoring and control of strategy implementation is not carried out in a theoretically founded and empirically verified manner.

Special hypotheses:

- There are direct links between successfully implemented initiatives and their strategic alignment.
- There is a direct link between the success of implementation of strategic initiatives and a systemic approach towards identification of priorities and selection of initiatives.
- There is a direct links between the success of implementation of strategic initiatives and clarity of their goals and implementation plans.
- There is a direct link between the success of implementation of strategic initiatives and implementation of strategy monitoring, control and evaluation systems.

Research on Implementation of Strategic Management in the Healthcare Institutions in Serbia

Sample description

There are around 218 primary, secondary and tertiary healthcare institutions in Serbia. The research focused on healthcare institutions in urban areas, assuming that they are more likely to implement strategic management concept. Out of the 150 organizations, 37 or 24.66% have responded to the survey, 3 questionnaires have been rendered invalid on the grounds of being incomplete, thus only 34 or 22.66% survey questionnaires have been taken into consideration.

Research Method

This research employed survey questionnaires as a primary source for collection of information. The objective of the survey questionnaire was to collect answers to the hypotheses defined and was distributed in June 2011 to the intended respondents. The survey consisted of 20 questions selected after conducting interviews with focus groups and performing an analysis of implementation of strategic management in healthcare institutions worldwide. The survey questions sought answers about the healthcare facility, strategic goals and priorities, strategic management methods and techniques used, and strategy implementation and

control modalities. The questions were close ended, multiple choice ones, with a choice of answers limited to one, and offering an option of scaling responses by means of Likert scale. All of the data obtained through the survey have been processed using the SPSS v.18 software package, and their description is presented in the text below.

Research Results

According to the analysis of implementation of particular strategic planning techniques (for analysis of both internal and external environment), the frequency of use of strategic planning techniques by type is as follows: SWOT analysis is used at the rate of 50%; PEST analysis at 23,5%; objectives tree at 14,7%, gap analysis at 17,6%; stakeholder analysis at 20,6%. The most frequently used forecasting methods are the scenario method (23.5%) and the simulation method (23.5%).

With respect to the strategic goals, the results of the research show that organizations under review do have formulated strategic goals, however the same does not apply to the priority setting methods. 23.5% organizations identify their priorities and select strategic initiatives in a systematically organized manner; 58.8% exhibit some parts of the system, whereas 17.6% do not take a systematic approach to identification of priorities and selection of strategic initiatives. When asked about how the most suitable strategic initiatives

Table 2. Crosstabs' statistics and measures of relation between successful initiatives and existence of prioritization and selection process

		Does the institution have a process of settings of priorities and selection of initiatives			
		No	Partly	Yes	Total
Initiatives were implemented successfully	Always	1 2.9%	0 .0%	4 11.8%	5 14.7%
	Never	1 2.9%	3 8.8%	0 .0%	4 11.8%
	Often	0 .0%	2 5.9%	3 8.8%	5 14.7%
	Rarely	3 8.8%	5 14.7%	1 2.9%	9 26.5%
	Sometimes	1 2.9%	10 29.4%	0 .0%	11 32.4%
	Total	6 17.6%	20 58.8%	8 23.5%	34 100.0%

are selected, as much as 83% respondents replied that this is normally done by senior management.

In response to the question on strategic alignment of the institutions' plans, 11.8% of the respondents maintained that they do give due consideration to the strategic alignment: 38.2% respondents stated that they do so nearly always; whereas 50% responded that it is only occasionally that they pay attention to strategic alignment of the initiatives in the process of their selection. Average score for the success of implementation of strategic initiatives is 3.64 on a scale ranging from 1 to 5.

Following the process of descriptive data processing and calculation of frequencies, a detailed analysis was performed by cross-referencing the data with the objective of confirming the general and specific hypotheses. The tests were performed using the Chi-squared test, thus confirming the hypothesis on the existence of interdependencies between the success of implementation of initiatives and the existence of a systemic approach to identifying priorities and selection of strategic initiatives. (Table 2 and Table 3)

Table 3. Chi-Squire Test of relation between successful initiatives and existence of prioritization and selection process

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	21,816 ^a	8	,005
Likelihood Ratio	25,392	8	,001
N of Valid Cases	34		

It can be concluded that most organizations in which strategic initiatives are successfully implemented have fully (23.5%) or partially (58.8%) taken a systemic approach towards establishing priorities and selection of strategic priorities. Additionally, the hypothesis that there is a correlation between the success of initiatives implemented and ensuring that they are strategically aligned was confirmed (Table 4).

The research shows the frequency with which organizations define their goals: 23.5% of them sometimes, 47.1% of them often and 29.4% always have clearly defined goals. In terms of criteria of specificity, measurability, attainability, re-

ality and timeliness only 11.8% of organizations maintain their goals meet all the criteria. 26.5% believe that the criteria are often met, 41.2% believe they meet them occasionally, whereas 20.6% believe that the specified criteria are never met.

Table 4. Chi-Squire Test of relation between successful initiatives and their strategic alignment

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	35,089 ^a	8	,000
Likelihood Ratio	30,420	8	,000
N of Valid Cases	34		

The analysis of data cross referencing leads to the conclusion that in most organizations in which strategic initiatives are successfully implemented, strategic initiative goals are either always (29.4%), or often (47.1%) clearly defined, thus confirming the hypothesis on existence of correlation between the success of implementation of strategic initiatives and existence of clearly defined goals (Table 5).

Table 5. Chi-Squire Test of relation between successful initiatives and defined goals

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	30,445 ^a	8	,000
Likelihood Ratio	35,665	8	,000
N of Valid Cases	34		

With respect to how strategic initiatives are implemented, the results indicate that 38.2% of respondents always have work implementation structure, 70.6% have a budget, 61.8% have a cash flow, 38.2% have a time schedule, while 35.3% of respondents have a schedule of resources. An interesting piece of information is that there are no organizations which have been able to successfully implement their strategic initiatives, without having a budget, cash flow or implementation schedule in place when planning for implementation.

Evaluation is carried out after each strategic initiative in 20.6% of the cases, a small percentage of which (under 3%) uses the Balanced Scorecard Method. In 64.7% of the cases evaluation is under-

taken partially, whereas 14.7% respondents says that evaluation is not undertaken after each strategic initiative. Research also indicates the existence of a straightforward correlation between the existence of partially or fully established system of reporting on the progress of implementation of all plans and the success of projects undertaken.

Likewise, the analysis of data cross-referencing, indicates that, in assessing the success of implementation of strategic initiatives, only a small percentage of organizations (under 3%) have scored over 4 on average. These organizations have, either fully or partially, implemented systems for monitoring, control and evaluation of strategies. In contrast, a large number of organizations (over 60%) that have scored very low on the success of implementation of strategic initiatives (below 2.5 on average) lack a systemic approach towards monitoring and control of strategy implementation altogether, thus confirming the hypothesis on the existence of correlation between the success of implementation of strategic initiatives and use of systems for strategy monitoring, control and evaluation.

Table 6. Chi-Square Test of relation between successful initiatives and existence of functional strategy monitoring, control and evaluation system

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	28,200 ^a	8	,000
Likelihood Ratio	26,911	8	,001
N of Valid Cases	34		

Based on all the above, it can be concluded that methods and techniques of strategic management help overcome certain problems in functioning an institution, create an environment for improvement of functioning of an institution, as well as an conditions for the institution to better adjust to the external environment and utilize opportunities for its development. The results of research indicate the need for existence of a systematic approach towards strategic management of an organization, which confirms the general hypothesis that the healthcare organizations in Republic of Serbia use methods for strategic analysis as a basis for formulation of goals and initiatives, but that the monitoring and control of strategies are not per-

formed in a theoretically founded and empirically verified manner. One of the ways for overcoming these faults in management, highlighted by the research results, is the use of strategic management models. The text below shows a modified model that has already been implemented in strategic management of integrated social welfare in local communities in Republic of Serbia. [30]

Strategic Management Model

The strategic management model for healthcare industry was developed after an extensive research and review of available literature and analysis of the practical implementation of a similar model deployed in the welfare sector. This model is a result of efforts to approach the national and local health protection issues in a new and innovative way, taking into consideration numerous empirical results, together with the assessment of the needs of service beneficiaries as key determinants of the goal oriented healthcare management. The model is shown in the Figure below.

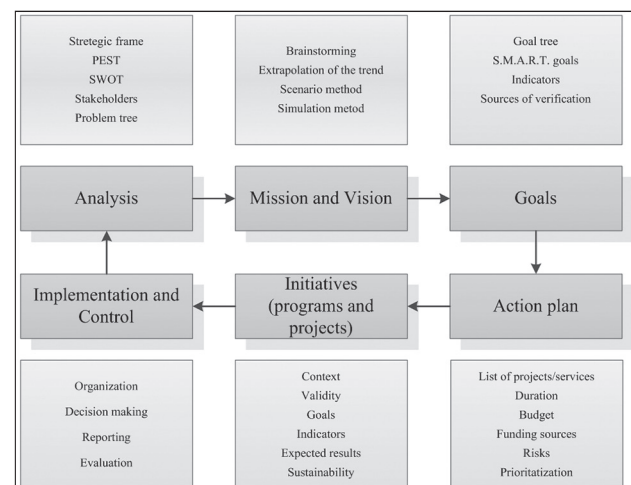


Figure 1. Strategic management model in health protection industry

In the first phase, the implementation of this model facilitates analysis of the strategic framework, mapping of needs and resources, analysis of internal and external environment and stakeholder analysis. The second phase entails defining of the vision and mission concurrent with the particular context in which strategic management is implemented. The third phase consists of defining the goals and identification of performance indi-

cators. The following phase involves the process of formulation of action plan for implementation of strategy, which incorporates determining the workload, schedule, required resources, persons responsible and risks. The fifth phase involves implementation and control of strategies, including the form of work arrangements and organization, decision-making procedures, systems for monitoring and reporting, as well as strategy evaluation.

The implementation of this model poses numerous challenges [31] that can be grouped and systematized along the lines of the defined phases. Similar to the implementation of numerous other models of strategic management, critical success factors in implementation of this model are: the manner in which analyses are performed, defining of goals and implementation of strategies through initiatives and projects, which was confirmed by the results of previous empirical research.

Conclusion

The demand for management disciplines in general, and implicitly for strategic management in particular, is constantly on the rise in organizations in all sectors. Numerous researches, some of which have been also been mentioned in this paper, suggest that strategic management is an inevitable factor of success of the healthcare institutions of modern day. In countries like USA, Canada, Denmark, Sweden healthcare organizations employ appropriate methods and approaches to strategic management in order to secure their beneficiaries with the best possible quality of healthcare in the times of ever shrinking resources. Serbia has also recognized the need for introducing improvements in management if healthcare sector. Numerous researches conducted, reform initiatives, as well as the increasing number of formal and informal forms of education specialized in the area testify to this fact.

The initial intention of this paper was not merely to prove the need for strategic management in healthcare institutions in Serbia, but also to propose a specific model which would facilitate and improve this process. The model shown here, in a format that is slightly modified compared to the original, has proven itself in practice in a number of occasions. 28 local governments in Serbia use

this model for strategic management in social welfare, which is quite similar to healthcare in a numerous aspects. Nevertheless, there are differences between the two systems, therefore the model has been slightly changed and tailored to provide better solutions in healthcare organizations. The model is specific, but also universal and can be applied on all levels of health protection regardless of the implementing organization, its size, number of employees, organizational arrangements and other elements of complexity. It can be applied to a particular organizational unit, organization or healthcare system in general. The model is designed to employ methods and techniques that the healthcare workers are fairly familiar with, thus creating conditions for its quick and efficient implementation. Strategic management is a necessity of the modern day healthcare institutions and the use of the model described in this paper may well be one of the paths towards more efficient and effective provision of healthcare services to the citizens of Serbia.

Acknowledgments

This paper is a result of the Project No. 179081 founded by Ministry of Education and Science of the Republic of Serbia: Researching Contemporary Tendencies of Strategic Management Using Specialized Management Disciplines in Function of Competitiveness of Serbian Economy.

References

1. Jakab M, Preker A, Halding A, *Linking organizational structure to the external environment: experiences from hospital reform in transition economies. A book chapter from Hospitals in a Changing Europe. Oxford: Open University Press; 2002.*
2. Hoeijmakers M, De Leeuw E, Kenis P, De Vries NK, *Local health policy development in the Netherlands: an expanded toolbox for health promotion. Health Promotion International, 2007; 22: 112–121.*
3. Glickman SW, Baggett KA, Krubert CG et al. *Promoting quality: the health-care organization from a management perspective. International Journal for Quality in Healthcare 2007; 19: 341–348.*
4. McKee M, Healy J, *Hospitals in a Changing Europe. Oxford: Open University Press, 2002.*

5. Exworthy M, *Policy to tackle the social determinants of health: using conceptual models to understand the policy process. Health Policy and Planning* 23. Oxford University Press in association with The London School of Hygiene and Tropical Medicine 2008; 318–327.
6. Hartwig K, Pashman J, Cherlin E, Dale M, Callaway M, Czaplinski C, Wood EW Abebe Y, Dentry T, Bradley HE, *Hospital management in the context of health sector reform: a planning model in Ethiopia. International Journal of Health Planning and Management*, 2008; 23: 203–2018.
7. Bahadori M, Nejati M, *Influential Determinants in Human Resources Development: a study of the managers in the health services sector; HealthMed Journal* 2011; Vol. 5, No 5: 1182–1186.
8. Jovanović P, Petrović D, Mihić M, Obradović V, *Necessary Skills of Managers in Transition Countries – The Case of Serbia, TTEM* 2012; 7(3).
9. Côté, MJ., *Patient flow and resource utilization in an outpatient clinic, Socio-economic Planning Sciences* 1999; 33 (3): 231–245.
10. Smits HL, Leatherman S, Berwick DM, *Quality improvement in the developing world. International Journal for Quality in Healthcare* 2002; 14 (6): 439–440.
11. Arah OA, Klazinga NS, Delnoij DMJ, Ten Asbroek AHA and Custers T, *Conceptual frameworks for health systems performance: a quest for effectiveness, quality, and improvement. International Journal for Quality in Health Care*; 2003; 15 (5): 377–398.
12. Rütten A, Röger U, Abu-Omar K, Frahsa A, *Assessment of organizational readiness for health promotion policy implementation: test of a theoretical model. Health Promotion International, Oxford University Press* 2009; 24 (3): 243–251.
13. Kudumovic M, Kudumovic A, *Economic analysis of health, HealthMed Journal*, 2008, 2(2); 100–103.
14. De Angelis V, Felici G, Impelluso P, *Integrating simulation and optimisation in healthcare centre management. European Journal of Operational Research* 2003; 150 (1): 101–114.
15. Swayne LE, Duncan WJ, Ginter PM, editors. *Strategic Management of Healthcare Organizations*. Oxford: Blackwell Publishing 2006; 102–29.
16. Jafari M, Bastani P, Ibrahimipour H, Dehnavieh R, *Attitude of health information system managers and officials of the hospitals regarding the role of information technology in reengineering the business procedures: A qualitative study, HealthMed Journal*, 2012, 6(1); 208–215.
17. Swinehart K, Zimmerer WT, *Adapting a strategic management model to hospital operating strategies: A model development and justification. Journal of Management in Medicine* 1995; 9 (2): 34–47.
18. Griffith RJ, Arbor A, White RK, *The Revolution in Hospital Management. Journal of Healthcare Management* 2005; 50: 3: 170–190.
19. Bart CK, Tabone JC, *Mission statement content and hospital performance in the Canadian not-for-profit healthcare sector. Healthcare Manage Review* 1999; 24: 18–29.
20. Janssen R, *Evaluation of the organization and financing of the Danish healthcare system. Health Policy* 2002; 59 (2): 145–159.
21. Vukašinović Z, Bjegović-Mikanović V, Jančić R, Spasovski D, Živković Z, Cerović S, Terzić Z, *Strategic Planning in a Highly Specialized Orthopaedic Institution. Srp Arh Celok Lek.* 2009; 137(1-2): 63–72.
22. Groene O, Brandt E, Schmidt W, Moeller J, *The Balanced Scorecard of acute settings: development process, definition of 20 strategic objectives and implementation. International Journal for Quality in Health Care*, 2009; 21 (4): 259–271.
23. Kollberg B, Elg M, *The practice of the Balanced Scorecard in healthcare services. International Journal of Productivity and Performance Management*, 2011; 60 (5): 427–445.
24. Grigoroudis E, Orfanoudaki E, Zopounidis C, *Strategic performance measurement in a healthcare organisation: A multiple criteria approach based on balanced scorecard. Omega* 2012; (40): 104–119.
25. Peters HD, Noor AA., Singh PL, Kakar KF, Hansen MP, Burnham G, *A balanced scorecard for health services in Afghanistan. Bulletin of the World Health Organization*, 2007; 85: 146–151.
26. Mills A, Hongoro C, Broomberg J, *Improving the efficiency of district hospitals: is contracting an option? Tropical Medicine and International Health*, 1997; 2(2): 116–126.
27. Berwick MD, *Lessons from developing nations on improving health care. BMJ*, 2004; 328: 1124–1129.
28. Garcia-Prado A, Chawla M, *The impact of hospital management reforms on absenteeism in Costa Rica. Health Policy and Planning* 2006; 21(2); 91–100.

29. Jafari M, Rashidian A, Abolhasani F, Mohammad K, Yazdani S, Parkerton P, Yunesian M, Akbari F, Arab M, Space or no space for managing public hospitals; a qualitative study of hospital autonomy in Iran. *International journal of health planning and management* 2011; 26: 121–137.
30. Medić S, Brkić M, Vlaović Vasiljević D, Vulević D, Mihić V, Obradović V, *Strateško upravljanje integralnom socijalnom zaštitom u lokalnoj zajednici*, SKGO, Beograd, 2010; p.131
31. White D, Patton J, *Closing Strategic Vision Implementation Gap*. PMI Annual seminars and Symposium, San Antonio, 2002.
32. Desmidt S, Heene A, *Mission statement perception: are we all on the same wavelength? A case study in a Flemish hospital*. *Healthcare Manage Review* 2007; 32: 77–87.

Corresponding author

Marko Mihic,

University of Belgrade,

Faculty of Organizational Sciences,

Department for Management and Specialized

Management Disciplines,

Serbia,

E-mail: mihicm@fon.bg.ac.rs

Effect of cigarette smoking on nasal mucociliary transport rate: Rhinoscintigraphic evaluation with using ^{99m}Tc -macroaggregated albumin

Zeki Dostbil¹, Yusuf Dag², Abdurrahman Abakay³, Salih Bakir⁴, Cengizhan Sezgi³, Ozlem Abakay³, Hadice Sen³

¹ Department of Nuclear Medicine, Dicle University Faculty of Medicine, Diyarbakir, Turkey,

² Department of Nuclear Medicine, Harran University Faculty of Medicine, Sanliurfa, Turkey,

³ Department of Chest Diseases, Dicle University Faculty of Medicine, Diyarbakir, Turkey,

⁴ Department of Ear Nose & Throat, Dicle University Faculty of Medicine, Diyarbakir, Turkey.

Abstract

Objectives: Cigarette smoking has harmful effects on mucociliary transport (MCT) in respiratory system. We aimed to investigate the association between nasal mucociliary transport rate (NMTR) and duration and amount of smoking in chronic cigarette smokers.

Materials and Methods: Fifty four current cigarette smokers and 40 healthy non-smokers were included in this study. In all cases, we measured the NMTR using ^{99m}Tc -macroaggregated albumin (^{99m}Tc -MAA) rhinoscintigraphy.

Results: The mean NMTR of the smokers was lower than that of the healthy non-smoker controls (5.63 ± 2.78 ; 9.44 ± 2.09 , respectively) ($p < 0.0001$). There were not statistically significant correlation between NMTRs and year of smoking, and smoking pack-year in smokers ($p > 0.05$; $r = 0.003$, $r = 0.2$, respectively) whereas there was a statistically significant correlation between NMTRs and cigarettes per day in smokers ($p = 0.024$; $r = -0.307$).

Conclusions: Our findings demonstrated that cigarette smoking decreases the nasal NMTR in chronic term. Impaired mucociliary transport in respiratory system may have harmful effects on the human health. The degree of impairment in NMTRs in smokers may increase as the number of cigarettes per day increases.

Key words: Tobacco smoke, smoking, mucociliary clearance, radionuclide imaging

moving. Inhaled foreign particles and micro-organisms are trapped by the mucus layer of the upper and lower respiratory system, and taken away if MCT works properly (1,2). This process has protective effect on upper and lower respiratory system and considered as first-line defence mechanism against hazardous environmental dusts, harmful physical and biological factors in men. If function of the MCT is impaired, the protective effect of mucociliary activity (MCA) may be lost (3,4). The efficacy of MCA in respiratory system depends on factors including the number of cilia and beat frequency, their co-ordinated movements, the amount of nasal fluid, and its viscoelastic properties (5). Impaired MCA may be associated with cigarette smoking, cystic fibrosis, bronchiectasis, immotile cilia syndrome, and nasal septum deviation, a history of nasal surgery or trauma, diabetes mellitus, adenoid hypertrophy, inflammatory process of the upper airway, allergic rhinitis, sinusitis, otitis media and many other factors (5-11).

Cigarette smoking has numerous harmful effects on the human health. It has been documented that the cigarette smoking diminishes ciliary beat frequency (6, 7, 12, 13), negatively affects ciliogenesis (14) and both active and passive smoking impairs MCT (2, 8, 15).

We aimed to investigate the association between nasal mucociliary transport rate (NMTR) and duration and amount of smoking using a radionuclide method.

Introduction

Mucociliary transport (MCT) in respiratory system is a physiological process in which the mucus layer on the ciliated cells of the epithelium is

Materials and methods

Study population

Fifty four current cigarette smokers and 40 healthy non-smokers were included in this study.

Non-smokers in control group had not been previously smoked cigarette or used any tobacco products. Any of subjects in smoker or control groups had not been previously exposed to intense environmental or occupational dusts. We used exclusion criteria as follows: any drug use, a history of acute or chronic upper respiratory tract infection in past two weeks, allergic rhinitis, nasal obstruction, chronic or current nasal drainage, nasal septal deviation, *nasal polyposis*, turbinate hypertrophy, cystic fibrosis, history of cilia-related disorders or a history of any chronic disease and nasal airway surgery. The local ethical committee approved the study protocol. All subjects were examined by an ear, nose and throat specialist for the detailed ear, nose and throat or head and neck examinations and by a pulmonologist for the detailed chest examination.

Scintigraphic procedure

Rhinoscintigraphy was performed by dripping one droplet (~50 μCi that corresponds to about 25 μSv radiation exposure) of $^{99\text{m}}\text{Tc}$ -macroaggregated albumin ($^{99\text{m}}\text{Tc}$ -MAA) (particle size ranged between 10-150 μm) on right side, on base of the nasal meatus and the anterior end of the inferior turbinate by using a 27G syringe. A scintigraphic procedure gives study subjects only a negligible gamma radiation exposure as a very small dosage of $^{99\text{m}}\text{Tc}$ -MAA is used. Room temperature was stabilized at 21°C. In the supine position, images were obtained by using a GE-millennium gamma camera system (GE Medical Systems, Milwaukee, WI, USA) with a “low energy general purpose” collimator and detectors were set laterally. Thirty-second dynamic images were obtained for a period of 20 minutes.

After the test, the images were processed to determine NMTR in millimetres per minute (mm/min). The distance between the point where the radiopharmaceutical was dropped and the point where the particles reached the nasal cavity was measured on a straight line using a system computer. Then, to determine the NMTR in mm/min, this length was divided by the time elapsed.

Statistical analysis

Statistical analysis was performed using the SPSS 15.0 software program (SPSS Inc., Chicago, Illinois, USA). Data were stated as mean $\pm$ standard deviation (SD). To compare cigarette smokers with control subjects in respect to NMTRs and ages, an independent samples *t*-test was used. Categorical data of gender was analyzed using Chi-square testing. Pearson's correlation coefficient was used to discover any relationships between NMTRs and smoking year, smoking pack-year and cigarettes per day. A *p* value of less than 0.05 was considered statistically significant.

Results

The mean age was 31.8 ± 9.9 years in the cigarette smokers and 28.9 ± 7.5 in control group. NMTRs, smoking pack-year, year of smoking and cigarettes per day were shown in Table 1. NMTRs distribution in smokers and control group were shown in Figure 1. The age and gender distribution of smokers and control groups were not significantly different from each other. The mean NMTR of the smokers was lower than that of the healthy non-smoker controls ($p < 0.0001$). There were not

Table 1. Some characteristics of the cigarette smokers and non-smokers (Values are mean $\pm$ SD)

	Cigarette smokers (n=54)	Non-smokers (n=40)	p-value
NMTR (mm/min)	5.63 ± 2.78	9.44 ± 2.09	<0.0001
NMTR range	(0.5-11.4)	(3.1-12.4)	
Age (year)	31.8 ± 9.9	28.9 ± 7.5	0.131
Gender			0.725
Male	46	33	
Female	8	7	
Cigarettes per day	22.3 ± 9	NA	NA
Duration of smoking (year)	13.4 ± 8.1	NA	NA
Pack-year	15.7 ± 13.4	NA	NA

NMTR, nasal mucociliary transport rate; NA, not applicable

statistically significant correlation between NMTRs and year of smoking, and smoking pack-year in smokers ($p>0.05$; $r=0.003$, $r=-0.2$, respectively) (Figure 2). However, there was a statistically significant correlation between NMTRs and cigarettes per day in smokers ($p=0.024$; $r=-0.307$) (Figure 3).

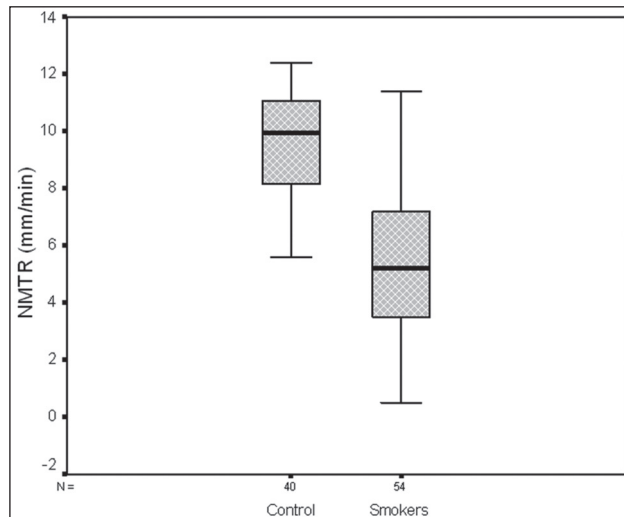


Figure 1. Nasal mucociliary transport rates (NMTR) distribution in cigarette smokers and non-smoking control groups

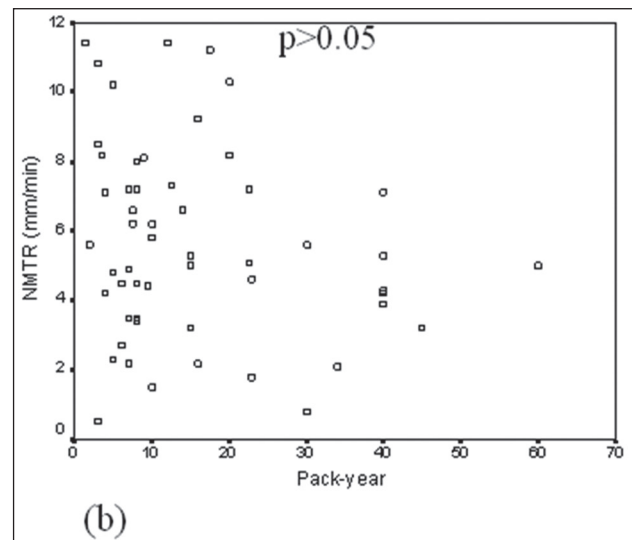
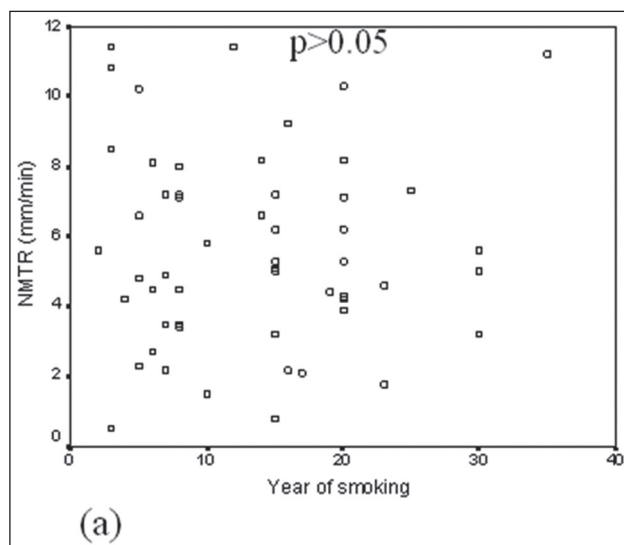


Figure 2. Scatter plots (a,b) show no correlation between nasal mucociliary transport rates (NMTR) and duration of smoking and pack-year in cigarette smokers ($p>0.05$)

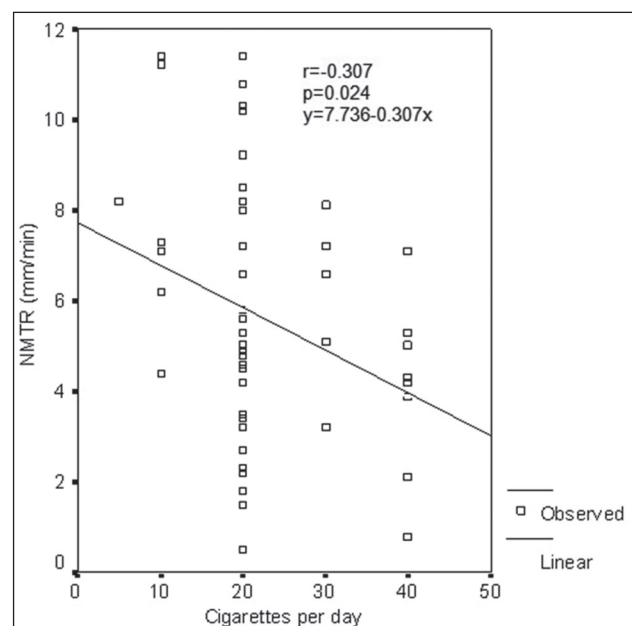


Figure 3. Linear regression analysis demonstrates significant correlation between nasal mucociliary transport rates (NMTR) and cigarettes per day in smokers

Discussion

Inhaled foreign particles, some pathogens, and toxins are eliminated by means of the mucociliary transport mechanism to obtain normal physiology of the respiratory system (1,2,16). In literature, it has been demonstrated that MCA may be affected from toxins, drugs, environmental heat, smo-

king, pressure, pH, and etc (2,17). It has also been shown that trauma, surgery, and some applications may have a deleterious effect on MCC (9). In this study, we found a statistically significant difference between cigarette smokers and control groups with respect to NMTR ($p < 0.0001$). Correlation analysis demonstrated that NMTRs did not significantly correlate with the year of smoking, and smoking pack-year in smokers ($p > 0.05$; $r = 0.003$, $r = -0.2$, respectively) (Figure 2), however there was a statistically significant correlation between NMTRs and cigarettes per day in smokers ($p = 0.024$; $r = -0.307$) (Figure 3).

There are several techniques for assessing ciliary activity in nasal mucosa. Of these, stroboscopy, roentgenography and photoelectron techniques evaluate ciliary activity and ciliary beat frequency. But, such techniques are not suitable for routine use (1,18). Most frequently used tests to measure MCA are rhinoscintigraphy and the saccharin test. The latter one is quite simple to perform. Main disadvantage of this test is that it relies on the patient's sense of taste (19). Rhinoscintigraphy can supply objective measurement of NMTR that reflects nasal MCA and allows quantitative analyses. Rhinoscintigraphy is an objective and sensitive nuclear medicine technique used for measurement of NMTR in nasal mucosa. In this method, tagged microparticles are dripped on anterior part of nasal meatus. If ciliary activity is intact, these particles move backwards, to nasopharynx. By the help of consecutive images, NMTR can be measured easily (1,18). For these reason, we preferred to use the radionuclide technique to measure NMTR in this study.

Proença et al. have studied the immediate and short term effects of smoking on nasal mucociliary clearance in smokers using a saccharin test (17). They found that eight hours after smoking saccharin transit time was reduced in smokers. In our study, we assessed the chronic effect of the smoking that NMTRs was reduced in smokers. Stanley et al. have also studied the effects of smoking on nasal mucociliary clearance in smokers using a saccharin test (8). They found that in the long term, smoking reduced saccharin transit time in smokers. Our results were consistent with their findings.

Singh et al. have studied the effects of smoking

on nasal mucociliary clearance in smokers using a saccharin test (15). In that study, smokers were observed to have prolonged nasal mucus clearance. They also reported that the clearance was prolonged as the number of cigarettes smoked and the duration of smoking increased. In our study, there was a statistically significant correlation between NMTRs and cigarettes per day in smokers ($p = 0.024$; $r = -0.307$) (Figure 3). This finding was consistent with their result. However, NMTRs in smokers did not significantly correlate with the year of smoking ($p > 0.05$; $r = 0.003$) (Figure 2). This finding was not consistent with their result. The possible causes for the different results of that study were as follows: **(a)** Their MCA method was the saccharin test whereas we used the rhinoscintigraphy with ^{99m}Tc -MAA to measure NMTR for this purpose. **(b)** The sample size of our study may be relatively small.

In conclusion, our study findings demonstrated that chronic cigarette smoking reduced NMTRs as a long term effect. The degree of impairment in NMTRs in smokers may increase as the number of cigarettes per day increases.

Disclosure

The authors declare that they have no financial relationship with any organization related to the research and no conflict of interest.

References

1. Dostbil Z, Polat C, Karakus A, Bakir S, Yuce S. Evaluation of the nasal mucociliary transport rate by rhinoscintigraphy in marble workshop workers. *Toxicol. Ind. Health* 2011; 27: 826-30.
2. Habesoglu M, Demir K, Yumusakhuylyu AC, Sahin Yilmaz A, Oysu C. Does Passive Smoking Have an Effect on Nasal Mucociliary Clearance? *Otolaryngol. Head. Neck. Surg.* 2012; Feb 29. DOI: 10.1177/0194599812439004.
3. Tawakir K, Yilmaz T, Sunucu S, Ergin T, Keith AB. Scanning electron microscopy of ciliae and saccharin test for ciliary function in septal deviation. *Laryngoscope* 2006; 116: 586-590.
4. Elahi MM, Frenkiel S, Fageeh N. Paraseptal structural changes and chronic sinus disease in relation to the deviated septum. *J. Otolaryngol* 1997; 26: 236-240.

5. Passàli D, Ferri R, Becchini G, Passàli GC, Bellussi L. Alterations of nasal mucociliary transport in patients with hypertrophy of the inferior turbinates, deviations of the nasal septum and chronic sinusitis. *Eur Arch Otorhinolaryngol* 1999; 256: 335-7.
6. Vander Top EA, Wyatt TA, Gentry-Nielsen MJ. Smoke exposure exacerbates an ethanol-induced defect in mucociliary clearance of *Streptococcus pneumoniae*. *Alcohol. Clin. Exp. Res.* 2005; 29: 882-7.
7. Cohen NA, Zhang S, Sharp DB, Tamashiro E, Chen B, Sorscher EJ, Woodworth BA. Cigarette smoke condensate inhibits transepithelial chloride transport and ciliary beat frequency. *Laryngoscope* 2009; 119: 2269-2274.
8. Stanley PJ, Wilson R, Greenstone MA, MacWilliam L, Cole PJ. Effect of cigarette smoking on nasal mucociliary clearance and ciliary beat frequency. *Thorax*. 1986; 41: 519-523.
9. Maurizi M, Paludetti G, Todisco T, Almadori G, Ottaviani F, Zappone C. Ciliary ultrastructure and nasal mucociliary clearance in chronic and allergic rhinitis. *Rhinology* 1984; 22: 233-240.
10. Gryczyńska D, Kobos J, Zakrzewska A. Relationship between passive smoking, recurrent respiratory tract infections and otitis media in children. *Int. J. Pediatr. Otorhinolaryngol* 1999; 49 Suppl 1: S275-8.
11. Mahakit P, Pumhirun P. A preliminary study of nasal mucociliary clearance in smokers, sinusitis and allergic rhinitis patients. *Asian. Pac. J. Allergy. Immunol* 1995; 13: 119-21.
12. Leopold PL, O'Mahony MJ, Lian XJ, Tilley AE, Harvey BG, Crystal RG (2009). Smoking is associated with shortened airway cilia. *PloS. One.* 4: e8157.
13. Agius AM, Smallman LA, Pahor AL. Age, smoking and nasal ciliary beat frequency. *Clin. Otolaryngol. Allied. Sci* 1998; 23: 227-30.
14. Tamashiro E, Xiong G, Anselmo-Lima WT, Kreindler JL, Palmer JN, Cohen NA. Cigarette smoke exposure impairs respiratory epithelial ciliogenesis. *Am. J. Rhinol. Allergy* 2009; 23: 117-22.
15. Singh I, Mehta M, Singh J, Yadav J. Nasal mucus clearance in chronic smokers. *Indian. J. Chest. Dis. Allied. Sci* 1994; 36: 133-6.
16. Stannard W, O'Callaghan C. Ciliary function and the role of cilia in clearance. *J. Aerosol. Med.* 2006; 19: 110-115.
17. Proença M, Fagundes Xavier R, Ramos D, Cavalheri V, Pitta F, Cipulo Ramos EM. Immediate and short term effects of smoking on nasal mucociliary clearance in smokers. *Rev. Port. Pneumol.* 2011; 17: 172-6.
18. Di Giuda D, Galli J, Calcagni ML, Corina L, Paludetti G, Ottaviani F, De Rossi G. Rhinoscintigraphy: a simple radioisotope technique to study the mucociliary system. *Clin. Nucl. Med.* 2000; 25: 127-30.
19. Corbo GM, Foresi A, Bonfitto P, Mugnano A, Agabiti N, Cole PJ. Measurement of nasal mucociliary clearance. *Arch. Dis. Child.* 1989; 64: 546-50.

Corresponding Author

Zeki Dostbil,
Department of Nuclear Medicine,
Dicle University Faculty of Medicine,
Diyarbakir,
Turkey,
E-mail: zekidostbil@yahoo.com

Frequency of ischemic stroke subtypes in relation to risk factors for ischemic stroke

Natasa Turanjanin¹, Mirjana Jovicevic², Ksenija Bozic², Marija Zarkov²

¹ Health Care Center of Backa Palanka, Serbia,

² Clinic for Neurology, Clinical Center of Vojvodina, Serbia.

Abstract

Introduction/Aim: Risk factors for the development of ischemic disease may be divided into modifiable (arterial hypertension, diabetes mellitus and glucoregulation disorders, smoking, dyslipidemia, atrial fibrillation and other cardiac disorders, obesity, physical inactivity) and non-modifiable (age, sex, and inheritance). According to etiology (TOAST classification), ischemic stroke is classified into the following five subtypes: large vessel atherosclerosis, cardiac embolism, small vessel disease (lacunar stroke), other determined causes, and undetermined causes. The aim of the study was to determine frequency of individual ischemic stroke subtypes in relation to risk factors for ischemic stroke in patients aged 15-45 and 46-75 years and to confirm that synergistic effects of hypertension, diabetes mellitus and dyslipidemia predispose one to lacunar ischemic stroke.

Methods: The study sample comprised 120 men and women with ischemic stroke treated at the Institute for Neurology of Vojvodina, Novi Sad, in the period 2005-2008. The patients were classified into two age groups, 15-45 and 46-75 years, each comprising 60 patients. All study patients met the clinical and radiological criteria for the ischemic stroke diagnosis. Etiology of ischemic stroke was determined using the TOAST classification. The risk factors studied were family history, hypertension, diabetes mellitus, dyslipidemia, previous stroke or transient ischemic stroke (TIA), smoking, cardiovascular disease, obesity, and alcohol abuse.

Results: In both age groups lacunar ischemic stroke was the most frequent in patients with the following risk factors: hypertension (37.0% in the younger group and 46.3% in the older group), dyslipidemia (26.3% in the younger group and 48.9% in the older group), previous stroke or TIA (41.2% in the younger group and 47.6% in the older group) and smoking (31.2% in the yo-

unger group and 53.3% in the older group). Cardiac embolism was the most frequent cause in patients with cardiological diseases in both groups (70.6% in the younger group, 36% in the older group). Different ischemic stroke subtypes were found in both age groups: in patients with diabetes mellitus (large vessel atherosclerosis was found in 44.4% in the younger group and lacunar stroke in 41.7% of the older group); positive family history (undetermined cause in 25.7% of the younger group, lacunar stroke in 63.0% of the older group); obesity (in the younger group, the most frequent were large vessel atherosclerosis and undetermined cause, both found in 25%, and in the older group large vessel atherosclerosis was the cause in 45%); and alcohol abuse (in the younger group cardiac embolism and undetermined cause were the most frequent, each found in 30%, and in the older group it was lacunar stroke, 43.8%). We found that hypertension, diabetes mellitus and dyslipidemia acted synergistically and made patients more susceptible to lacunar ischemic stroke.

Conclusion: Our results show that different ischemic stroke subtypes occur in both younger and older patients with different stroke risk factors. Synergistic effects of hypertension, diabetes mellitus and dyslipidemia predispose one to lacunar ischemic stroke.

Key words: Risk factors, ischemic stroke, etiology, brain ischemia, brain infarction

Introduction

Stroke is the cause of death of more than 5.5 million people per year, which makes 10% of overall mortality worldwide, and cerebrovascular diseases are the third most common cause of death in many countries (1). Acute stroke is one of the most important neurological diseases, and it is classified into two major categories: ischemic (75-80%) and hemorrhagic (20-25%) (2).

Risk factors for ischemic stroke contributing to the progression of the *pathological process in blood vessels* often precede the development of the disease by many years (3). Combination of multiple risk factors most frequently poses higher risk for stroke than the single risk factor.

Risk factors for ischemic brain diseases are classified according to their potential for modification and include modifiable (arterial hypertension, diabetes mellitus and glycoregulation disorders, smoking, dyslipidemia, atrial fibrillation and other cardiac dysfunction, obesity, lack of physical activity and alcohol abuse) and non-modifiable (age, gender and heredity) etiologies (2).

The TOAST classification denotes five subtypes of ischemic stroke, according to their etiology, i.e. blood vessel atherosclerosis, cardiac embolism, small-vessel occlusion (lacunar), stroke of other determined etiology, and stroke of undetermined etiology (2). Factors causing stroke differ considerably between young and elderly patients. According to some reports, some 21% cases of ischemic stroke in younger patients remain etiologically undetermined (4). Large-artery atherosclerosis and small-vessel occlusion are prevalent in patients older than 60, whereas large-artery atherosclerosis is highly uncommon in patients under 45 years of age, who frequently have diseases such as dissection, inflammatory artery diseases, migrainous infarction and cardiac embolism (5).

The aim of our research was to determine the proportional representation of ischemic stroke subtypes associated with different risk factors in patients with ischemic stroke from Vojvodina region, including age groups 15-45 and 45-75 years, and to establish whether synergistic effects of hypertension, diabetes mellitus and dyslipidemia predispose a person to lacunar ischemic stroke.

Methods

The study sample comprised 120 male and female ischemic stroke patients treated at the Institute for Neurology of the Clinical Center of Vojvodina in Novi Sad, Serbia, in the period from October 14, 2005 to March 21, 2008. Study subjects were divided into two age groups – 60 patients aged 15-45 years and 60 patients aged 46-75 years. All study subjects met the clinical and radiological cri-

teria for the diagnosis of ischemic stroke. Due to the low incidence of stroke in young patients and therefore small numbers of young stroke patients enrolled prospectively, the study was partly retrospective, by a retrospective review of medical records (data was collected from medical histories).

Information about the patients who were enrolled prospectively was obtained from the patients themselves or their relatives.

The risk factors for ischemic stroke studied were family history, hypertension, diabetes mellitus, dyslipidemia, previous stroke or TIA, smoking, cardiological disease, obesity and alcohol abuse. According to etiology (TOAST classification), ischemic stroke is classified into the following five subtypes: large vessel atherosclerosis, cardiac embolism, small vessel disease (lacunar stroke), other determined causes, and undetermined causes.

Data were analyzed using standard statistical methods. All analyses were performed using the software package SPSS 15.0 for Windows. Numerical data were presented with mean arithmetic values and standard deviations, and comparisons were performed using the t-test. The differences in frequencies were tested with the χ^2 test. The level of statistical significance adopted for all analyses was 0.05.

Results

Proportional representation of ischemic stroke subtypes associated with particular risk factors was analyzed in 120 patients with ischemic stroke aged 15-45 (60 patients) and 46-75 (60 patients).

In both groups, the highest incidence of same ischemic stroke subtypes was observed in patients with hypertension (younger 37.0%, older 46.3%), dyslipidemia (younger 26.3%, older 48.9%), previous stroke or TIA (younger 41.2%, older 47.6%) and smoking (younger 31.2%, older 53.3%) when it comes to the lacunar ischemic stroke, and cardiac diseases (younger 70.6%, older 36%) when it comes to cardiac embolism.

In both groups, the occurrence of different stroke subtypes was observed in following risk factors: diabetes mellitus (large-artery atherosclerosis in 44.4% of younger patients, lacunar stroke in 41.7% of older patients), heredity (undetermined etiology in 25.7% of younger patients, lacunar stroke in 63.0% of older patients), obesity (equal incidence

Table 1. Incidence the etiological subtype of ischemic stroke in relation from risk factors of ischemic stroke in the different age groups in ischemic stroke patients

Group risk factors			Etiology of ischemic stroke					
			large vessel atherosclerosis	cardiac embolism	small vessel disease (lacunar)	other determined causes	undetermined causes	total
15-45 yrs	hipertension	N	5	3	10	1	8	27
		%	18,5%	11,1%	37,0%	3,7%	29,6%	
	diabetes mellitus	N	4	0	2	1	2	9
		%	44,4%	0,0%	22,2%	11,1%	22,2%	
	family history	N	7	8	8	3	9	35
		%	20,0%	22,9%	22,9%	8,6%	25,7%	
	dyslipidemia	N	7	8	10	5	8	38
		%	18,4%	21,1%	26,3%	13,2%	21,1%	
	previous stroke or TIA	N	2	5	7	1	2	17
		%	11,8%	29,4%	41,2%	5,9%	11,8%	
	smoking	N	4	7	10	3	8	32
		%	12,5%	21,9%	31,2%	9,4%	25,0%	
	cardiological disease	N	0	12	3	0	2	17
		%	0,0%	70,6%	17,6%	0,0%	11,8%	
46-75 yrs	obesity	N	3	2	2	2	3	12
		%	25,0%	16,7%	16,7%	16,7%	25,0%	
	alcohol consumption	N	2	3	2	0	3	10
		%	20,0%	30,0%	20,0%	0,0%	30,0%	
	total	N	11	12	15	7	14	59
	hipertension	N	17	9	25	0	3	54
		%	31,5%	16,7%	46,3%		5,6%	
	diabetes mellitus	N	9	3	10		2	24
		%	37,5%	12,5%	41,7%	0	8,3%	
	family history	N	7	2	17	0	1	27
		%	25,9%	7,4%	63,0%		3,7%	
	dyslipidemia	N	13	7	23	0	4	47
		%	27,7%	14,9%	48,9%		8,5%	
	previous stroke or TIA	N	4	3	10	0	4	21
		%	19,0%	14,3%	47,6%	0	19,0%	
	smoking	N	4	2	8		1	15
		%	26,7%	13,3%	53,3%	0	6,7%	
	cardiological disease	N	7	9	7		2	25
		%	28,0%	36,0%	28,0%	0	8,0%	
	obesity	N	9	2	8		1	20
		%	45,0%	10,0%	40,0%	0	5,0%	
	alcohol consumption	N	5	4	7		0	16
		%	31,2%	25,0%	43,8%	0	0,0%	
	total	N	18	9	29	0	4	60

Table 2. Incidence of ischemic stroke patients with all three aforementioned risk factors (hypertension, diabetes mellitus et dyslipidemia) in relation to the etiologic subtype of ischemic stroke

Etiologic subtype of ischemic stroke.	provided N	expected N	rezidual
large vessel atherosclerosis	6	5,0	1,0
cardiac embolism	2	5,0	-3,0
small vessel disease (lacunar)	11	5,0	6,0
undetermined causes	1	5,0	-4,0
Total	20		

χ^2 is statistically significant. $\chi^2 = 12,400^a$ df(3) $p = 0,006$

of large-artery atherosclerosis and undetermined etiology in 25.0% of younger patients, large-artery atherosclerosis in 45.0% of older patients) and alcohol abuse (equal incidence of cardiac embolism and undetermined etiology in 30% of younger patients, lacunar stroke in 43.8% of older patients) (Table 1).

Analysis of synergistic effects of hypertension, diabetes mellitus and dyslipidemia as a predisposing factor for lacunar ischemic stroke encompassed only patients exhibiting all three risk factors. Table 2 displays the incidence of patients with all three aforementioned risk factors in relation to the etiologic subtype of ischemic stroke.

The most prevalent etiologies are shown in frequency table (Table 2). The highest frequency, but also the highest positive residual was observed in lacunar ischemic stroke. It indicates that its observed frequency is statistically significantly higher than the expected frequency, provided that ischemic strokes of various etiologies are equally probable.

Discussion

Abundant research has been conducted worldwide, addressing risk factors for ischemic stroke and incidence of different subtypes of ischemic stroke associated with particular risk factors (6).

In both age groups, the highest incidence of lacunar ischemic stroke was observed in patients with hypertension (younger 37.0%, older 46.3%) in our research, as well as in reports of other authors (6). Also, the lacunar subtype of ischemic stroke was the most common in both age categories of patients with dyslipidemia (younger 26.3%, older 48.9%), previous stroke or TIA (younger 41.2%, older 47.6%) and smoking (younger 31.2%, older 53.3%) in our research, whereas this subtype was reported as the second and the third most prevalent in the reports of aforementioned authors (6) when it comes to smoking and dyslipidemia, and previous stroke or TIA, respectively.

Arterial hypertension influences the atherosclerosis process by initiating formation of atherosclerotic lesions, accelerating and intensifying atherosclerosis and enhancing lipid deposition in small vessel walls (arterioles). Consequently, stenosis, obliteration of atherosclerotic plaque associated with accumulation of thrombotic masses may de-

velop (7). In time cerebrovascular insult may occur. Meta analysis of nine prospective studies revealed that 1 kPa (7.5 mmHg) increase in diastolic pressure increases the risk of stroke for 46% (8).

Substantial decrease in HDL cholesterol and relative proportion of HDL/LDL was observed in patients with ischemic brain disease, and changes tend to be most pronounced by the middle of sixth decade of life (9). High total cholesterol and low HDL-cholesterol were independent predictors of carotid stenosis (10).

Previous stroke and transient ischemic attack are important risk factors for ischemic stroke. American research revealed a 10-20 fold risk of recurrent stroke after the first one (11), whereas risk of brain infarction ranges from 24 to 29% within five years after transient ischemic attack (TIA) (12).

Smoking accelerates the atherosclerosis process, which is the leading cause of myocardial and brain infarction (13), but also the most important predictor of pronounced atherosclerosis of the extracranial segment of carotid arteries (14).

In younger and older patients with diabetes mellitus, the most prevalent subtypes were large-vessel atherosclerosis (44.4%) and lacunar stroke (41.7%), respectively. This is in accordance with reports of other researchers, indicating that diabetes mellitus is better predictor of lacunar stroke (15) than of the other stroke subtypes. Cerebrovascular insult occurs more frequently in patients with Type 2 diabetes (16), and an association of insulin resistance and thickening of intima-media complex and development of carotid disease has already been well-established (17).

In our research, the most prevalent subtypes in patients with hereditary risk factor were stroke of undetermined etiology in younger (25.7%) and lacunar stroke in older patients (63.0%). Reports of other authors also demonstrated high correlation between heredity and etiologic subtypes such as large-vessel atherosclerosis, lacunar stroke and stroke of undetermined etiology (18). Genetic factors play an important role in occurrence of cerebrovascular insult, as patients with family history of early atherosclerosis are at increased risk to suffer stroke. A range of probable causes of atherosclerosis, such as lipid disorders, endothelial dysfunction and possible effects of environmental factors might contribute to stroke events (19).

In younger as well as in older patients with cardiac diseases the most frequent stroke subtype was cardiac embolism (younger 70.6%, older 36%). Persons with any symptomatic or asymptomatic cardiac disease, regardless of blood pressure value, are at two-fold risk for developing ischemic stroke compared to persons who do not suffer from heart problems (11). Atrial fibrillation (AF) carries a high risk of cerebral embolism (2). Research on etiology of ischemic stroke in young patients identified paradoxical embolism as a possible etiopathogenic mechanism in 3.3% of patients (20).

In younger obese patients, equal rates (25%) were determined for large-vessel atherosclerosis and stroke of undetermined etiology, whilst the large-vessel atherosclerosis was determined in 45% of obese older patients. Other researchers identified the abdominal obesity as an independent risk factor for all subtypes of ischemic stroke (21). *Obesity is a problem not just esthetic*, but it involves severe health issues and is often associated with other pathological conditions and diseases, accelerating their progression. Thus, obesity doubles the risk of an ischemic stroke (22).

Alcohol abuse as a risk factor was associated with equal rates of cardiac embolism and stroke of undetermined etiology in younger patients (30%) and with lacunar stroke in older ones (43.8%). However, effects of alcohol as a risk factor for ischemic stroke are still controversial, and most likely dependent upon the amount consumed (23). Some authors established the association between alcohol consumption and an increased risk of stroke (13), as well as that alcohol is a toxin affecting negatively (directly or indirectly) all organs (24) including the central nervous system. Alcohol tends to have more disruptive effect on women, and even relatively small amount of alcohol may cause severe complications (25).

Our research confirmed that synergistic effect of hypertension, diabetes mellitus and hypercholesterolemia predispose a person to lacunar stroke. American authors identified hypertension as a predictor for all subtypes of ischemic stroke. Smoking and diabetes mellitus are strong predictors for both lacunar and non-lacunar stroke, though somewhat stronger for the lacunar one (15).

Prospective study encompassing 4,736 elderly Americans (the majority was Caucasian popula-

tion) revealed that smoking and diabetes mellitus were independently associated with increased risk of lacunar stroke, but not the atherosclerosis- or embolism-related ones (26). Another prospective study that included American females revealed association of diabetes mellitus with all subtypes of ischemic stroke (27). Prospective study carried out on 1,621 subjects of both sexes in Japan demonstrated significant correlation between smoking and glucose intolerance and the incidence of lacunar stroke in women, but not in men (28).

Conclusion

The results obtained in this research indicated difference in proportional representation of diverse etiologic subtypes of ischemic stroke associated with different risk factors, both in younger and elderly patients with ischemic stroke. It was established that synergistic effect of hypertension, diabetes mellitus and dyslipidemia predisposes the patient to lacunar ischemic stroke. The existence of risk factors for ischemic stroke, especially concomitant presence of multiple risk factors, substantially increases the risk of stroke. Prevention measures are crucial for the strategy aimed at decreasing the number of patients suffering ischemic stroke, and particular attention should be paid to risk factors in all age groups.

References

1. Truslen T, Bonita R, Jamrozik K. Surveillance of stroke: a global perspective. *Int J Epidemiol.* 2001; 30: 1-16.
2. Akutni ishemijski moždani udar. Nacionalni vodič. Beograd: Republička stručna komisija za izradu i implementaciju vodiča u kliničkoj praksi, Ministarstvo zdravlja Republike Srbije; 2004.p.4-13.
3. Petrović G. Faktori rizika u pojavi cerebrovaskularnog inzulita. *Med Pregl.* 2000; (3-4): 207-13.
4. Jovičević M. Etiologija ishemičnog moždanog udara kod mladih ljudi (doktorska disertacija). Novi Sad: Univerzitet u Novom Sadu, Medicinski fakultet; 2005.
5. Hankey J G. *Stroke, Your questions answered.* Sydney: Churchill Livingstone; 2002.
6. Božić K, Gvozdenović S. Podtipovi ishemijskog moždanog udara: profil faktora rizika i demografske karakteristike (monografije: 85). Novi Sad: Univerzitet u Novom Sadu, Medicinski fakultet; 2010.

7. Petrov-Kiurski M. Esencijalna arterijska hipertenzija i njene komplikacije kao aktuelan kardiološki problem, (magistarski rad). Novi Sad: Univerzitet u Novom Sadu, Medicinski fakultet; 1990.
8. MacMahon S, Peto R, Cutler J, Collins R, Sorlie P, Neaton J, et al. Blood pressure, stroke and coronary heart disease. Part 1: Prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. *Lancet* 1990; 335: 765-74.
9. Jovičić A, Marić P. Lipidi i ishemijska bolest mozga. *Bilten odbora za lipide*; 1994; (4): 17-20.
10. Mathiesen EB, Joakimsen O, Bonna KH. Prevalence of and risk factors associated with carotid artery stenosis. *The Tromso Study. Cerebrovasc Dis.* 2001; 12: 44-51.
11. Dyken ML. Risk factors predisposing to stroke. In: Moored W, ed. *Surgery for cerebrovascular diseases*. Philadelphia: WB Saunders Company; 1996. p. 33-42.
12. Kostić V, Raičević R. Karotidna bolest, etiologija, patofiziologija, dijagnostika i terapija. VMA: Beograd: Medicinski fakultet u Beogradu; 2004.
13. Gorelick PB. Stroke related to alcohol and drug abuse. *Ammel courses, cerebro-vascular disorders. AM Academy of Neurology* 1990; 3: 91-119.
14. Živković M, Šternić N, Kostić V. Ishemička bolest mozga. Beograd: Zavod za udžbenike i nastavna sredstva; 2000.
15. Al Rajeh S, Awada A. Stroke in Saudi Arabia. *Cerebrovasc Dis.* 2002; 13: 3-8.
16. Diabetes mellitus. Nacionalni vodič kliničke prakse. Beograd: Nacionalni komitet za izradu vodiča kliničke prakse; 2002.
17. Mijajlović M. Značaj insulinske rezistencije u ishemijskoj bolesti mozga. In: Treći simpozijum Srbije i Crne gore o moždanom udaru, Tara, 8-11 septembra. Niške sveske 2005. p.66-71.
18. Jood K, Ladvall C, Rosengren A, Blomstrand C, Jern C. Family history in ischemic stroke before 70 years of age. *The Sahlgrenska Academy study on ischemic stroke. Stroke* 2005; 36: 1383-93.
19. Nichols FT III. Atherosclerosis. In: Fisher M, ed. *Stroke therapy*. London: Butterworth-Heinemann; 1995. p.171-218.
20. Jovičević M, Divjak I, Žarkov M, Jovanović A, Rabi-Žikić T, Ružička S. Uzroci ishemičnog moždanog udara kod mladih ljudi. *Aktuelnosti iz neurologije, psihijatrije i graničnih područja*. 2003; 11(3): 1-6.
21. Suk SH, Sacco RI, Boden-Albala B, Cheun JF, Pittman JG, Elkind MS, et al. Abdominal obesity and risk of ischemic stroke. *The Northern Manhattan study. Stroke* 2003; 34: 1586-92.
22. Tom OS. Other risk factors. *Cerebrovasc Dis.* 2003; 15(Suppl 2): 37-41.
23. Boden-Albala B, Sacco R. Lifestyle factors and stroke risk: exercise, alcohol, diet, obesity, smoking, drug use, and stress. *Curr Atheroscler Rep* 2000; 2: 160-6.
24. Davidović D, Petrović D, Petrić M. Psihijatrija sa medicinskom psihologijom. Kragujevac: Astra; 1998.p.118.
25. Jovičević M, Divjak I, Žarkov M, Jovanović A, Rabi-Žikić T, Ružička S. Uzroci ishemičnog moždanog udara kod mladih ljudi. Novi Sad: Aktuelnosti iz neurologije, psihijatrije i graničnih područja. 2003; 5(3): 38-43.
26. Davis BR, Vogt T, Frost PH, Burlando A, Cohen J, Wilson A, et al. Risk factors for stroke and type of stroke in persons with isolated systolic hypertension. *Systolic hypertension in the elderly program cooperative research group. Stroke* 1998; 29: 1333-40.
27. Iso H, Rexrode K, Hennekens CH, Manson JE. Application of computer tomography-oriented criteria for stroke subtype classification in a prospective study. *Ann Epidemiol.* 2000; 10: 81-7.
28. Tanizaki Y, Kiyohara Y, Kato I, Iwamoto H, Nakayama K, Shinohara N, et al. Incidence and risk factors for subtypes of cerebral infarction in a general population: the Hisayama study. *Stroke.* 2000; 31: 2616-22.

Corresponding author
 Natasa Turanjanin,
 Health Care Center of Backa Palanka,
 Serbia,
 E-mail: ntnatasa4@gmail.com

Contraception use and attitudes of women and health care providers

Aleksandra Kapamadzija¹, Tihomir Vejnovic¹, Slobodana Mihaldzic Tubic¹, Radojka Ratkovic², Sladjana Koledin¹, Gordana Radeka¹, Vesna Kopitovic¹

¹ Department of Obstetrics and Gynecology, Medical Faculty, University of Novi Sad, Serbia,

² Innotech International, Belgrade, Serbia.

Abstract

Introduction: Very few women use modern methods of contraception in Serbia and the number of abortions is still high. The aim of this research was to analyze factors affecting non-use of contraception in women as well as the attitudes of health care providers in order to influence them and therefore lower the number of abortions and preserve the reproductive health of women.

Methods: We surveyed 600 women from Northern Serbia, aged 20-44 who were gynecologically healthy with no desire to conceive and give birth at that moment. We also surveyed health care providers – 50 gynecologists (aged 30-65), 70 general practitioners (aged 25-55) and 100 nurses (aged 20-54). Both groups completed separate questionnaires constructed for this research, one for women and one for health care providers, and two standardized psychological questionnaires: The locus of control test and Planning and Future Orientation test.

Results and discussion: Women used the method of withdrawal most often (70.5%). The same method was used by 46.5% of health care providers. Health care providers use a condom most commonly – 57.7%, while 53.5% women do so. Effective methods – combined oral contraception (COC) and the intrauterine device (IUD) were used more by gynecologists (28% and 27.5%) than women (19.2%, 13.3%), but even they used it insufficiently. Only one half of women see a gynecologist for counseling about contraception. Gynecologists recommend effective methods of contraception most often but not even they use them to a satisfactory extent. Women and their partners often consider these methods harmful to health hence they do not use them sufficiently. A greater number of health care providers (61.4%) than women (43.3%) have a positive attitude toward effective methods of contraception. Prerequisites for better use of con-

traception are internal locus of control and orientation to future and planning. There are differences regarding the use and method of contraception with regard to marital status and age.

Conclusion: In order to increase the use of effective contraception and, therefore, to decrease the number of abortions, a systematic action is needed, with the emphasis on education and dissemination of knowledge about the benefits of modern contraception among women, their partners and health care providers.

Key words: Use of contraception, health care providers, determinants of contraceptive use

Introduction

The use of modern methods of contraception is of vital importance in family planning, giving birth to healthy children, preserving women's reproductive health, as well as reducing the number of abortions to a minimum. The problem of high abortion rate due to insufficient use of modern contraception is still present in Serbia (1, 2). Withdrawal is the predominant method of protection from unwanted pregnancies. Whereas lack of information regarding hormonal contraception and intrauterine devices (IUD) results in prejudice against these methods, fear and refusal to use them. There is no sex education in schools with the exception of occasional lectures on these topics. According to certain studies not even all the gynecologists in Serbia possess the necessary knowledge and positive attitude toward modern contraception (3, 4). The aim of our study is to examine how much contraception is used in Serbia, to identify the reasons why and to what extent women as well as health care providers (gynecologists, general practitioners and nurses) have negative attitudes toward modern contraception – hormonal contraception and intrauterine devices. We wanted to grasp to what extent health care

providers have an influence on the use of modern methods of contraception in our country as well as which other factors effect this use in order to undertake action with the objective to increase the use of contraception and reduce the number of abortions.

Methods

The study included 600 women, from the city territory of Novi Sad and neighboring areas (northern Serbia), aged 20-44 who were gynecologically healthy with no desire to conceive and give birth at that moment. Health care providers were also surveyed – 50 gynecologists (aged 30-65), 70 general practitioners (aged 25-55) and 100 nurses (aged 20-54). Both groups completed separate questionnaires constructed for this research, one for the women and one for the health care providers, and two standardized psychological questionnaires: The locus of control test and Planning and Future Orientation test. Ethical consideration - this study was approved by the Ethical Committee of Faculty of Medicine, University of Novi Sad and by the Ethical Committee of Clinical Centre of Vojvodina. The data were collected without personal identification of patients and all data were strictly confidential. All participants signed a voluntary consent form in order to participate in the study.

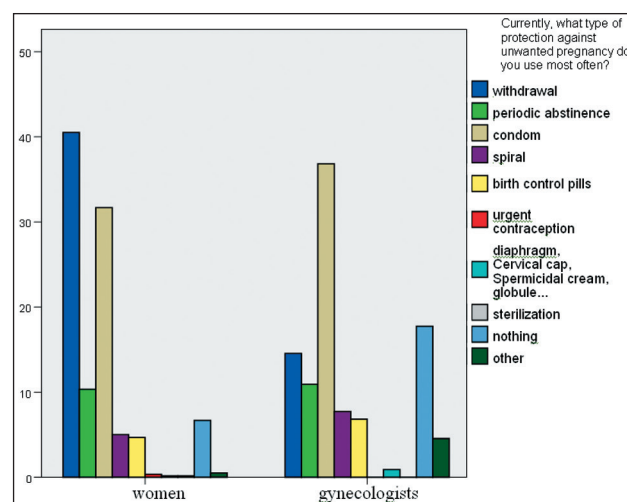
Statistical analysis

Descriptive statistics was used for each subsample. This was followed by correlational analyses in order to establish a potential connection between women's and health care providers' behavior, attitudes toward and prejudice against contraception. We compared results obtained on the subsample of women and the subsample of health care providers regarding contraception. Standard statistical methods of analysis were used in Excel, SPSS. The analyses were done in the statistical software SPSS for Windows 14 and 15.

Results

The use of contraception – Women surveyed currently use unreliable methods of contraception more – 40.5% uses withdrawal, 10.3% periodic abstinence, whereas 6.7% of the women do not use any form of contraception. Reliable methods

of contraception are used by only 41.4% of the women: condoms are used by 31.7%, while the most effective methods are used the least - 5% IUD and 4.7% combined hormonal contraception-pills (COC - combined oral contraception). One woman is sterilized; one uses a diaphragm and one spermicides; two women use urgent contraception; three women use other methods. Comparison of the current use of contraceptives between women and gynecologists is presented in Graph 1, showing a considerable difference. Methods that the women have used so far in their lives (multiple answers were possible): withdrawal, the most frequent form of contraception (three quarters of the women); one half of the women have used a condom; one third periodic abstinence; only 19.2% have used COC; 13% IUD; and 2% urgent contraception. No form of contraception was used by 9.7% of the women. The health care providers have so far in their lives used condom the most, then withdrawal (mostly nurses 58%), and periodic abstinence. One quarter of the health care providers have used COC, and one quarter IUD. More University clinic gynecologists used COC, while more outpatient clinic gynecologists used IUD. Urgent contraception was used most frequently by the University clinic gynecologists. Withdrawal was used significantly more often by the women than the health care providers, and more effective methods - IUD and COC - significantly less often. The health care providers use condoms most often (Chi-square test significant, Table 1).



Graph 1. Current use of contraception in women and gynecologists
Chi-square test shows significant differences

Table 1. The use of contraception by women and health care providers hitherto

	Women N (%)	Health care providers N (%)	Gynecologists N (%)
Withdrawal	423(70,5)	102 (46,4)	
Condom	321(53,5)	127(57,7)	
Periodic abstinence	201(33,5)	78(35,5)	
COC	115(19,2)	55(25)	11(36,7) from University clinic
IUD	80(13,3)	58(26,4)	7(35) from outpatient clinic
Urgent contraceptation	12 (2)	6(2,7)	2(6,7) from Univeristy clinic
Nothing	58(9,7)	25(11,4)	

Chi-square test shows significant differences.

Table 2. Attitudes of women and health care providers toward the most important reason for non-use of contraceptives

			What is the most important reason for your non-use of contraceptives?								Total
			Health risks	Insufficient reliability	The feeling is not the same	Interferes with spontaneity	Complicated use	I am insufficiently informed	Expensive	Other	
sample	women	N	132	67	60	47	45	47	11	26	435
		%	30,3%	15,4%	13,8%	10,8%	10,3%	10,8%	2,5%	6,0%	100,0%
	Health care providers	N	31	16	9	18	12	2	1	27	116
		%	26,7%	13,8%	7,8%	15,5%	10,3%	1,7%	,9%	23,3%	100,0%
	total	N	163	83	69	65	57	49	12	53	
		%	29,6%	15,1%	12,5%	11,8%	10,3%	8,9%	2,2%	9,6%	100,0%

Chi-square test is significant.

Table 3. Attitudes toward modern methods of contraception

	Women N (%)	Health care providers N (%)
Positive attitude	260 (43,3)	135 (61,4)
Abstained	225 (37,5)	75 (34,1)
Negative attitude	115 (19,2)	10 (4,5)
	600 100%	220 100%

Chi-square test is significant.

Reasons for non-use of contraception: Women and health care providers who have not used effective methods of contraception (COC and IUD) list health risks as the main reason for not using them (30.3% and 26.7% respectively). A higher percentage of women think that contraception is unreliable and that the feeling is not the same with it. Health care providers state more often that these methods interfere with the spontaneity of the intercourse, whereas they list lack of information about the methods less frequently. Only 2.7% of

the women say that the price of contraception is a negative factor. Women and health care providers differ significantly in the reasons for non-use of effective methods of contraception. Chi-square test is significant (Table 2).

Attitudes toward modern methods of contraception. Health care providers have a positive attitude toward modern methods of contraception more often than women (61.4% vs. 43.3%) (Chi-square test significant). Outpatient clinic gynecologists, who advise on the use of contraceptives most often, have

the most positive attitude toward COC and IUD (90%). They are followed by University clinic gynecologists (70%), nurses (63%) and general practitioners (47%). These differences in the attitudes are significant (Chi-square test is significant, Table 3)

Counseling: One half of the women (51%) have not had any counseling with the gynecologist regarding the use of contraception because they believe they have sufficient knowledge about it (62.4%) and that none of the methods are good enough (24.8%). Women from the urban area go to a gynecologist for counseling about contraception more often than women from the rural area ($p < 0.01\%$). Those who had had counseling received most recommendations to use a condom (45.1%), the IUD (37.9%) and birth control pills (31.1%). Only 3.8% were recommended to use withdrawal, 2% periodic abstinence, while none was recommended to use urgent contraception or spermicides. Some women have been advised about two methods of contraception. A significant number of women were satisfied with the counseling (87.7%).

Health care providers were questioned about how often they give counseling concerning contraception and which methods they recommend, as well as those they never recommend. Gynecologists from the outpatient clinics provide counseling about contraception most often - 80%, due to the fact that the Contraception Counseling services are a part of primary health care. They recommend and use a condom most frequently, while they regularly recommend the most efficient modern methods (COC, urgent contraception and IUD) but use them the least often. They almost never recommend withdrawal, but half of them have applied this method (Table 4). Only one third of the gynecologists from the University clinic provide counseling regarding contraception. General practitioners do not address this issue and only 5.7% provide counseling often, whereas 12% of nurses do so.

As a method of contraception, up to 79.7% of health care providers never recommend withdrawal (although women use it most often) and 59.3% of them do not recommend periodic abstinence either, due to the inefficiency of this method. Only 10% of gynecologists never recommend COC, however, 36% of nurses and 25% of general practitioners never recommend it either. IUD is never recommended by 16% of gynecologists, 14.6% of general practitioners and 36% of nurses. One third of the nurses do not support modern and effective methods of contraception. The differences in recommended methods between gynecologists, general practitioners and nurses are statistically significant (Table 5). *Table 4. Counseling and use of contraception among gynecologists from outpatient clinics*

Method of contraception	Recommend N (%)	Have used N (%)
Condom	18 (85)	12 (60)
COC	18 (85)	4 (20)
Urgent contraception	16 (80)	1 (5)
IUD	16 (80)	7 (35)
Periodic abstinence	9 (45)	8 (40)
Withdrawal	2 (10)	10 (50)

One half of the health care providers believe that the use of contraception is somewhat harmful to health (53.2%), 6.8% consider it very harmful, 55.5% believe that it is difficult to use, and 22.8% think that it is morally disturbing. Birth control pills are believed to be harmful to health by 20.8% of general practitioners, 25.3% of nurses, and only 3.4% of University clinic doctors and none outpatient clinic doctors. These differences are statistically significant and point to the fact that health care providers, apart from gynecologists, are not sufficiently educated about the safety of hormonal contraception.

Psychological personality traits. It has been examined whether certain personality traits – locus of control, and future orientation and planning -

Table 5. I never recommend these methods due to health risks:

	COC N (%)	IUD N (%)	Urgent contraception N (%)	Sterilization N (%)
Gynecologists outpatient clinic	0	1 (5)	3 (15)	0
Gynecologists University clinic	1 (3,4)	4(13)	1 (3,4)	4 (13,8)
General practitioners	10 (20)	4(18,3)	7 (14,6)	9 (18,8)
Nurses	19 (2)	12 (16)	13 (17,3)	7 (9,3)
Total	30 (17)	21(12,2)	24 (14)	20 (11,6)

affect the use of contraception. Respondents from the urban area have an internal locus of control more frequently (one can control the course of events in one's life). Whereas participants from the rural areas, as well as younger respondents (including nurses compared to doctors) have an external locus of control more frequently (believing in fate and that one does not have effect on the events in one's life) (T test significant, Table 6). Women from the urban area are more oriented to future and planning (T test is significant $p < 0.05$). Orientation to future and planning is expressed the most by the 25-29 and 35-39 age groups, while it is least expressed among the youngest, 20-24, and the oldest, 40-44, age groups. These two groups, in fact, use contraception the least. Three groups have the most expressed internal locus of control (table 7) and the strongest orientation to future and planning (table 8): women who consult a gynecologist, women who use effective contraception and women with the lowest number of abortions. Respondents who have not used contraception have a more expressed external locus of control.

The role of the partner in the selection of contraception. The final decision about the type of contraception they are going to use is made together with their partners in 60.6% of women and 57.1% of health care providers with no statistically significant difference. Partners of health care providers object to the use of contraception to a statistically significant lower degree (36%) than

the partners of women (47.8%). Chi-square test is positive. Partners who object to some methods of contraception most frequently do so to the use of condom (52.3%) and this tendency increases with age, because it interferes with spontaneity and the sensation during intercourse. On account of the "health risks" 50.3% are against contraceptive pills and 48.2% are against intrauterine spirals. Forty-three percent of partners are against periodic abstinence as well as urgent contraception, whereas 37.6% are against sterilization. In 66% of cases partners believe that withdrawal is the best method as well as the simplest and cheapest. In the cases of women from the rural areas, significantly more often is the final decision about the type of contraception joined and the partners' only (5.1% to 2.3% $p < 0.05$) than in the cases of women from the urban area where the women's and joined decision is more frequent.

The use of contraception varies according to *age group and marital status*. The use of condoms decreases with age (42.1% - 18.9%), whereas periodic abstinence and IUD increase (periodic abstinence - 5.8% - 16.4 %; IUD - 0% to 9%). Withdrawal is used in a similar percentage in all age groups. The youngest use condoms the most (20-24 years), whereas young women use birth control pills (25-29 years). Chi-square test is significant.

Married women use withdrawal (43.4%) and periodic abstinence (12.3%) more often than unmarried ones (withdrawal 35.4% and periodic abstinence

Table 6. Locus of control test values in women from the urban area and rural area

	Place of residence	N	AS	SD	Std. gr.
Locus of control test score (higher score – external locus of control)	Urban area	399	28.7068	8.84778	.44294
	Rural area	197	31.2183	7.46885	.53213

$P < 0,001$

Table 7. Use of effective contraception compared to the values of Locus of control test

	Used at least one method	N	AS	SD	Std.gr.
Locus of control test score (higher score – external locus of control)	NO	187	31.5027	8.75986	.64058
	YES	413	28.6513	8.27820	.40734

$P < 0,001$

Table 8. Use of effective contraception compared to the scores on Planning and future orientation test

	Used at least one method	N	AS	SD	Std.gr.
Planning and future orientation test score (higher score - greater orientation to future and planning)	NO	187	18.2299	2.14666	.15698
	YES	413	18.9685	2.04001	.10038

$P < 0,001$

4.3%), whereas unmarried women use condoms more often (48.8%) than married ones (25.5%). IUD is more often used by married women (married 6.4%, unmarried 1.2%), whereas unmarried women use contraceptive pills – 6.1% compared to married ones 4.2%. Chi-square test is significant.

Thirty-three point five percent of women had an *abortion* with no significant difference between the women from rural areas and the ones from the urban area, and 41.8% of health care providers, which is statistically significantly higher ($p < 0.01$). More than one abortion had 42.8% of women. Two thirds of health care providers (64.1%) had more than one abortion. Considering that the group of health care providers is older than the group of women, age group analysis indicates that 57.4% of women aged 40-44 had an abortion. Whereas this percentage is statistically significantly lower in the case of health care providers and gynecologists of the same age - 40%. Nurses had an abortion in 41% of cases which is significantly more than the women.

Discussion

The use of contraception – The results of this research confirm the assumption that withdrawal is the most frequently used method of contraception in Serbia, and, since this method is also highly unreliable, this is the main cause of the high number of abortions. Serbia is among the countries with the highest abortion rate in Europe, which is the result of lack of knowledge about and prejudice toward modern, effective methods of protection from unwanted pregnancies (1, 2, 3, 4). Women and their partners believe that withdrawal is a natural method, with no health risks, and does not require a visit to the gynecologist's, counseling or any examination and tests. Health care providers refer to withdrawal in a significantly lower degree, because they understand its ineffectiveness. Only 3.8% of gynecologists suggested this method to women and 79.7% of health care providers never recommend this method. At the moment, 40.5% of women use withdrawal (as opposed to 14.5% of health care providers), and 70.5% of all women used this method at some point in their lives (46.4% of health care providers). Withdrawal is used in Germany in only 2.5-7.4% of cases (5),

8% in the USA (6), and 28.8% in Greece (7). A very small proportion of women in Serbia use COC (4.7%) and only every fifth woman has used COC once in her life. COC (8) is used most in five European countries (Germany, France, United Kingdom, Spain and Italy). Forty-one percent of women in Germany use hormonal contraception (9), 35% in France, 33.6% in Australia (10). The use of hormonal contraception among adolescents is 75% in the Netherlands and this country has the lowest adolescent pregnancy and abortion rates. All countries that have compulsory sex education in schools have a lower rate of abortions, while the rate of use of modern methods of contraception is high. Globally, in the world IUD is used in 21% of cases, whereas in Serbia, only 5% of women use it at the moment (up to now 13% of women and 36% of gynecologists used it). Urgent contraception was used by only 2% of women (although it was not recommended by any of the gynecologists) and 2.7% of health care providers. Adolescents use urgent contraception in 13.8% of cases in Serbia (11). At the time the research was conducted sterilization was not a viable option at the request of women, but only for medical indications, and this method is one of the most commonly used worldwide. Slightly more than half of women and health care providers have used a condom. It is used the most by the Chinese – 90.2%, then by the English – 80.2% (12). Japan is the country where condom is used the most by married couples. Three quarters of married couples who currently do not want to have children are using it (13).

Health care providers have hitherto in their lives used condom the most, followed by withdrawal, then periodic abstinence, and lastly IUD and hormonal birth control pills. Women have significantly more often used withdrawal than health care providers, and significantly less often effective methods – IUD and hormonal contraception.

Reasons for non-use of effective contraception methods according to women – the most common reason is concern that these methods are hazardous to health. Women still believe that these methods are not sufficiently effective. Furthermore, women are inadequately informed about them, believe that the feeling is not the same with them, that they interfere with the spontaneity of the intercourse and are complicated to use. The least

number of women (2.7%) states that the price of contraception is a negative factor. Health risks are listed as the reason for not using contraception by 71% of women in Finland (14) and 23% of women in Australia (10). Price is the reason for non-use of contraception in 12% of women in the USA (15).

Attitude toward modern and effective contraception (IUD and COC) – Only two thirds of health care providers have a positive attitude toward modern methods of contraception, but that puts them ahead of women. The encouraging aspect is that nearly all gynecologists at outpatient clinics, who provide counseling about contraception most often, have a positive attitude toward effective methods. However, the negative aspect is that less than one half of general practitioners have a positive opinion regarding these methods.

The influence of health care providers. Merely one half of women consult with the gynecologist about contraception, women from the urban area do this more often. Every other woman was recommended to use a condom, while one in three women received a recommendation for the IUD and COC. None were recommended to use urgent contraception, despite the fact that 80% of gynecologists claim that they recommend urgent contraception. Gynecologists who most frequently provide counseling regarding birth control often use methods that they recommend the least – withdrawal and periodic abstinence. On the other hand, they least frequently use effective, modern methods which they recommend the most (IUD and COC). The conclusion to be drawn from this is that gynecologists have an ambivalent attitude toward modern methods thus cannot be completely assuring in counseling. Gynecologists from Serbia recommend condoms more (89%) than the world average (50%) (5).

One half of health care providers believe that the use of contraception is somewhat harmful to health and complicated to apply. Gynecologists do not consider COC to be harmful to health, unlike one in five general practitioners and one in four nurses which brings us to the conclusion that they are insufficiently educated regarding hormonal contraception. Gynecologists have a more positive attitude toward modern methods of contraception than women; however, not even they use it to a sufficient degree (although they are ahead of women in this)

and have a significant number of abortions. Gynecologists in Russia most frequently recommend the IUD (59%) and COC (50%). Despite these being the most used methods, there still is a large number of abortions in Russia (16). These methods are also recommended and used the most in the Czech Republic and Slovakia but the number of abortions in these countries has lowered significantly in the past 20 years or so (17). Only 5.7% of general practitioners in Serbia provide counseling about contraception frequently, as opposed to 25% in Japan (18), and the USA where this percentage has increased to 41% of general practitioners (19). Gynecologists employed at University clinics in Europe, similarly to those in Serbia, do not provide counseling about contraception often (33%) (20).

Psychological personality traits. According to the locus of control, the respondents are in the middle between external and internal. Women with an internal locus of control and a stronger orientation to future and planning seek counseling with a gynecologist more often, use effective contraception more often and have fewer abortions. Women from the urban area have a more pronounced internal locus of control and future orientation and planning than women from the rural areas. Younger women have an external locus of control more often, while future orientation and planning is weaker among the youngest and oldest women. Internal locus of control is considered to be one of the most important determinants of effective contraception use (21, 22). Occurrence of pregnancy is left to chance by 20.2% of Australian females (10).

Influence of partner. More than one half of women make a decision regarding the use of contraception with their partners, who are, in nearly one half of the instances, against contraception, thus the number of women using effective contraception is decreased. Two thirds of male partners believe that the method of withdrawal is the best – it is available, with no health risks and is free. Partners of health care providers are against contraception in a lesser degree than women, while the influence of partners is greater among women in the rural area than in the urban area. Disagreement with a partner regarding contraception occurs in 10% of cases in the USA (15).

Influence of marital status. Marital status has influence on the choice and use of contraception. Married women use ineffective methods of contra-

ception (withdrawal and periodic abstinence) more often than unmarried women and the latter use condom more often than married women. The IUD is used more by married women, whereas single women use contraceptive pills more often. Contraception is used by 45% of married women in the world – USA and China 70%, Nigeria 6% (23, 24). Condom is used the most in marital relationships in Japan (13).

Influence of age. The use of condoms decreases as the age increases, while the use of periodic abstinence and intrauterine spirals increases with age. Withdrawal is used in similar percentages in all age groups. Younger women use birth control pills more often, while the youngest people use condom the most. Adolescents in Serbia use condom and combined methods – 84.2% (25). Turkish male students often use condoms (26).

Influence of place of residence. Women from the rural area have an external locus of control more often which implies less counseling with a gynecologist and less use of effective contraception. This is contributed to by their male partners who object to effective methods of contraception more often and make the decision regarding the use of contraception more frequently.

One in three women has had an *abortion*, and less than half of them have had more than one abortion. Two thirds of health care providers (female gynecologists or female partners of male gynecologists) with experience in abortion had more than one abortion. The analysis of the age group 40-44 shows that more than one half of women and less than one half of general practitioners and gynecologists had an abortion. Nurses had an abortion in 41% of the cases, which is significantly more than women. A study in Serbia shows that 61.8% of female gynecologists or the wives of male gynecologists have had an abortion, and two thirds (67.7%) have had more than one termination of pregnancy. (3, 4)

On the basis of previous data, it can be concluded that there are several obstacles on the road to the use of effective, modern contraception in Serbia. Merely one half of all women in need of contraception seek counseling with a gynecologist. One third of this half is given advice to use hormonal contraception (15%), for example. Two thirds of those women (10%) make the decision

about the method with their partners who are in 50% of the cases against these methods, which brings us to the percentage of about 4.5% plus 5% of women who make the decision by themselves. One half of this number abandon the idea because they have concerns regarding health risks, which, again, brings us to the fact derived from the study that only about 4.7% of women use hormonal contraception. It is necessary to react at several levels. Until sex education is introduced in schools, which essentially solves nearly the entire problem, campaigns should be started and women educated to go to regular controls and counseling with gynecologists. Gynecologists should constantly be reminded of health benefits of modern and effective contraception, although gynecologists in Serbia have performed well in this study. Other health care providers should be educated about these methods. Male partners should also attend counseling as they are in need of education as well.

Conclusion

Reliable and modern methods of contraception are used insufficiently, and the number of abortions is high in Serbia. Factors that influence these are as follows: negative attitudes and prejudice of women and health care providers toward contraception resulting from lack of knowledge; lack of counseling with a gynecologist; certain psychological components of personality in women; influence of partners; age; marital status. Comprehensive education is necessary – in schools, for women and their partners, and health care providers as well.

References

1. Sedlecki K, Rašević M. *The abortion issue in Serbia. The European Journal of Contraception and Reproductive Health Care* 2009; 14(6): 385-90
2. Kapamadzija A, Vejnovic T, Novakov A, Vukelic J, Bjelica A, Kopitovic V. *Reducing the number of abortions – possibilities and solutions – situation in Serbia 11th International Symposium „Interdisciplinary Regional Research” ISIRR 2010 HUNGARY – ROMANIA – SERBIA, Szeged 13-15 October, 2010*
3. Sedlecki K, Rašević M. *Ginekolozi i abortusno pitanje u Srbiji. Stanovništvo* 2007; 45(1): 33-45

4. Sedlecki K, Rašević M. Are Serbian gynaecologists in line with modern family planning? *The European Journal of Contraception and Reproductive Health Care* 2008; 13(2): 158-63
5. Finer LB, Henshaw SK. Abortion incidence and services in the United States in 2000. *Persp Sexual Reprod Health* 2003; 35-6
6. Speroff L, Darney P. *A Clinical Guide for Contraception*. Fourth edition, Philadelphia, USA; 2005: 3-5
7. Tountas Y, Dimitrakaki MC, Antoniou A, Boulamatsis D, Creatsas G. Attitudes and behaviour towards contraception among Greek women during reproductive age: a country-wide survey. *Eur J Obstet Reprod Biol* 2004; (116): 190-5
8. Skouby, SO Contraceptive use and behavior in the 21st century: a comprehensive study across five European countries. *The European Journal of Contraception and Reproductive Health Care* 2004; 9(2): 57-68
9. Oddens B. Women's Satisfaction With Birth Control: A Population Survey of Physical and Psychological Effects of Oral Contraceptives, Intrauterine Devices, Condoms, Natural Family Planning and Sterilisation Among 1466 Women. *Contraception* 1999; 59: 277-86
10. Richters J, Grulich AE, de Visser RO, Smith AM, Rissel CE. Sex in Australia: Contraceptive practices among a representative sample of women. *Aust N Z J Public Health* 2003; 27: 210-6,
11. Kapamadžija A, Vukelić J, Bjelica A, Stojšić V. Urgent contraception in adolescent age in Serbia, 10th ESC Seminar Unwanted pregnancy or abortion, 2009, Belgrade, 16
12. Condom use around the world—WHO statistics 2011. Available from www.who.int
13. Population Reports published by the Population Information Program, Center for Communication Programs, The Johns Hopkins School of Public Health, Baltimore, Maryland, USA 1999; 27(1) Available from (http://www.k4health.org/pr/h9/h9chap1_1.shtml)
14. Sihvo S, Hemminki E, Kosunen E. Contraceptive health risks-women's perceptions. *J Psychosom Obstet Gynaecol* 1998; 19: 117-25
15. Jones R, Darroch J, Henshaw S. Contraceptive Use Among U.S. Women Having Abortions in 2000-2001. *Perspectives on Sexual and Reproductive Health* 2001; 6: 294-303
16. Visser AP, Remennick L, Bruyniks N. Contraception in Russia: attitude, knowledge and practice of doctors. *Plan Parent Eur* 1993; 22(2): 26-9
17. Visser A, Uzel R, Ketting E, Bruyniks N, Oddens B. Practice, attitudes and knowledge of Czech and Slovak gynaecologists concerning contraception. *Plan Parent Eur* 1994; 23(1): 19-23
18. Kitamura K, Feters MD, Ban n. Contraceptive care by family physicians and general practitioners in Japan: attitudes and practices. *Fam Med* 2004; 36(4): 279-83.
19. Chuang CH, Freund KM. Emergency contraception: an intervention on primary care providers. *Contraception* 2005; 72: 182-6
20. Bajos N, Leridon H, Goulard H, Oustry P, Job-Spira N. Contraception: from Accessibility to efficiency. *Human Reproduction* 2003; 5: 994-9
21. Alves AS, Lopes MH. Locus of control and contraceptive knowledge, attitude and practice among university students. *Rev Saude Publica* 2010; 44(1): 39-44
22. Visser S. The relationship of locus of control and contraception use in adolescent population. *Journal of adolescent health care*. 1986; 7(3): 183-6
23. United Nations Population Division. *World Population Prospects. The 2002. Revision*, available from www.un.org/esa/population/unpop.htm 2003.
24. Mosher WD, Martinez GM, Chandra A, Abma JC, Willson SJ. Use of contraception and use of family planning services in the United States: 1982-2002. Advance data from Vital and Health Statistics 2004: 350
25. Kapamadžija A, Vejnovic T, Novakov Mikic A, Vukelić J, Kopitovic V, Bjelica A. Sexual knowledge, attitudes and practice of adolescents in Northern Serbia – are we making any progress? Follow up study 2000-2008. *J Reproduktionsmed Endokrinol* 2010; 7 (1): 106-11
26. Polat S, Yüzer S, Başer M. Turkish male university students' knowledge and attitudes about use of condom. *HealthMED* 2011; 5(3): 633 – 8

Corresponding Author
Aleksandra Kapamadžija,
Department of Obstetrics and Gynecology,
Medical Faculty,
University of Novi Sad,
Serbia,
E-mail: kapamagia@gmail.com

Human ischemia modified albumin can be a predictive biomarker for the detection of peripheral ischemia duration

Celal Yavuz, Ahmet Caliskan, Suleyman Yazici, Oguz Karahan, Orkut Guclu, Sinan Demirtas

Medical School of Dicle University, Department of Cardiovascular Surgery, Diyarbakir, Turkey

Abstract

Background: Human ischemia modified albumin (IMA) provides diagnostic and prognostic information for acute coronary ischemia. However, its role in peripheral ischemic disorders is unclear. The aim of this study is to detect the association between ischemia duration and the discriminator value of serum IMA levels in rat model with created peripheral ischemia.

Methods: Thirty-two male Sprague–Dawley rats were included in the study. The rats were divided into four equal groups. The rats in Group I were sacrificed to determine the basal serum values of IMA without any application. The rats in Group II, the sham group, were applied with simple femoral incision only. The rats in Group III and IV had their common femoral artery clamped with classic femoral incision. Blood samples were taken after 120 minutes of ischemia in Group III and after 360 minutes of ischemia in Group IV, respectively. The serum ischemia modified albumin levels were detected using the blood samples. The results were compared statistically.

Results: Obtained IMA levels were similar in the sham (Group II) and baseline (Group I) groups ($p>0.05$). The serum IMA levels were determined as 33 ± 4 (33) μL , 36 ± 9 (34) μL and 57 ± 19 (61) μL in Groups I, III and IV, respectively. High IMA levels were found in advanced ischemia duration. The increase in serum IMA levels with time was statistically significant as can be seen in Figure 1 ($p<0.05$).

Conclusion: Peripheral ischemic disorders can cause extremity loss if not treated immediately. In addition, delayed treatments may have fatal results. Therefore, timing is important in such cases. We suggest that serum IMA levels may be beneficial for the determination of ischemia duration in peripheral ischemia. They may also improve the predictive values of other standard biomarkers of ischemia.

Key words: Human ischemia modified albumin, peripheral ischemia, biomarker, treatment timing

Introduction

Acute critical ischemia is a severe obstruction of the major arteries. This condition can seriously reduce blood flow to the tissues. The duration of ischemia is an important determinant for the recovery of the basal cellular grade from organismal responses. Prolonged ischemia may result to irreversible tissue loss. Similarly, delayed treatment may cause fatalities due to the release of radicals into the circulation with reperfusion (1-3). Critic limb ischemia is such a condition. Failure to treat this condition immediately can result to major amputations. Conversely, if appropriate and timely revascularisation is performed, there may be a chance of saving the limb (4). Recent studies are investigating new biomarkers for the therapeutic or diagnostic process of acute peripheral ischemia (5, 6).

Ischemic conditions can cause the deterioration of the last amino terminal of the albumin structure, which contains a binding area for transition metals, such as cobalt, copper and nickel. This new variant of albumin is called ischemia modified albumin (IMA) (7). The usefulness of this biomarker is described in several *in vivo* and *in vitro* studies in ischemia before the onset of irreversible cardiac injury (8, 9). Current studies suggest that it may be beneficial to perform management of ischemic conditions in the emergency room (9). Some reports claim that IMA levels can increase peripheral ischemia and that they are sensitive to skeletal muscle ischemia (10). Reduced IMA levels have been noticed in exercised induced limb ischemia (11). Chronically elevated IMA levels in persistent limb ischemia have been mentioned in previous studies (10). However, the correlation

between IMA levels and acute peripheral ischemia duration still remains unclear.

We aim to investigate the correlation between acute peripheral ischemia duration and serum IMA levels in the rat model.

Materials and Method

Study Design

The study was designed as a randomised, controlled, single-blinded, interventional animal study. This study was approved by the Local Animal Ethics Committee and was conducted in accordance with the Animal Welfare Act and the Guide for the Care and Use of Laboratory animals prepared by the Local Animal Ethics Committee.

Animal Subjects

Thirty-two male Sprague–Dawley rats (aged 8 to 12 weeks), weighing 230 ± 30 g (mean $\pm$ standard deviation) and obtained from the Laboratory Animal Production Unit were used in the experiment. The rats were placed in a temperature ($22 \pm 2^\circ\text{C}$) and humidity ($50 \pm 5\%$) controlled room where 12-hour light/dark cycles were maintained for one week before the experiment was commenced. A standard diet and tap water were provided *ad libitum*. The rats were given only water 12 hours before starting the experiment procedures.

Study Protocol

The rats were randomised into four different groups of eight animals each. All operations were performed simultaneously for sample standardisation. We anaesthetised all subjects with ketamine (Ketalar, Pfizer) at a 130 mg/kg dose and xylazine (Rompun, Bayer) at a 20 mg/kg dose via an intraperitoneal line. Ketamine HCL (50 mg/kg) was used for the maintenance of anaesthesia. Breathing rate, pulse, oxygen saturation (sO_2) and body temperature were continuously monitored. A heating pad was applied during anaesthesia to maintain body temperature.

The first group (Group I) was separated in order to determine the basal values and normal range of ischemia modified albumin in the animal genus. Blood samples were taken at the start of the study. The second group (Group II), the sham group, underwent a classic femoral incision and blood samples were taken 30 minutes thereafter.

The common femoral artery was clamped during a classic femoral incision conducted on the rats in the third and fourth groups (Groups III and IV) and blood samples were taken after 120 minutes in Group III and after 360 minutes in Group IV, respectively. The blood samples were obtained within the critical six hours. The rats were sacrificed after the procedures were completed.

Laboratory Analysis

Each collected blood sample was immediately centrifuged at 4,000 rpm and $+4^\circ\text{C}$ for 10 minutes and then transferred into an Eppendorf tube. Samples were transferred on ice and kept in -70°C deep freeze until the end of the study, which was completed within one week.

Serum ischemia modified albumin levels were measured in all blood samples by a biochemist who was blinded as to which groups the animals came from.

IMA Measurement

The plasma IMA levels were determined using the enzyme-linked immunosorbent assay method (USCN Life Science Inc; Wuhan, China) as reported by Dikensoy *et al.* (12).

Statistical Analysis

The results were expressed in mean $\pm$ standard deviation (SD) and median. The peripheral ischemia parameters of the animal subjects were compared using a paired t-test. The Lilliefors test was also performed to check the normal distribution of the parameters. All statistical procedures were performed using SPSS software version 15.0 (SPSS Inc., Chicago, IL). A p value of 0.05 was considered statistically significant.

Results

The baseline value of IMA was detected as 33 ± 4 (33) μL in Group I. Serum IMA levels were detected as 34 ± 7 (34) μL in the sham group (Group II). Derived values were compared in each of the ischemia groups and the differences, according to base values, were evaluated. The serum IMA levels were determined as 36 ± 9 (34) μL and 57 ± 19 (61) μL in Groups III and IV, respectively. IMA levels were not significantly higher in Group III compared to the baseline values in Group

Table 1. Comparison of Serum IMA Levels in Each Group

	Group I Baseline (n: 8)	Group II Sham Group (n: 8)	Group III 2nd Hour PI* (n: 8)	Group IV 6th Hour PI (n: 8)
IMA**(μ/L)	33±4 (33)	34±7 (34)	36±9 (34)	57±19 (61)
p***		0.572	0.427	0.015

*PI: Peripheral Ischemia, **IMA: Ischemia modified albumin, ***p< 0.05 is significant

I ($p>0.05$), although the higher values of serum IMA levels were obtained than others. However, the increase were significantly higher in Group IV ($p<0.05$) compared to the other groups (Table 1).

The peak values of IMA were obtained in Group IV. This elevation was statistically significant as a scatter graphic in Figure 1.

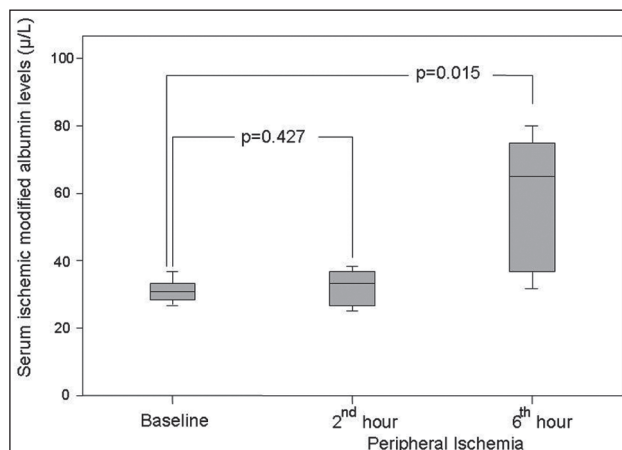


Figure 1. Alterations in serum IMA levels in early and advanced periods of peripheral ischemia

The manner of obtaining IMA values was similar in the sham (Group II) and baseline (Group I) groups. This means that the serum IMA levels were not affected by simple femoral incision ($p=0.572$)

Discussion

Critical limb ischemia is the most common cause of extremity loss according to the presented reports (13). In addition, it may have fatal outcomes, with 15 to 25% mortality rates. Spending time is important after presentation to intervene for the improvement of the outcomes (14). Therefore, the detection of ischemia duration is important. It requires early diagnosis and urgent intervention (14). Delayed interventions can lead to the development of Haimovici's myoneuropathic-metabolic syndrome (15). Moreover, intervention

to prolonged ischemia is as life threatening as not interfering with the condition.

New biomarkers have been investigated for the management of ischemic conditions in the literature. Some of them are about the determination of hypoxic condition while others are related with ischemia-reperfusion injuries (16, 17). However, the biomarker descriptive studies for the detection of ischemia duration are still insufficient.

Recent studies have been focused on the changes in albumin structure during ischemia. The last amino terminal of albumin is impaired. This terminal generates a binding area for transition metals. This new variant of albumin is called ischemia modified albumin (IMA) (7-9). IMA is a recently identified valuable ischemic biomarker for the diagnosis and management of acute coronary syndromes (8, 9). Numerous studies explored this marker in peripheral ischemic conditions. Roy *et al.* reported that IMA is significantly reduced immediately after exercise-induced leg ischemia in patients with peripheral vascular disease (11). The produced lactate from the skeletal muscle is blamed for this reduction (11). Gunduz *et al.*, on the other hand, reported that serum IMA levels were significantly reduced in limb ischemia (18). They claimed that IMA is 81.8% sensitive and 81.8% specific in patients with clinically severe lower limb ischemia (18). Marcus *et al.* reported that IMA levels elevated shortly after peripheral vascular intervention. They specified that IMA levels were strongly associated with acute plaque disruption/rupture (19). Existing studies were conflicting as shown. We detected that the IMA levels were elevated with prolonged ischemia duration in the rat peripheral ischemia model. The increase of IMA levels was statistically significant in Group IV ($p=0.015$), where blood samples were taken after 360 minutes compared to the other groups (Table 1). Lower elevation of IMA levels were detected in Group III, which was insignifi-

cant ($p=0.427$). The results of our study support the report of Gunduz *et al.*, which stated that IMA levels increase during peripheral ischemia.

The conflicting results of our experiment indicate that further studies are required for the detection of definitive prognostic or descriptive value of serum IMA levels for peripheral ischemia duration. However, the results confirmed that IMA levels may be beneficial for the detection of prolonged ischemia duration. In addition, monitoring the serum IMA levels may be an appropriate biomarker for the estimation of the efficacy of clinical approaches.

References

1. Collard CD, Gelman S. Pathophysiology, clinical manifestations, and prevention of ischemia-reperfusion injury. *Anesthesiology*. 2001; 94(6): 1133–8.
2. Tarantini G, Cacciavillani L, Corbetti F, Ramondo A, Marra MP, Bacchiega E. *et al.* Duration of ischemia is a major determinant of transmural and severe microvascular obstruction after primary angioplasty: a study performed with contrast-enhanced magnetic resonance. *J Am Coll Cardiol*. 2005; 46(7): 1229–35.
3. Al-Mubarak HA, Alamri TM, Aljabab SA, Atteya M, Quan A, Teoh H. *et al.* Effects on duration of post-operative ischemia and patterns of blood flow recovery in different conditions of mouse hind limb ischemia. *Vasc Cell*. 2011; 3(1): 14.
4. Beard JD. Chronic lower limb ischemia. *West J Med*. 2000; 173(1): 60–3.
5. Smadja DM, Duong-van-Huyen JP, Dal Cortivo L, Blanchard A, Bruneval P, Emmerich J. *et al.* Early endothelial progenitor cells in bone marrow are a biomarker of cell therapy success in patients with critical limb ischemia. *Cytotherapy*. 2012; 14(2): 232–9.
6. Fadini GP, Losordo D, Dimmeler S. Critical reevaluation of endothelial progenitor cell phenotypes for therapeutic and diagnostic use. *Circ Res*. 2012; 110(4): 624–37.
7. Bar-Or D, Lau E, Winkler JV. A novel assay for cobalt–albumin binding and its potential as a marker for myocardial ischemia—a preliminary report. *J Emerg Med*. 2000; 19: 311–315.
8. Dominguez-Rodriguez A, Abreu-Gonzalez P. Ischemia-modified albumin: we are ready for use in the emergency room? *Int J Cardiol*. 2011; 151(2): 247.
9. Sbarouni E, Georgiadou P, Voudris V. Ischemia modified albumin changes—review and clinical implications. *Clin Chem Lab Med*. 2011; 49(2): 177–84.
10. Lippi G, Montagnana M. Ischemia-modified albumin in ischemic disorders. *Ann Thorac Cardiovasc Surg*. 2009; 15: 137.
11. Roy D, Quiles J, Sharma R, Sinha M, Avanzas P, Gaze D. *et al.* Ischemia-modified albumin concentrations in patients with peripheral vascular disease and exercise-induced skeletal muscle ischemia. *Clin Chem*. 2004; 50(9): 1656–60.
12. Dikensoy O, Celik N, Kul S, Gogebakan B, Bayram H, Light RW. Ischemia modified albumin in the differential diagnosis of pleural effusions. *Respir Med*. 2011; 105(11): 1712–7.
13. Jordan RW, Marks A, Higman D. The cost of major lower limb amputation: a 12-year experience. *Prosthet Orthot Int*. 2012 DOI: 10.1177/0309364612441489.
14. Lee WS, Lee KJ, Ryu WS. Acute embolic occlusion of the left common iliac artery treated with intra-arterial thrombolysis and percutaneous thrombectomy. *Korean J Intern Med*. 2009; 24(2): 153–5.
15. Haimovici H. Muscular, renal, and metabolic complications of acute arterial occlusions: myonephropathic-metabolic syndrome. *Surgery*. 1979; 85(4): 461–8.
16. Brahimi-Horn MC, Ben-Hail D, Ilie M, Gounon P, Rouleau M, Hofman V. *et al.* Expression of a Truncated Active Form of VDAC1 in Lung Cancer Associates with Hypoxic Cell Survival and Correlates with Progression to Chemotherapy Resistance. *Cancer Res*. 2012; 72(8): 2140–2150.
17. Sadayappan S. Cardiac myosin binding protein-C: a potential early-stage, cardiac-specific biomarker of ischemia-reperfusion injury. *Biomark Med*. 2012; 6(1): 69–72.
18. Gunduz A, Mentese A, Turedi S, Karahan SC, Mentese U, Eroglu O. *et al.* Serum ischaemia-modified albumin increases in critical lower limb ischaemia. *Emerg Med J*. 2008; 25(6): 351–3.
19. Hacker M, Hoyer HX, la Fougère C, Akcakoyunlu E, Schuhmann C, Förster S. *et al.* Effects of peripheral vascular intervention on ischemia-modified albumin. *Coron Artery Dis*. 2007; 18(5): 375–9.

Corresponding Author

Celal Yavuz,
Medical School of Dicle University,
Department of Cardiovascular Surgery,
Diyarbakir,
Turkey,
E-mail: celalyav@hotmail.com

Case study: school experience of children with attention deficit hyperactivity disorder

Olivera Knezevic-Florici¹, Sladjana Zukovic¹, Stefan Ninkovic¹

¹ Department of pedagogy, Faculty of Philosophy, University in Novi Sad, Serbia

Abstract

Understanding subjective school experiences of children with attention deficit hyperactivity disorder (ADHD), as well as educational experiences of their mothers is the aim of this paper, as well as the interest of the author. In the research of case study draft eight children with ADHD and their mothers participated (included in work of the Clinic of developmental paediatrics, Novi Sad, Serbia). Data are collected by two unstructured interviews constructed for the needs of this study. Material collected is processed by procedures of quantitative analysis. The most striking finding of this study shows that mothers of children with ADHD are familiar with models of educational processes that are adapted to ADHD symptoms, which should be a basis in education of teachers for work with ADHD children. Analysis of material collected has also shown that teachers by their behaviour (criticism and punishments) contribute negative experiences of hyperactive children at school. In that sense, familiarity of teachers with ADHD children's experiences could contribute to redirecting of teacher's attention to creation of school environment that would facilitate educational success of children with ADHD.

Key words: ADHD, children, parents, teachers, education.

Introduction

Attention-deficit hyperactivity disorder is a label for most widely present behavioural disorder in childhood and adolescence (1). ADHD is a cognitive and behavioural disorder whose manifestations are high level of attention-deficit, impulsivity and hyperactivity (2). Frequency of ADHD in school population moves from 3 to 7% (3). Disorder is 4-5 times more frequent in case of boys, while in older ages the ratio of genders is lower.

In the last two decades, it has come to significant progress in understanding the nature of this type of

disorder. However, in comparison with achievements of biological and cognitive deficits that cause ADHD, studies of social and interpersonal aspects of ADHD are relatively neglected (1). Having this in mind, there is a clear need for a better insight in impacts of ADHD on academic and social life of children, by an insight into parents' perception of ADHD. As one of the authors in this field points out (4), interest of future researches will be aimed to issues how the disorder affects everyday life of a child.

With the aim of understanding school experience of children with ADHD and their parents, we have applied the design of case study in this research. First part of the paper is dedicated to considerations of ADHD nature and etiology of disorder. In the second part of the paper, we have shown the results of case study on school experiences of pupils with ADHD, as well as educational experiences of their mothers. Finally, the last part of the paper refers to discussion of results aimed at performing pedagogical implications and improvement of teaching process with ADHD children.

Etiology of ADHD: Current state of the science

Most authors agree that heterogeneity of ADHD expression points to its multi-causal nature (3). Although there are standpoints claiming that ADHD is primarily genetically determined (1), all attempts of setting aside unique, universal cause of disorder were unsuccessful. Social, clinical and behavioural complexity of ADHD has aimed scientific researches towards development of etiological models which in different way attempt to connect genetic, biological and social factors.

Many researchers accept the standpoint that key element of ADHD is *inability of behaviour inhibition* (2). In other words, when children with ADHD do something which does not include the ability of behaviour inhibition, stimuli from environment will not bother them more or less than other children. Neuropsychological studies have shown that behaviour inhibition is related to four executive neuropsychological

abilities that are called executive functions. *Working memory* enables retaining of events in consciousness and performing the activities based on them. From this function, the term of time also results, more precisely the feeling that the time passes, as well as understanding verbal instructions. *Inner speech* enables thinking about own behaviour prior to its performance; underdevelopment of this function results in impulsiveness in behaviour. *Self-regulation of emotions and level of excitation* provides assuming the control and self-regulation of motivation, as well as participating in behaviour that is purposeful. *Reconstruction* includes combination of pieces of information which we communicate to other people; it refers to speed, accuracy and fluency by which certain cognitive content turns into messages that are addressed to other people.

Although studies in the last decade were aimed at strengthening the positions mentioned, latest findings show that ADHD complexity is mediated by different combinations of genetic and social factors (3). One of alternative understandings is offered by transactional model of developmental psychopathology (1) which stresses the importance of situational circumstances and their impact on social behaviour. According to that model, on one end of continuum there are children in case of whom hyperactivity is dominantly determined by genetic factors of risk, with relatively weak contributions of social factors (family, school, peers). On the other end of continuum, there are high risk social environments which, in combination with minimal child's predispositions, function as primary determinant of ADHD symptoms.

This theoretical orientation allows the assumption that social environment does not have a causal impact on ADHD, but on development of disorders that are related to it (1). This model of explanation assumes that interaction of ADHD state with social circumstances can contribute to development or prevention of problems in behaviour that are usually related to hyperactive children. For example, it is known that symptoms of ADHD child can seem as a "trigger" for aversive parental actions (bad supervision of child's behaviour, inconsistent disciplinary processes) that contribute to the development of oppositional behaviour, depression, dyslexia etc. (3). In those cases, persons with ADHD are exposed to specific type of risk for appearance of other types of disorders in social behaviour. In this way, social

factors become related to ADHD, not as its cause, but as impacts that follow and maintain its flow.

In accordance with assumptions of this theory of relationship between social environment and hyperactive child, attention needs to be aimed at all segments of intervention measures and activities that are aimed at successful social integration of children with ADHD or those in case of which there is a risk of that type of disorder. Therefore, in this model, the need for good management of the process of educating ADHD children is particularly expressed (which includes both child and parents and teachers), so all the elements of social field, at least the closest ones, will become „big social classroom“.

Review of ADHD treatments

It is unequivocally that etiological complexity of attention disorder with hyperactivity causes professional, most frequently pedagogical-psychological treatment. The very treatment of children who manifest emotional and/or disorders in social behaviour sets its ethical boundaries. Diversity of access in treatment of children and adolescents with ADHD comes from different theoretical standpoints and scientific cognitions on causes of disorders.

Although exceeded medicalization of ADHD is criticized from many aspects, pharmacological access is still widely present. It is estimated that about 85 % of children in which ADHD has been diagnosed takes some kind of medicine (5). However, although pharmacological therapy significantly improves concentration and reduces impulsiveness, there are evidences that its effects are short-term, as well as that they do not lead to the improvement of academic success of hyperactive children, i.e. their social skills (6). Purdie et al. (6) mention the finding that pharmacologically treated hyperactive children do not go to college more frequently, nor they take part in delinquent behaviour in relation to ADHD children who were not included in medicament therapy. It is significant to mention that as side effects of pharmacological treatments, particularly often there appear fatigue and confusion, insomnia, muscle tension, trembling (6). Listed and many other controversial factors have contributed to the fact that there are still no clear ethical standpoints towards the application of psychotropic treatments in treating ADHD.

Alternative etiological standpoints, although they do not deny the significance of medicament tre-

atments, primary significance is attributed to social factors and stress is on psychosocial interventions aimed at children, parents and teachers. Moreover, it points out that psychosocial interventions are efficient regardless whether a child simultaneously takes part in pharmacological therapy (6). One of the most frequent forms of psychosocial treatment are *parent trainings* that educate parents in techniques of recognizing and manipulating positive and negative consequences of ADHD. Parent trainings are aimed towards the development of skills of leading a family, monitoring and supervision of children's behaviour, mastering the skills of recognition and encouragement of positive behaviour, as well as reactions to unacceptable behaviours of children.

The second significant group of psychosocial interventions are those aimed at school, i.e. management of a class. The most famous technique from this group, used for changing unfit behaviour of hyperactive children in school, are different forms of *token economy*. Main principle of this technique is that a child obtains agreed number of tokens for daily agreed manifestations of behaviour, which are then exchanged for some kind of reward. The essence of the procedure is for a child to voluntarily decide whether it will try, and motivation for that effort is maintained by token encouragement. Negative token encouragement is carried out in a way that a child loses the tokens each time it manifests undesired behaviour (for example, interrupts writing the assignment in order to deal with something else). This method is also known by the name „response cost“.

The second significant group consists of behavioural-cognitive techniques, which integrate two perspectives: cognitive and behavioural. Their standpoint is that child's emotions and behaviour depend on the way in which it interprets the situation. One of the most famous techniques is practicing the self-instructions. Technique is applied by: a) model solves a problem loudly, giving instructions to itself, b) child executes the same problem and model provide verbal instructions, c) child executes a task by whispering the instructions, d) child executes a task by using inner speech.

Method

There are almost no scientific-research papers in our environment on the problem of school experi-

ence of children with ADHD, although it is known that it is the most present cognitive and behavioural disorder in the period of childhood and adolescence. Our interest is aimed at understanding the experiences of the mothers of hyperactive children, as well as school experience of their children with ADHD. We tended to get closer to experiences of participants and their subjective constructions, starting from the attitude that process of studying personal narratives is reciprocal process that does not diminish the distance between researchers and participants.

Participants

This research included eight children with ADHD, 2 girls and 6 boys. Age of the children was from 7 to 10 years. In addition, research included mothers of those children, who were included in program of the Clinic of developmental paediatrics which acts within the Service of health protection of Novi Sad (Serbia). Age of the mothers was from 31 to 40.

Research design

Having in mind that our research is based on studying the manners in which students with ADHD experience their own experiences at school, design of *case study* was applied in the research. Although case study most frequently refers to the individual, case is not always related to one person, it can be one school, class within a school, family, as well as programme and certain relations and processes (7). Case, i.e. subject of our research, is a group of students with ADHD and their mothers.

Instruments

For the needs of this study, two interviews were constructed with questions of open type: one for students and the other for mothers. Questions in interview meant for mothers were: What kind of attitude towards the child or what kind of behaviour strategy helps your child the most in performing everyday activities?; Is there a way in which you can support (prolong) the attention and concentration of your child?; How should a teacher react to unexpected, different behaviour or deviation from expected behaviour of your child?; What else is important in order to draw attention of teachers, and it concerns your child?

For the needs of the research, an interview meant for examination of school experience of children is also constructed. The questions were:

What would help you to keep up with teaching activities more carefully?; In what ways could the teacher help you to perform teaching activities more successfully?; What is the biggest problem in teaching process to you personally?; Is there something that makes you feel bad at school?

Having in mind that our study is of explorative character, we have chosen a qualitative analysis of the material collected. Analytical process that is classified in qualitative thematic analysis, which implies search for dominant patterns in material collected, is used (8). In order to identify the themes that repeat in participants' opinions, their answers are classified by similarities and differences. During analytical process, comparison between our categories and initial answers of students in research was performed.

Results

The first task of our study was to establish the type of relationship of mothers towards the disorder of their children. More than a half of mothers have said that they know that in case of ADHD children it is important to insist on routine, structure (clear schedule of activities) and predictability of activities and actions, as well as clear communication accompanied by simple, positive and consistent instructions. There is an answer of one mother which illustrates all the above-mentioned:

In our home there are problems, but what helps our child the most in that moments is everyday routine. For example, it does the homework every day at the same time, has lunch at the same time, goes to bed at the same time. Consistency in daily activities provides the child to focus on something without worrying. When it comes to encouragement of attention and concentration of ADHD child, all mothers have pointed out how important it is to enable for a child to perform two activities simultaneously, as well as exposing a child to certain smells. Here is the answer of one mother:

Smell can encourage their concentration. I have discovered how the scent of lemon or peppermint helps a lot... Daughter of my friend is a „drummer“, one of those who constantly tap the fingers when doing something else. My friend has solved it by buying her a ball for release of stress which she squeezed while she was learning. I am planning to do the same thing.

It is known that difficulties in maintaining the attention, hyperactivity and impulsiveness are often not taken into consideration as a part of ADHD, due to which environment often sets too high and inadequate requirements before a child. Findings of the research show that all the mothers point out that ADHD children do not mean anything bad when they behave different than expected and that they believe such behaviour is not a consequence of children's choice.

Many children do not mean anything bad when they are moving and fidgeting. Accept different behaviour instead of fighting against it. It is probably not realistic to expect that children, for example, stand during the class, but perhaps there are some other ways of including the movements in teaching.

Above-mentioned statements of the mothers of hyperactive children point to difficulties with self-control and self-direction of children ADHD are not an issue of child's choice, but an issue of neurological state of a child. Almost all mothers point to this in answering the question how should a teacher react to unexpected behaviour of their child.

Results show that mothers believe that the biggest problem for children with ADHD is the lack of time, i.e. inability to orient in time perspective, which is in accordance with assumptions that ADHD delays the development of this executive function which creates difficulties for a child in sense of time.

My son has no sense of time, i.e. he cannot estimate how much time he needs to do something. For example, my son can read his comic books stunningly fast. Of course, it is not the same when he needs to read something for school.

In the second phase of research, we attempted to explore the experiences of school children with ADHD, i.e. their experience in interaction with teachers. Children with ADHD interviewed, such as their mothers believe that it would mean them a lot if during the learning in teaching they could simultaneously perform another activity.

I need to touch something because it helps me to concentrate on the things that are asked from me. I do not know how could I do that without going on my teacher's nerves.

Children mention that their problem in teaching process is that they often do not understand the teachers and thus they cannot answer their requirements. These findings show that due to lack of

attention, hyperactive child often hears only some parts of a message that a teacher sends him and it is not able to retain the information sufficiently in order for them to obtain their meaning. In case of children with ADHD, this is not a difficulty in reading or listening, but in working memory and inner speech. Here is a part of the answer that illustrates the above-mentioned:

I really find it difficult to listen many things. Sometimes I hear a few words, but not what should follow, and then anyway I forget the first part of the task. Every time I get several tasks, it confuses me.

Analysis of data collected confirms that children believe that it would mean them a lot if they had more time in performing teaching tasks. ADHD children live in the moment given, so Barkley (2) justifiably refers to ADHD as *time myopia*. This explains why ADHD children do everything in the last minute, why they are always late. Most children have replied that it is very important for them to timely obtain the warning about how much time they have left. One of the boys said:

I really need some warning when I need to stop working. I need to know how much time will something take.

Children with ADHD cannot predict the events in future and direct their behaviour in accordance with it. Having in mind that children with ADHD function in terms “right now” and “now”, postponed encouragement such as grade will not have a big impact on them – for them a reward needs to be contained in the task itself.

I find it difficult to wait my turn. I wish if the teacher could immediately say whether I do something good or bad. I need to know that.

Behaviour of ADHD child is often criticized and punished at school. Analysis of material collected shows that ADHD children often feel bad at school. There are numerous reasons for that. Answers of more than a half of children illustrate some of them:

Because the teacher always yells at me. I know that I do stupid things and that it is wrong, but I do not do it to upset him. I don't know why am I doing it. I am not really good at math and that stuff. Although sometimes I hit something, majority of my tasks are mottled by a red pen.

One of the answers of students points out that some teachers do not understand the inability of children with ADHD to concentrate.

I don't like to sit next to the people or things for which I know they will distract me. I cannot manage not to pay attention to the people who sit next to me or something I see through the window... often some things in the walls encourage me to constantly look at them.

This finding is in accordance with recommendations that hyperactive child should sit in the first row, because there it will the least be distracted by actions in class and there is the smallest possibility of interaction with other students during the teaching.

Discussion

Until now, relatively small number of studies dealt with knowledge of teachers and parents on ADHD, i.e. relation between their knowledge and behaviour. On the other hand, main source of information on this type of disorder for the parents is school system (9) so the consequence is that teachers often inaccurately inform the parents.

The most striking finding of this study is that mothers of ADHD children are familiar with models of procedures that are adapted to ADHD symptoms, which is in contrast with findings of some previous studies in which it was established that mothers were not sufficiently informed (10). Most mothers find it very important to provide a clear structure and predictability of daily activities for ADHD children. In addition, mothers have expressed their familiarity with the fact that their children have difficulties when orientating in time.

In this study, it is established that children with ADHD experience negative experiences in school, which was also pointed out by previous studies (9). It is usual to assume that those difficulties are a consequence of nature and symptomatology of their disorder. For example, underdevelopment of the functions of working memory and inner speech causes difficulties in understanding and following instructions of teachers (2). However, analysis of material collected has shown that teachers contribute to the negative experiences of hyperactive children by their actions (criticism and punishment). This points to the fact that teachers do not understand sufficiently the complex etiology and phenomenology of ADHD, most likely because child's behaviour is estimated through requirements that educational system sets before all the participants.

Having in mind the fact that they will most likely teach the students with ADHD, teachers need a comprehensive training on ADHD in order to prevent their wrong attributions of ADHD children's actions. For example, if a teacher knows that ADHD is primarily a neurologically caused disorder, he will not start from the assumption that a child is a source of problems which can prevent their wrong actions.

Limitations of the study

All the mothers that took part in this research attend the programme of the Clinic of developmental paediatrics. Therefore, it is justified to assume that new experiences and perceptions of their children's disorders are not equal to perceptions of parents who do not cooperate with the Clinic. Actually, it is possible that parents who do not cooperate with the institution do not see ADHD of their children as a disorder, but as normal, transient developmental phenomenon, which does not require a special treatment. The need for acquiring an insight into perceptions of those parents who do not look for institutional help and who independently face the behaviour and problem of their children.

Conclusions

This study, as many others, has shown that school and particularly the classroom represent a place of hardship for children with ADHD. Hyperactivity, lack of attention, impulsiveness are the characteristics that represent an obstacle in requirements and expectations of teachers. It is known that comorbidity in case of ADHD is intensive and that this disorder is often accompanied by other disorders such as depression, dyslexia, oppositional behaviour that additionally interfere with academic success of children with ADHD (4).

Due to current tendency towards inclusive education, teachers and professors assume the responsibility for students with ADHD. It is very important that the teachers understand the specific way in which a ADHD child functions, as well as to be better familiar with confirmed teaching strategies with children that are hyperactive and/or inattentive. In addition, familiarity of teachers with parents' experiences with ADHD children can contribute to redirection of

attention of teachers on creating the environment that stresses their "strong sides". Transactional, two-way model encourages the cooperation between school and family, insists on division of responsibility for child's learning. Through the collaboration, school-family and support of the community, we can improve the relationship between children and school environment and thus increase the chances for better school success of children with ADHD (11).

References

1. Johnston, C., Mash, E. *Families of children with ADHD: Review and recommendation for future research. Clinical Child and Family Psychology Review.* 2001; 4: 183-207.
2. Barkley, R. A. *Behavioral inhibition, sustained attention, and executive functions: Construing a Unifying Theory of ADHD. Psychological Bulletin.* 1997; 121: 65-94.
3. Singh, I. *Beyond polemics: science and ethics of ADHD. Nature Reviews Neuroscience.* 2008; 9: 957-964.
4. Harpin, V.A. *The effect of ADHD on the life an individual, their family, and community from preschool to adult life. Archives of disease in childhood.* 2005; 90: 2-7.
5. Chronis, A. M., Jones, H. A., Veronica, V. L. *Evidence-based psychosocial treatments for children and adolescents with attention-deficit/hyperactivity disorder. Clinical Psychology Review.* 2006; 26: 486-502.
6. Purdie, N., Hattie, J., Carrol, A. *A review of the research on interventions for ADHD: What works best?. Review of Educational Research.* 2002; 72: 61-99.
7. Ristić, Ž. *O istraživanju metodu i znanju. Beograd: IPI, 2006.*
8. Creswell, W. J. *Qualitative inquiry & research design: choosing among five approaches. London: SAGE, 2007.*
9. Kos, J. M., Richdale, A., L., Hay, D. A. *Children with Attention Deficit Hyperactivity Disorder and their Teachers: A review of the literature. International Journal of Disability, Development and Education.* 2006; 53: 147-160.
10. Ghanizadeh, A. *Educating and counseling of parents of children with attention-deficit hyperactivity disorder. Patient Education and Counseling.* 2007; 68: 23-28.
11. Jurin, M., Sekušak-Galešev, S. *Poremećaj pozornosti s hiperaktivnošću-multimodalni pristup. Pediatrica Croatia.* 2008; 52: 1-12.

Corresponding Author

Olivera Knezevic-Florico,

Faculty of Philosophy,

University in Novi Sad,

Serbia,

E-mail: florico@ff.uns.ac.rs

Thromboelastographic comparison of the effects of different fluid preloading regimens delivered before spinal anesthesia

Irsat Ozen, Turkan Togonal, Mustafa Said Aydogan, Mehmet Ali Erdogan, Hamza Nakir, Nurcin Gulhas, Huseyin Ilksen Toprak, Mehmet Ozcan Ersoy

Department of Anesthesia and Reanimation, Faculty of Medicine, Inonu University, Turkey

Abstract

Introduction: Various fluids used for preloading purposes prior to spinal anesthesia. Coagulation disorders can occur due to use of those fluids at large volumes [1]. We aimed to compare the impact of different preloading fluids over coagulation parameters.

Method: Sixty-eight patients of ASA I-II physical status who were aged between 18 and 75 years, and scheduled for orthopedic surgery under spinal anesthesia, were included in the study. Prior to the spinal anesthesia, preloading was carried out by RL in Group R (n=16), HES (130/0.4) in Group H (n=16), polygeline in Group P (n=16), and succinylated gelatin 7 ml/kg in Group S (n=16). RL was used as the maintenance fluid in all the groups. Thromboelastography, CBC, PTT, aPTT, fibrinogen values were assessed at baseline and 2 hours.

Results: Groups P and S displayed significantly prolonged PTT values. While Groups R and P showed significantly prolonged PTT-INR values, groups R and H exhibited significantly prolonged aPTT values. Groups R, P, and S demonstrated significant decreases in TEG parameters including R, K, CI, and TMA. The increase in α angle was significant in groups R and S.

Conclusion: Fluid preloading with HES was not found to affect the coagulation parameters, however, polygeline and succinylated gelatin were observed to cause moderate hypercoagulation. Therefore, we believe that HES may be preferred over succinylated gelatin and polygeline in cases with hypercoagulability.

Key words: Hypercoagulability, thromboelastography, preloading fluid, spinal anesthesia.

Introduction and objective

The optimal dose of preloading fluids is a focus of ongoing discussion [1,2]. When used at large volumes, they have been shown to have a dilution effect over blood coagulation parameters [3,4]. Disruption of coagulation factors is an important event because it may lead to thromboembolization and hemorrhage particularly in cases with coagulation disorders or in patients with a history of postoperative immobility [5,6]. Clinical and in vitro studies show that the use of colloids and crystalloids including RL, is associated with results involving hypercoagulation and hypocoagulation. While it is likely that the amount of the administered fluid and coagulation tendency play determinative roles in these results, it is also remarkable that cases demonstrating increased coagulation following fluid loading are generally orthopedic cases [7-9]. In this study, we aimed to compare the effects of various colloids, used as preloading fluids in patients about to receive orthopedic surgery under spinal anesthesia, over coagulation parameters with those of Ringer's lactate by thromboelastography. So, we suggest to describe which fluids should be used in cases with hypercoagulable state.

Material and method

Ethical approval for this study "Thromboelastographic Comparison of the Effects of Different Fluid Preloading Regimens Delivered Before Spinal Anesthesia" (Ethical Committee N° Inonu University 2009/77) was provided by the Ethical Committee of İnönü University Hospitals, Malatya, Turkey (Chairperson Prof Ayse Kafkasli) on 27 October 2009. Following provision of informed writ-

ten consent, 68 adult patients of American Society of Anesthesiologists physical status grade I and II, who were aged between 18 and 75 years, and scheduled for orthopedic elective hip replacement surgery by the department of orthopedics, were included in the study. Exclusion criteria were known coagulation disorders, prothrombin time less than 85%, known liver or renal diseases. Our study design was of prospective and double-blind character. The cases were divided into 4 groups in a randomized fashion: Group R, Ringer's Lactate (RL); Group H, HES 6% (130/0.4); Group P, polygeline; and Group S, succinylated gelatin. All patients received regional anesthesia with hyperbaric bupivacaine 0.5% (spinal anesthesia 2.5–3 mL). Patients were actively warmed with fluid warmers and a convective warming system. Before spinal anesthesia was administered, all patients received 500 mL of RL to prevent hypotension associated with neuronal block. While calculating the pre-existing fluid deficit, patients were regarded as fasting for the last 8 hours. Hourly fluid requirement was recognized as 4 ml/kg/h for the first 10 kg, 2 ml/kg/h for the next 10 kg, and 1 ml/kg/h for each subsequent additional kg. Half of the fluid deficit was delivered within the first hour, while the other half was administered over the next 2 hours. Fluid loss at the operation site was considered as 4 ml/kg/s and it was replaced throughout the surgery. Fluid deficits associated with the hemorrhages were completely substituted by the corresponding preloading fluid of each group. Total blood volume was assumed as 65 ml/kg in women and 75 ml/kg in men; hemorrhages above 20% of total blood volume were replaced with erythrocyte suspension. Patients requiring administration of erythrocyte suspension were excluded from the study. In cases where the operation ended early, fluid replacement performed due to fasting, was continued. The follow-up of the cases was realized by an anesthesiologist blinded to the study. Prior to the anesthesia, blood samples, collected from were assessed with thrombelastography (TEG) before the surgical procedures and fluid resuscitation. This TEG trace is described by specific variables. Reaction time (r) is the interval between the start of the recording until an amplitude of 2 mm is reached (normal value 12.0 (2.3) mm). It reflects the function of the coagulation factors. Coagulation time (k) is defined as the time interval from the end

of r until the amplitude of the TEG tracing reaches 20 mm (normal value 4.2 (1.6) mm); k is influenced not only by coagulation factors but also by fibrinogen and the number and function of platelets. Maximum amplitude (MA) of the TEG tracing reflects clot strength as a function of platelets and fibrinogen (normal value 63.5 (4.5) mm). The angle α is formed by the slope of the TEG tracing from the r to the k value and is, similarly to MA, influenced by the function of platelets and fibrinogen (normal value 60.2 (6.7) °). Clot lysis can be described by the clot lysis index (CLI), defined as the amplitude of the TEG trace at 60 min after MA (A60) divided by MA ($CLI = A60/MA \times 100, \%$) or by Ly30 and Ly 60. The fibrinolysis indexes, Ly30 and Ly60, computed by the current TEG device, are defined as the percentage reduction of the computed area under the curve 30 and 60 min after reaching MA (normal value for Ly30 $\leq 7.5 \%$ and Ly60 $\leq 15 \%$). All normal value apply to plastic cups and plastic pins with 1% celite activation. The temperature of the TEG was maintained at 37.0°C. Each group received their corresponding preloading fluid at 7 ml/kg dose for 30 minutes. Two hours after the fluid preloading, second blood sample was obtained from the catheter in the other arm; CBC (Beckman Coulter-780 analyzer), PTT, aPTT, PTT-INR, fibrinogen (Dade Behring BCS XP Analyzer), and TEG (5000 analyzer) were evaluated according to the same protocol.

The results were analyzed by SPSS 16,0 package program and expressed as mean and frequency values. Following assessment of the intergroup differences by Kruskal-Wallis test, intergroup variables were reassessed by Mann-Whitney U and Wilcoxon W tests. The intragroup differences between the assessments at baseline (t1) and 2 hours (t2) were analyzed by Wilcoxon signed-rank test.

Results

Patient characteristics and surgery were comparable between groups (Table 1). There was no statistically significant difference between the groups in terms of clinical and biological data.

None of the hematologic parameters showed an intergroup difference, and all of them demonstrated a statistically significant reduction between t1 and t2 values in Table 2 ($p < 0.05$).

Table 1. Demographic characteristics and surgical data relative to the groups

Variable	Group R (n=16)	Group H (n=16)	Group P (n=16)	Group S (n=16)
Age (yr)	36±15	41±23	48±14	37±15
Weight (kg)	72±11	70±13	76±12	69±11
Height (cm)	168±9	167±7	169±8	168±7
Tourniquet time (min)	74±15	80±17	84±27	83±22
Duration of surgery (min)	93±37	101±32	105±36	98±34
Intraoperative blood loss (mL)	129±253	115±222	60±111	86±205
Hemoglobin (g/dL)	14,2±1,7	13,3±1,9	14,0±2,9	14,2±1,5
Urinary output (mL)	180±106	221±211	154±73	251±154
Loading fluid (mL)	617±253	588±239	579±161	591±279
Maintenance fluid (mL)	1355±322	1240±310	1368±222	1443±266
Total fluid administration (mL)	1948±497	1897±376	1903±298	1985±279

No significant differences among groups (administration of IV fluids according to study protocol).

Data are given as mean ± SD.

Table 2. Measurements of Routine Coagulation parameters Tests During Knee Replacement Surgery (mean ± SD)

Variable	Group R (n=15)	Group H (n=16)	Group P (n=17)	Group S (n=16)
PT (s)				
t ₁	12,3±1,0	12,1±0,5	12,1±1,8	12,2±1,1
t ₂	12,9 (10,8-14,5)	13,3 (12,1-15)	12,3 (2,2-16)	12,2 (1,2-16)
INR				
t ₁	1,1±0,1	1,0±0,2	1,0±0,1	1,1±0,1
t ₂	1,1(0,9-1,2)	1,1(1-1,3)	1,05(0,9-1,4)	1,05(0,9-1,4)
aPTT (s)				
t ₁	24,6±3,2	23,3±8,6	23,0±3,3	25,6±9,9
t ₂	24,3(20,7-32) ^a	26,9(22,5-35,1) ^b	25,9(12,4-53,4)	23,2 (16,7-74,5)
PLT (10 ⁹ /L)				
t ₁	250,7±50,6	276,8±84,6	237,1±42,4	246,8±68,8
t ₂	228,3±45,6	244,5±43,8	215,8±37,6	231,5±67,8
FIB (mg/dL)				
t ₁	340 (214-796)	386 (210-842)	454 (217-776)	385 (133-768)
t ₂	348,1±114,2	423,0±146,7	367,5±151,2	357,8±153,3

t₁ = baseline; t₂ = 2 h later; PT = prothrombin time; aPTT = activated partial thromboplastin time; PLT = platelets;

FIB = fibrinogen; Statistically significant difference : ^a group R versus H; ^b group H versus group S (P<0.05)

Coagulation parameters showed no statistically significant difference relative to t₁ values, as well. Regarding the aPTT values at t₂, Group R exhibited a statistically significant difference compared with Groups H and P. Comparison of PTT values at t₁ and t₂ revealed statistically significantly prolonged PTT values in Groups R, P, and S. Groups R and P showed statistically significantly prolonged PTT-INR values in Groups R and P. aPTT values at t₂ were significantly higher in Group R compared with other groups. Moreover, comparison of aPTT values at t₁ and t₂ in Groups R and H, revealed significantly prolonged values.

TEG values at t₁ showed no intergroup difference. R at t₂ was significantly lower in Group R than in Groups P and H. Moreover, Group R had a significantly shorter TMA at t₂ than Group P. SP value at t₂ was significantly shorter in Group R than in Groups H and P. Regarding the intragroup comparisons of TEG values in Table 3 (p<0.05); as R, K, TMA, and SP values showed a shortening at t₂ in Groups R, P, and S; CI was significantly increased. Only TPI value at t₂ exhibited a significant increase in Group H. Although α angle at t₂ was increased in all the groups, it was statistically significant only in Groups R and S.

Table 3. TEG variables before (t_1) and after (t_2) surgery in groups (mean $\pm$ SD)

Variable	Group R (n=15)	Group H (n=16)	Group P (n=17)	Group S (n=16)
r (mm)				
t_1	14,9 $\pm$ 5,1	14,1 $\pm$ 4,4	15,1 $\pm$ 7,3	16,4 $\pm$ 5,2
t_2	8,1(1,5-16,5)*	6,3(3,7-18,1) ^{&}	11,2(7,2-18,1) [£]	11,5(4,1-27,4)
k (mm)				
t_1	7,6 $\pm$ 3,6	6,8 $\pm$ 3,0	6,9 $\pm$ 3,2	8,7 $\pm$ 3,1
t_2	4,3(2-11,2)*	3,6(2,3-22,6) ^{&}	4,4(2,3-13,5)	7,4(2,7-22,3)
α (°)				
t_1	30,1 $\pm$ 10,9	30,5 $\pm$ 10,9	32,4 $\pm$ 11,4	26,4 $\pm$ 8,7
t_2	39,8 $\pm$ 12,2	41,7 $\pm$ 13,2	39,9 $\pm$ 13,7	39,4 $\pm$ 12,5
MA (mm)				
t_1	56,3(42,4-73,6)	60,2(17,5-89,7)	61,7(46,4-69,7)	52,5(9,1-72,5)
t_2	60,8 $\pm$ 7,7	59,6 $\pm$ 11,1	62,6 $\pm$ 9,5	60,8 $\pm$ 9,5

t_1 = baseline; t_2 = 2 h later.

r = Reaction time, k = Clotting time, α = rate of clot formation, MA = maximum amplitude,

Statistically significant difference : * group R versus H; [&] group H versus group S ; [£] group P versus group S ($P < 0.05$).

Discussion

In this study, we found dilution-related changes and moderate hypercoagulation effect in patients who received colloid preloading. Large volume colloid administration is known to have a negative impact over the coagulation profile [10]. When colloidal infusion solutions are delivered at large volumes, they can influence the coagulation potential and corpuscular elements of the blood. In the current study, t_2 values showed a significant decrease compared with the t_1 values in all the groups with regard to hemoglobin, and platelet parameters. However, the reduction in the hemoglobin and platelet values did not require fresh blood or thrombocyte transfusion. The impact of HES on coagulation may also occur by hemodilution and direct effect. However, in our study, coagulation was affected more moderately in the HES group compared with the other groups. While RL, polygeline, and succinylated gelatin groups demonstrated significantly elevated PTT results at t_2 compared with the baseline values, RL and polygeline groups displayed significant increases in PTT-INR values at t_2 . aPTT value was significantly elevated in RL and HES groups at t_2 .

In thromboelastography, reaction time (r) represents the speed of clot formation which begins with the measurement and ends with the time of formation of first clot. While anticoagulant drugs prolong the r value, hypercoagulants shorten it. k

is the interval from the formation of the first clot until the clot reaches 20mm size. MA value reflects the maximum elasticity and amplitude. As g represents the elasticity of the clot, CI is the abbreviation of *Coagulation Index*; CI values smaller than -3 indicate hypercoagulability, whereas values higher than +3 suggest a hypocoagulable state (20-25). In TEG measurements; r , k , TMA, and SP values were observed to be reduced at t_2 compared with the intragroup baseline results in RL, HES, polygeline, and succinylated gelatin groups, whereas CI values were observed to be significantly prolonged. Only global coagulation index showed a significant prolongation in the HES group. The α angle at t_2 was observed to be increased in all the groups, however, this increase was at significant levels only in the RL and gelatin groups.

In TEG measurements; r , k , TMA, and SP values were observed to be reduced at t_2 compared with the intragroup baseline results in RL, HES, polygeline, and succinylated gelatin groups, whereas CI values were observed to be significantly prolonged. Only global coagulation index showed a significant prolongation in the HES group. The α angle at t_2 was observed to be increased in all the groups, however, this increase was at significant levels only in the RL and gelatin groups. Ruttmann and colleagues [11] conducted an in vitro study in 1996 where 1/4 modified gelatin and isotonic were used for dilution and both groups displayed decreased r , k , and rk values compared with

the controls, whereas α angle and MA values were found to be elevated in both of the study groups; the changes were not significant only in the modified gelatin group.

In the study of Ruttman et al [11], HES (200/0.5) 1000 ml and isotonic solution 1000 ml were delivered for hemodilution. The comparison of the baseline values with those at 30 minutes in the isotonic group revealed the following results: r and k values were reduced, α angle and MA values were increased, the reduction in the MA value in HES group was significant, the decreases in r and k values in the HES group were clinically significant, and PTT and aPTT values at 30 minutes were prolonged compared with the baseline values in both of the groups. Fibrinogen and anti-thrombin III values showed a decrease as well. The results of the above mentioned studies were consistent with those of our study. Ruttman [11], noted that hemodilution induced thrombin formation which in turn reduced the fibrinogen and antithrombin III levels. The authors explained the prolonged PTT and aPTT values by dilution of the coagulation factors within the platelet-poor plasma. Moreover, they associated the absence of elevated platelet aggregation in the HES group by compensation of hypercoagulability due to antiplatelet effect of the HES [11]. In our study, antiplatelet effect of HES may be explained by the absence of changes in the TEG values despite hemodilution.

In the study of Karoutsos et al [7]; modified gelatin 6%, HES (200/0.62), and albumin 5% solutions were administered in patients undergoing knee and hip replacement surgery, and blood parameters before and after surgery were compared. TEG studies showed that r and rk values were reduced after surgery compared with the baseline values in the gelatin and albumin groups, which was a statistically significant decrease in the succinylated gelatine group. Moreover, postoperatively, α angle was increased and MA values remained the same in the gelatin and albumin groups. Authors associated this hypercoagulability tendency of gelatin with the inhibition of fibrin polymerization by gelatin-fibronectin complex, and noted this process as a dose-independent event. Many of the studies focusing on the effects of colloids over hemostasis and comparing HES 130/0.4 with medium molecular-weight starches or gelatin, have

shown that it increases coagulation tests less and reaches normal values faster [12,13]. In our study, no statistically significant intergroup difference was determined with regard to all the parameters except moderate hypercoagulable state.

Innerhofer et al [8] used 500 ml Ringer's Lactate as the loading and maintenance fluid on 60 cases undergoing knee replacement surgery under regional anesthesia. HES (200/0.5), modified fluid gelatin, and RL were delivered at varying doses in order to maintain normovolemia. They evaluated PTT, aPTT, antithrombin III, fibrinogen, fibrinogen values at baseline and 2 hours by ROTEG analysis which is a modified version of TEG device. Coagulation was increased only in the RL group, whereas intrinsic coagulation was shortened in the RL and gelatin groups, but it was prolonged in the HES group. Moreover, extrinsic coagulation was shortened in the RL group and prolonged in the colloid groups. In this study, since the decrease in the antithrombin III concentration was low in the crystalloid group, it was observed to be inconsistent with the relationship between the antithrombin III and hypercoagulability. The hypercoagulable state occurring with RL and gelatin, was consistent with our study.

Mittermayer et al [14], conducted a study on orthopedic cases with low blood volumes: They initially administered fibrinogen and used HES (130/0.4), modified fluid gelatin, and RL in order to achieve normovolemia. As clot formation time did not change in none of the groups, clot dissolution time was observed to increase in all the groups, but this increase was more remarkable in the HES group compared with the others.

Ulukaya et al [15], performed an in vitro study about hemodilution where 20%, 30%, and 40% dilutions with HES (130/0.4) and succinylated gelatin were used. While r values did not display a significant increase relative to dilution, k values exhibited a significant prolongation in the HES group, however, only 40% subgroup showed a significant increase in the gelatin group. Egli et al [16], observed decreased r , k , and MA values in the 30% dilution subgroup of saline group, whereas in the 60% dilution subgroup the drops in r and k parameters were improved, but the decrease in MA was found to be aggravated. In the same study, as r values showed no change in the 30%

dilutions with HES (200/0.5), succinylated gelatin, and albumin; 60% dilutions caused an increase in those values, but the decline in MA persisted.

Colloids and crystalloids including RL, is associated with results involving hypercoagulation and hypocoagulation [7-9]. This explains the moderate hypercoagulability effect induced by the fluid loading through dilution-related changes in our study. Probably, the fluids stimulate coagulation at certain doses and eventually coagulation causes dilution in the anticoagulant system [11], which in turn leads to an uncertainty similar to a different kind of consumptive coagulopathy. All those changes are reflected by decreased r and k values, and increased α angles along with prolonged PT and aPTT values in TEG.

As a result of using colloids were found to have no impairing effect over the hemorrhage and coagulation profiles of the cases that would deteriorate their clinical status. Although, unlike other colloids, HES was observed to balance the hypercoagulability at the applied dose, polygeline and succinylated gelatin were found to generate moderate hypercoagulability. These results indicate that gelatin and polygeline should be preferred in cases with hypocoagulable state, whereas HES should be used in cases with hypercoagulable state. In conclusion, we believe that colloid infusions are safe for prophylactic use in the prevention of hypotension associated with spinal anesthesia.

References

1. Morgan G.E. JR, *Clinical Anesthesiology* fourth edition, Appleton & Lange 2006; 289-322.
2. Morgan P.J. Halpern S.H. Tarshis J. *The effects of an Increase of Central Blood volume before spinal anesthesia for Cesarean Delivery: A Qualitative Systematic Review.* *Anesth Analg* 2001; 92: 997-1005.
3. Boldt J. Suttner S., *Plasma substitutes, Minerva Anesthesiol* 2005; 741-758.
4. De Jonge E, Levi M. *Effects of different plasma substitutes on blood coagulation: A comparative review.* *Crit Care Med* 2001; 29: 1261-1267.
5. Uzun S. Saricaoglu F. Celiker V. *Deep Vein Thrombosis: Review, Türkiye Klinikleri J Med Sci* 2007, 27: 853-861.
6. Guyton AC. *Hemostaz ve kan pıhtılaşması, Textbook of medical physiology 10th ed. Türkçe Nobel yayınevi* 2001, 36: 419-431
7. Karoutsos S. Nathan N. Lahrimi A. *Thrombelastogram reveals hypercoagulability after administration of gelatin solution.* *Br J Anaesth* 1999; 82: 175-182.
8. Innerhofer P, Fries D, Margreiter J. *The effects of perioperatively administered colloids and crystalloids on primary platelet-mediated hemostasis and clot formation,* *Anesth Analg* 2002; 95: 858-865.
9. Jones S.B., Whitten C. W. *The influence of crystalloid and colloid replacement solutions in acute normovolemic hemodilution: A preliminary Survey of haemostatic Markers,* *Anesth Analg* 2003; 96: 363-368
10. Vercauteren MP. Hoffman V. Copejans H.C. *Hydroxyethylstarch compared with modified gelatin as volume preload before spinal anaesthesia for caesarean section.* *Br J Anaesth,* 1996; 76: 731-733.
11. Ruttman T.G. James M.F. *In vivo investigation into the effects of haemodilution with hidroxyethyl strach (200/0.5) and normal saline on coagulation,* *Br J Anaesth* 1998; 80: 612-616.
12. Coriat P. Voluven, a lower substituted novel hydroxyethyl starch (HES 130/0.4), causes fewer effects on coagulation in major orthopedic surgery than HES 200/0.5. *Anesth Analg* 2001; 92: 855-862.
13. Grauer M.T., Baus D., Woessner R. *Effects on general safety and coagulation after long-term, high-dose volume therapy with 6% Hydroxyethylstarch 130/0.4 in patients with acute ischemic stroke, 21st International Symposium on Intensive Care and Emergency Medicine; 20-23 March 2001, Brussels, Belgium: Crit Care; 2001, S53.*
14. Mittermayr M. *Hemostatic changes after crystalloid or colloid fluid administration during major orthopedic surgery: The role of fibrinogen administration,* *Anesth Analg* 2007; 105: 905-917.
15. Ulukaya S. Alper S., Balcioglu S.T. *% 6 Hidroksietil Nişasta (130/0.4) ve % 4 süksinilli Jelâtin solüsyonlarının koagülasyonu etkileri, J Turk Anaesth Int Care* 2009; 37(5): 280-286.
16. Egli G.A, Zollinger A. *Effect of progressive haemodilution with hydroxyethyl starch, gelatin and albumin on blood coagulation.* *Br. J. Anaesth.* 1997; 78: 684-689.

Corresponding Author
Mustafa Said Aydoğan,
Inonu University School of Medicine,
Department of Anaesthesiology and Reanimation
Malatya,
Turkey,
E-mail: dr_mustafasaid@hotmail.com

The reasons for sharing needle using and syringe among injection drug users in the city of Ahvaz: A qualitative study

Morteza Mansourian¹, Mahnaz Solhi¹, Tahereh Dehdari¹, Mohamad Hosain Taghdisi¹, Fereshteh Zamani-Alavijeh², Hadi Rahimzadeh Barzoki³, Hamid Asayesh⁴

¹ Tehran University of medical sciences, Tehran, Iran,

² Ahvaz University of medical sciences, Ahvaz, Iran,

³ Golestan University of Medical Sciences, Gorgan, Iran,

⁴ Qom University of Medical Sciences, Qom, Iran.

Abstract

Introduction and goals: The prevalence of HIV and hepatitis among injection drug users (IDUs) who shares needle and syringe is by far more than those who do not share syringe. Therefore, the purpose of this qualitative study was to explain the reasons of sharing needle and syringe in Ahvaz IDUs.

Materials and method: This article is a part of qualitative study which has been performed by the content analysis method and purposeful sampling in drop in center (DIC) of Ahvaz city. 39 semi-structured individual depth interviews and two focus group discussions (FGD) were performed in this study. The subjects were asked by the causes of using shared needle, prison background and stricken by disease. After the first interview, the analyzing of data was started and continues up to data saturation.

Result: After coding and analyzing of data, inaccessibility and limitation of provision to sterile syringe, the lack of knowledge about result of sharing needle, disappointment and eagerness to die thought the sharing needle and sharing needle by self-deception were four causes of using sharing syringe.

Discussion: According to the increasing in IDU and incidence of STDs disease in IDUs, it seems increasing of harm reduction programs and distributing of sterile syringe with the perform educational program for IDUs and helping them to quit can be useful for the control of addiction.

Key words: Needle and Syringe Exchange, Injection Drug User, Qualitative Study, Drop in Centers

Introduction

According to United Nations Office on Drugs and Crime (UNODC) report in 2008 about 11- 21 million people in the world have injecting addiction. These reports express that 20% of Iranian population, ranging from 15-60 years old attempted to use illegal narcotic drug. In 2008, there was about 250000 IDUs in Iran and 5-20% of them had the HIV virus (Justice Tettey, 2010) and only 7.5 percent of IDU have access to DICs and another centers for given sterile syringe and needle. Survey of three decade trend of addiction in Iran showed that injecting drug use in Iran has 330% growth in three recent decades (an average 10% for every year). (Tanibuchi et al., 2010) Also, In the USA, between 1970–2002, the tendency toward the injecting addiction has been rising and in this country, the number of IDUs was more than 440000 in which male users was more than female ones (Rahimi Movaghar A, 2002). During recent years, the total number of addicted people and the number of IDUs have increased (Rahimi Movaghar A, 2002). Additionally, injecting drug is causing mental and physical problems such as abscess, skin infection and the possibility an increase in depression. It will cause (Anglin MD, 2000) disease such as HIV/AIDS and hepatitis (Hamamoto & Rhodus, 2009; Marcondes, Flynn, Watry, Zandonatti, & Fox, 2010; Semple, Patterson, & Grant, 2002). Another study also has shown that prevalence of HIV+ and hepatitis in IDUs who have used sharing needle is, significantly, more than those who have not used sharing syringe (Abiona TC, 2010; Kheirandish P, 2009; Kolovrat A, 2010; Loue S, 2011). In the fuller

study (Fuller CM, 2002), the results showed that the chance of getting HIV in IDUs is, significantly, more than non IDUs. Neaigus (Gyarmathy VA, 2011) showed that the IDUs have extra problems such as the probability of an increase in becoming homeless, losing jobs, long usage of drug and doing injecting himself. Considering the importance of using the sterile syringe and also the importance of understanding the reasons of using sharing syringe in the IDUs it is possible to solve needle and syringe exchange problem. This study was performed by using qualitative approach in order to achieve first-hand information in explaining the reasons of needle and syringe exchange in Ahvaz city IDUs.

Material and method

This article is a part of a qualitative research that was done on content analysis method participants were selected by purposive sampling. For the implementation of this research, after getting permission from Ahvaz Welfare Organization, the researchers refer to drop in centers (DICs). The participants in the study have been selected from among IDU who were willing to participate in the study to offer their experiences about injection drug phenomenon. After the introduction of the subjects, the participants have been ensured that the data have been anonymous and were collected only through recordings. In order to comply with the ethical issues, all of the participants signed the testimonial form and the research proposal was approved by the Ethics Committee of the University of Tehran's Medical Sciences (grant No. 91-01-27-16609). Data gathering was performed by purposeful sampling methods and in depth semi-structured individual interviews and focus group discussion (FGD). Polit et al believed that the main source of information on the qualitative study will be in depth interviews between the researchers and the participants (Beck, 2007). In this study, 39 semi-structured interviews and two FGD were done. Due to constant relation between DICs personnel to IDUs an interview took place with two experts in centers where one of them had injection addiction four years of prior. The time of every interview varied according to the situation and procedure of interview and it was between

30 to 70 minutes. The interviews and FGDs were performed in March 2010 until July 2011 in the DIC offices. The interviews started by the introduction of participants and a history of their drug use and then they were asked questions about the reasons for using shared syringe, having a history of imprisonment and stricken by STDs disease. After doing the first interview, the recorded conversations were transcribed word by word and entered into the open code software in order to be analyzed. Constant comparative analysis of data have began and it continued in three levels of open coding, axial, and selective (Streubert Speziale J.H., 2003). The obtained codes by the method of external check were reviewed and amended by sending them to three professors at Tehran University of Medical Sciences and one professor at Ahwaz University of Medical Sciences. In order to increase the acceptability of credibility, the researcher was, consistently, in relationship with the participants for having a better understanding of their behavior. The triangulation in data collection was used including semi-structured interview, observation and FGD. The data gathering continued up to data saturation (Victoria D. Ojeda, 2011) and until we had a description of the causes of needle and syringe sharing.

Results

Thirty-seven cases out of the 39 interviews have used crystal meth and crack together and only two people used just inject crack. All of them used crack and crystal meth by injecting crack and smoking crystal meth except one person who also injected crystal meth.

Ethnically, 51.4% were Bakhtiarian lor, 34.3% Arab and the rest were from another ethnicity. 62.9% of participants were single, 14.3 married and the rest were separated. Fifty-eight percent of the participants had, at least, one addict in their family, 85.7 % had history of prison, 3 subjects had hepatitis type C, 14 subjects had HIV+ and two subjects had both hepatitis C and HIV+. Some of the participants always used sterile syringe, purchased from pharmacy or DICs but some people exchanged syringe and used shared syringe frequently. After analyzing and categorizing, the causes of used shared needle and syringe were classified into 4 following categories:

1. The lack of access and having limitation at supplying sterile syringe
2. The lack of awareness about the dangers of using shared needles
3. Hopelessness and Tendency to die through the use of shared needles
4. The use of shared needle with Justification and self-deception.

1 - The lack of access and limitation at supply sterile syringe

One of the reasons for using shared syringe in IDU was the access to sterile syringe and limitation to supply sterile syringe for injection drugs. These categories consist of five sub-categories including: not to sell syringes by pharmacies, lack of access to sterile syringes due to pharmacies and DICs begin closed on holidays, having no time due to extreme hangover for supplying sterile syringe, and not having enough money and being in prison. Addiction has been considered to be a crime in our country for a long time. Participant NO 7 expressed that "Nowadays community has a view on addicted people as an illness and the people's view of us has become better". No selling syringes to IDUs were affected by this attitude and this factor had a lot of influence on the spread of AIDS and hepatitis. Participant No 30 said, "I used many shared syringes and in those days, pharmacies didn't give us sterile syringes because my hands had tattoo and my appearance showed that I'm an addict" (30 years old man and HIV+). Also, the participant NO 45 stated, "Three people bring one syringe and they inject by that syringe orderly. There were no syringes, previously, and pharmacies did not give syringes either (38 years old, HIV+). Another participant who has wife and a son in FGD said, "In those days, syringes were not sold and some even would sharpen syringes by stone and injected them to me. The syringes were used collectivity. There was just one syringe and ten people injected with it. We took a syringe that had fallen into the sewage and injected with that it. One of the main problems for IDUs in supplying syringes was the pharmacies and DICs being closed. Participant NO 6 expressed, "Most of our problems were holidays in which all drug-stores and DICs were closed and we used our syringe so many times or took it from another person".

Participant NO 1 said, "Previously, there were no sterile syringes and I had found syringes from the ground and did inject ". Another participant stated, for example, Friday was off and syringes were out of reach, so, the addicts had to share their syringes (man 40 years old). The other reason to use shared syringes was hangover that makes us to think just about injection and don't pay attention to healthy injection. Some participants were talking about a situation in which they did not think about the consequences of using shared syringe due to having hangover. Participant NO 3 stated that two or three times, I used shared syringe, I had hangover and I had to take syringe from someone (21 years old man). Participant no 41 said, "When I would become hangover, I used shared syringes because my drug use is high" (26 years old man). Also NO 42 said, "I used shared syringes many times, you know, I was having an extreme hangover, I could not afford to buy it, and did not have the patience to buy it". Another participant stated that "when somebody takes his drug, he merely wanted to use it and doesn't think about consequences and dangers. Nobody is worried about HIV, hepatitis and other things" (38 years old man, HIV+). One of the participant in the FGDs said, "It was never important for me to become sick or not, I just wanted to I survive the hangover and syringe had no importance to me" (woman 40 years old). Participant NO 35 stated "I picked up the dirty syringes from the ground and I washed it. Sometime, when I had a terrible hangover, maybe, I didn't wash it due to pain. My body was insensible (35 years old man and HIV+)

In some cases IDUs people wanted sterile syringe for injection, but they didn't have enough money to buy syringes. Participant NO 1 said, "You know, sometimes when I have money just enough for buying a drug I had to use non- sterile syringes to inject the drug. Participant NO 43 who was married and had a daughter said, "I myself as an addict couldn't even buy one bread, how could I spend any money for syringes.

In some cases, although, the IDUs were aware of the dangers of sharing needles anyway because they did not have enough money. One of the participants in the FGDs said, "I couldn't work and earn money and I found syringes on the ground and injected, myself despite the fact that I knew

they might make me sick. Before the harm reduction program in prison, shared syringe was used a lot in the prisons. One of the experts of DICs said, "Now in the prisons, there are both HIV and drugs. Thirty people injected by one needle and often those who were referred from the prison to start methadone therapy, had HIV. One of participants in FGD said, "I saw ten people in prison that shared one syringe for injection".

2 - Lack of awareness about the dangers of using shared needles

In some cases people did not have enough knowledge about HIV and other STDs and there were shared syringe in prisons". At those times, we were not aware about diseases. After three years of using injection drugs, I saw a few of my friends that we shared syringes together died, so I I've tested and found that I'm HIV+" (32 years old man and HIV+). In some cases, participants have complained because the community had not given them awareness about HIV/AIDS. Participant NO 35 who got HIV from unprotected sex stated, "In the past they had not trained us about sex and such thing was like a taboo". In some cases, the subjects was aware about transmitted disease through sharing syringes, but had no choice but using shared syringes. One of the participants in FGD said, "I had hangover. I knew that I would get sick injecting with someone that I knew he had the disease (28 years old man and HIV+).

3 - Hopelessness and Tend to death through the use of shared needles

Disappointment and eagerness to death through sharing syringe. Some of IDUs were eager to become ill by using shared syringes and die sooner because they were tired from injecting drugs and problems associated with injecting.

Participant NO 13 who was an addict and started working for DIC helping drug addicts after quitting drugs said, "Some of young IDUs say to me: I like to die and get HIV, I'm tired from injecting ". Participant no 22 said, "My situation was so bad that I injured my blood vessel in order to die and get rid of the injection drugs". Participant NO 21 stated, "I injected dense heroin to die, but I didn't".

4 - The use of shared needle with Justification and self-deception

In this category we have two categories including: washing syringes of other people and taking syringes from friends. Using of shared syringes by IDUs who were aware of the transition of disease by sharing syringes was accompanied by a series of self deception and justification. In some cases, in which the addict had to use shared syringes, he/she tried to wash the syringe in order to make it clean. One of the participants said, "We took somebody else's syringe or picked them up from the ground and then, we washed them and used them at the time of overwhelming pressure of hangover (23 years old man who was suffering from hepatitis C). IDUs that get a syringe from their friends due to the belief they think they are not sick. Participant NO 7 said, "Sometime, it has happened that I had to use shared syringes, but you know, it shouldn't be contaminated and I would wash it by water and I took it from someone who I knew had no diseases. This person when asked by the researchers: How do you know that he had no illness? He answered, orally, but not quite sure about it.

One of the participants hints to a specific way of supplying syringes by the means of IDUs. He said, "Some addict selling syringes, for example gather 20 dirty and contaminated syringes. He would, then somebody a syringe that did not have one and then said to him, give me some money or some drops of everything that you are using". Another participant in FGD also said, "Some participant gather syringe from the ground that it whether has been clean or not for holiday or when there was no access to syringe and they would sell to another IDU.

Discussion and Conclusion

In our study some of the participant said that they had to use shared syringe due to the lack of selling syringes by pharmacies. According to the studies conducted bychakrapani (Chakrapani V, 2010), Strathdee) Strathdee SA, 2005(and Sendziuk (P, 2007), one of the reasons to use shared syringes was the limitation in access to sterile syringe in drug-stores and needle and syringe programmes (NSPs) centers. The main reason was the obstinacy of drugstore in the distribution of

syringes and the fear of label as being known as an addicted person by addict. Some people weren't aware about the existence of NSP and those who weren't receiving syringes sufficiently. In our study, also, DICs being closed causes the lack of access to the sterile syringes and Ahvaz has got just two DICs. Although, the results of Bryant (Bryant J, 2011) and Ngo (Ngo, Schmich, Higgs, & Fischer, 2009) showed that access to centers for the distribution of syringes has no significant relation with the use of sterile syringes. Therefore, it seems that encouraging IDUs to use sterile syringes and training them about the risks of shared syringes can affect the control of needle and syringe exchange problem.

Another reason for sharing syringe in IDUs was time limitation due to the hangover and limitation of payments to supply syringes. In some studies, such as Prat (Prat & Adan, 2011), Gjired (Gjerde H, 2010) and Mahmud (Mahmood OM, 2010) studies, it has been mentioned that IDUs are experiencing pressure and hangover between two drug consumption. According to participants' statements about the pressure of hangover in our study, it seems that we need to develop harm reduction centers and further access to sterile syringe by IDUs.

Another limitation for the use of sterile syringe in our country was imprisonment. In the studies by Chu (Chu, 2009) and Afriandi (Afriandi et al., 2009), there has been a reference to the importance of prison in increasing of HIV/AIDS. Although, recently, in most prisons in our country harm reduction and methadone maintenance therapy (MMT) program for HIV/AIDS patients has been implementation but according to uncertainty about the effectiveness of these programs (Takacs & Demetrovics, 2009), it seems that the survey of effectiveness of this program can be a research priority in our country. In our study, some of the participants said that they did not have enough knowledge about the risks of sharing syringes. In different studies, this issue has been verified that many people, specially, those who have seen education of a low level have little information about HIV/AIDS transition ways; see Ming (Ming, Liang, Yap, Liu, & Wu, 2002) and Bryant (Bryant J, 2011) studies. It seems that the implementation of educational program for IDUs and another high

risk groups can be effective in the control of HIV/AIDS in our country. Another reason for sharing syringes in IDUs was disappointment and eagerness for premature death. In some studies, the act to suicide by IDUs has been mentioned in the study conducted by Backmund (Backmund, Meyer, Schutz, & Reimer, 2011) in which factors like female gender, older age, lack of drug user counseling and emergency treatment were associated with attempted suicide in IDUs. In Sarin (Sarin, Samson, Sweat, & Beyrer, 2011) study, human rights abuses and in Havens (Havens JR, 2006) factors associated with injection drug users' lifestyles and mental health status have been accounted for the higher prevalence of suicidal ideas in IDUs.

In the present study, emotional problem and effort for getting rid of addiction have been mentioned as factors associated with suicidal ideas but according to researcher's observation, their bad life conditions and being driven out of DIC in Ahvaz due to summer hot days and finishing DIC time working season and deprivation of human right, it maybe some the other reasons associated with attempted suicide in IDUs in our study.

Some of the participants in our study said that they were aware about the risk of sharing syringes and they have been washing the syringes before use. These results have, also, been confirmed in other studies such as ones by Payne-James (Payne-James JJ, 2005) and Sarang (Sarang A, 2006). In this study, two of the participants have mentioned the special kind of shared syringe selling for money and drug. Sarathdee (Strathdee SA, 2005) hinted there are some hints in regards to the same cases that used syringes were sold for money or in exchange for drugs. It seems by increasing the harm reduction programs and supplying syringe distribution, ways such as self-furbisher machines of syringe, supporting the IDUs and supplying boarding shelter with training IDUs and the use of MMT program can help to reduce the amount of HIV/AIDS and injecting drug use in our country.

Limitations of this study were including

- 1 – Lack of a private environment for the interview forced to stop the interviews, temporarily, with the entries to the interview room.

- 2 - Euphoria or the hangover of some of the participants would cause the jabber or scattering in some cases.

Acknowledgments

This article was part of a thesis research project which was approved and supported by Tehran University of Medical Sciences [grant number 91-01-27-16609]. The Article writers thank and appreciate the Welfare Officials of Drop in Service Centers (DIC) of Ahwaz in implementation and collaboration of the study.

References

1. Abiona TC, B. J., Adefuye AS, Sloan PE. (2010). Body art practices among inmates: Implications for transmission of bloodborne infections *Am J Infect Control*, 38(2), 121-129.
2. Afriandi, I., Aditama, T. Y., Mustikawati, D., Oktavia, M., Alisjahbana, B., & Riono, P. (2009). HIV and injecting drug use in Indonesia: epidemiology and national response. *Acta Med Indones*, 41 Suppl 1, 75-78. doi: 040579197 [pii]
3. Anglin MD, B. C., Perrochet B, Stamper E, Dawud-Noursi S. (2000). History of the methamphetamine problem. *J Psychoactive Drugs*, 32(2), 137-141.
4. Backmund, M., Meyer, K., Schutz, C., & Reimer, J. (2011). Factors associated with suicide attempts among injection drug users. *Subst Use Misuse*, 46(12), 1553-1559. doi: 10.3109/10826084.2011.564443
5. Beck, D. F. P. C. T. (2007). *Nursing Research: Generating and Assessing Evidence for Nursing Practice* (7th ed.). London: Philadelphia, Pa. ; London : Lippincott Williams & Wilkins, 2011.
6. Bryant J, P. D., Wilson H. (2011). Syringe Coverage in an Australian Setting: Does a High Level of Syringe Coverage Moderate Syringe Sharing Behavior? *AIDS Behav journal*.
7. Chakrapani V, N. P., Shunmugam M, Dubrow R. (2010). Social-structural contexts of needle and syringe sharing behaviours of HIV-positive injecting drug users in Manipur, India: a mixed methods investigation, *BMC Public Health* 2010, . *BMC Public Health*, 721-730.
8. Chu, S. (2009). Clean switch: the case for prison needle and syringe programs. *HIV AIDS Policy Law Rev*, 14(2), 5-19.
9. Fuller CM, V. D., Ompad DC, Shah N, Arria A, Strathdee SA. (2002). High-risk behaviors associated with transition from illicit non-injection to injection drug use among adolescent and young adult drug users: a case-control study. *Drug Alcohol Depend*, 66(2), 189-198.
10. Gjerde H, C. A., Moan IS, Yttredal B, Walsh JM, Normann PT, Mørland J. (2010). Use of alcohol and drugs by Norwegian employees: a pilot study using questionnaires and analysis of oral fluid. *J Occup Med Toxicol*.
11. Gyarmathy VA, N. A., Li N, Ujhelyi E, Caplinskiene I, Caplinskis S, Latkin CA. (2011). Infection disclosure in the injecting dyads of Hungarian and Lithuanian injecting drug users who self-reported being infected with hepatitis C virus or human immunodeficiency virus. *Scand J Infect Dis*. 2011 Jan;43(1):32-42. Epub 2010 Sep 15, 43(1).
12. Hamamoto, D. T., & Rhodus, N. L. (2009). Methamphetamine abuse and dentistry. *Oral Dis*, 15(1), 27-37. doi: OD11459 [pii]
13. 10.1111/j.1601-0825.2008.01459.x
14. Havens JR, S. S., Sapun M, Strathdee SA. (2006). Prevalence and correlates of suicidal ideation among young injection vs. noninjection drug users. *Subst Use Misuse*, 41(2), 245-254.
15. Justice Tetley, B. H., Matthew Nice, Barbara Remberg. (2010). *WORLD DRUG REPORT 2010 Vol. 1*. (pp. 310).
16. Kheirandish P, S. S., Jahani M, Shirzad H, Seyed Ahmadian M, Majidi A, Sharifi A, Hosseini M, Mohraz M. (2009). Prevalence and correlates of hepatitis C infection among male injection drug users in detention, Tehran, Iran. *J Urban Health*, 86(6), 902-908
17. Kolovrat A, J. I., Maric Z, Cvitkovic A. (2010). Prevalence of hepatitis B, hepatitis C and HIV among injecting drug users treated outpatiently and in therapeutic community in Brod-Posavina County. *Acta Med Croatica*, 64(4), 287-296.
18. Loue S, S. M., Mendez N. (2011). Substance use and HIV risk in a sample of severely mentally ill Puerto Rican women. *J Immigr Minor Health*, 13(4), 681-689.
19. Mahmood OM, J. J., Bava S, Scarlett A, Tapert SF. (2010). Learning and memory performances in adolescent users of alcohol and marijuana: interactive effects. *J Stud Alcohol Drugs*, 71(6), 885-894.

20. Marcondes, M. C., Flynn, C., Watry, D. D., Zandonatti, M., & Fox, H. S. (2010). Methamphetamine increases brain viral load and activates natural killer cells in simian immunodeficiency virus-infected monkeys. *Am J Pathol*, 177(1), 355-361. doi: S0002-9440(10)60091-0 [pii]
21. 10.2353/ajpath.2010.090953
22. Ming, Z., Liang, S., Yap, L., Liu, W., & Wu, Z. (2002). [Qualitative study of drug-using and sexual behaviors of drug users in Guangxi]. *Zhonghua Liu Xing Bing Xue Za Zhi*, 23(2), 111-113.
23. Ngo, A. D., Schmich, L., Higgs, P., & Fischer, A. (2009). Qualitative evaluation of a peer-based needle syringe programme in Vietnam. *Int J Drug Policy*, 20(2), 179-182. doi: S0955-3959(07)00272-1 [pii]
24. 10.1016/j.drugpo.2007.12.009
25. P, S. (2007). Sendziuk P, Harm reduction and HIV-prevention among injecting drug users in Australia: an international comparison. *Can Bull Med Hist*, 24(1), 113-129.
26. Payne-James JJ, W. I., Bailey C. (2005). 6x Patterns of illicit drug use of prisoners in police custody in London. *J Clin Forensic Med*, 12(4), 196-198.
27. Prat, G., & Adan, A. (2011). Influence of circadian typology on drug consumption, hazardous alcohol use, and hangover symptoms. *Chronobiol Int*, 28(3), 248-257. doi: 10.3109/07420528.2011.553018
28. Rahimi Movaghar A, M. K., Razaghi EM. (2002). Trend of drug abuse situation in Iran: A three-decade survey. *HAKIM RESEARCH JOURNAL*, 5(3), 171-181.
29. Sarang A, R. T., Platt L, Kirzhanova V, Shelkovnikova O, Volnov V, Blagovo D, Rylkov A. (2006). Drug injecting and syringe use in the HIV risk environment of Russian penitentiary institutions: Qualitative study. *Addiction*, 101(12), 1787-1796.
30. Sarin, E., Samson, L., Sweat, M., & Beyrer, C. (2011). Human rights abuses and suicidal ideation among male injecting drug users in Delhi, India. *Int J Drug Policy*, 22(2), 161-166. doi: S0955-3959(10)00137-4 [pii]
31. 10.1016/j.drugpo.2010.09.011
32. Semple, S. J., Patterson, T. L., & Grant, I. (2002). Motivations associated with methamphetamine use among HIV+ men who have sex with men. *J Subst Abuse Treat*, 22(3), 149-156. doi: S0740547202002234 [pii]
33. Strathdee SA, F. W., Case P, Firestone M, Brouwer KC, Perez SG, Magis C, Fraga MA. (2005). Vivo para consumirla y la consumo para vivir" ["I live to inject and inject to live"]: high-risk injection behaviors in Tijuana, Mexico. *J Urban Health*, 82(3), 58-73.
34. Streubert Speziale J.H., C. R. D. (2003). *Qualitative Research in Nursing* (3th ed.). New York Lippincot Williams & Wilkins
35. Takacs, I. G., & Demetrovics, Z. (2009). [The efficacy of needle exchange programs in the prevention of HIV and hepatitis infection among injecting drug users]. *Psychiatr Hung*, 24(4), 264-281.
36. Tanibuchi, Y., Shimagami, M., Fukami, G., Sekine, Y., Iyo, M., & Hashimoto, K. (2010). A case of methamphetamine use disorder treated with the antibiotic drug minocycline. *Gen Hosp Psychiatry*, 32(5), 559 e551-553. doi: S0163-8343(09)00285-0 [pii]
37. 10.1016/j.genhosppsych.2009.12.005
38. Victoria D. Ojeda, A. M. R., Sarah P. Hiller, Remedios Lozada, Wayne Cornelius, Lawrence A. Palinkas, Carlos Magis-Rodriguez, and Steffanie A. Strathdee, A (2011). Qualitative View of Drug Use Behaviors of Mexican Male Injection Drug Users Deported from the United States, *Journal of Urban Health*. 88(1), 11524-11530.

Corresponding Author
 Tahereh Dehdari,
 Faculty of Health,
 Tehran University of Medical Sciences,
 Health Education Department,
 Tehran,
 Iran,
 E-mail: dehdarit@yahoo.com

Surgical treatment of retroperitoneal Pelvic tumors

Ljiljana Ivanovic¹, Srdjan Djurdjevic¹, Mirjana Bogavac¹, Dragan Nikolic², Marijana Basta-Nikolic³

¹ Department of Obstetrics and Gynecology, Clinical Center of Vojvodina, Novi Sad, Serbia,

² Department of Vascular surgery, Clinical Center of Vojvodina, Novi Sad, Serbia,

³ Department of Radiology, Clinical Center of Vojvodina, Novi Sad, Serbia.

Abstract

Introduction: Primary retroperitoneal tumors account for 3% of all tumors, with sarcoma and schwannoma being the most common. Their growth period is rather long, without presence of characteristic symptoms related to the location and tumor size. Basic therapeutic procedure is complete surgical removal of tumor. Definitive diagnosis is made intraoperatively and after hystopathological examination.

Objective: To present the results of surgically treated retroperitoneal tumors localized in female pelvis.

Method: Eight (8) patients with different histological types of retroperitoneal tumors were operated in the period 2001-2010. Only in 4 (50 %) cases, imaging diagnostic methods reliably confirmed retroperitoneal localization of pelvic tumors. Stage of the disease was determined according to staging classification of soft tissue sarcomas.

Results: In the period 2001-2010, 4015 of women were operated for different pelvic tumors, out of which 8 (0.19 %) had retroperitoneal tumors. 5 (62.5 %) patients had malignant tumors of mesenchymal origin (sarcomas), while 3 (37.5 %) patients had benign tumors. In all cases, tumors were completely removed. Average length of operation was 189 minutes, and intraoperative blood loss was 360 ml. In 2 (25 %) patients with malignant retroperitoneal schwannomas, bleeding from presacral veins and arteries of greater omentum occurred following the surgery, which required second look surgery.

Conclusion: In spite of utilization of modern diagnostic methods, primary retroperitoneal tumors are in 50% of cases discovered intraoperatively. Successful treatment means complete surgical tumor removal. The total of 6 (75 %) patients is alive and without clinical signs of tumor, while average survival rate is 4.3 years.

Key words: Retroperitoneal pelvic tumors, surgical treatment

Introduction

Primary retroperitoneal tumors are rare neoplasms comprising 0.1 - 3 % of all tumors (1,2). Regarding their malignant potential, they can be benign or malignant, with the highest incidence of sarcomas and schwannomas (3-5). The incidence of soft tissue sarcomas is 1/1.200 cases or about 1 % of all malignant tumors in adults (6). In 15 % of cases, soft tissue sarcomas are localized in retroperitoneal space of abdomen and pelvis, with most common types being liposarcoma, fibrosarcoma, malignant fibrous histiocytoma, rhabdomyosarcoma, leiomyosarcoma and angiosarcoma (7, 8) . Occurrence of any tumor masses beneath deep fascial structures should arise suspicion on the presence of these tumors. Schwannomas are tumors of nerve fibers sheath, mainly composed of Schwann cells, and localized in pelvis in 3% of cases. Although they can be hemorrhagic or cystic, most commonly they manifest as solid, well circumscribed and encapsulated tumors which can grow large in size (9,10). Primary retroperitoneal tumors have a long growth period without the presence of characteristic symptoms related to the localization and tumor's size. The first symptoms usually occur when tumor reaches large size and make pressure on surrounding organs. Pain and feeling of pressure are the first symptoms, especially if bleeding or necrosis within the tumor occur (1-3). If tumor makes pressure on blood or lymph vessels, lower extremities edema may occur, and if the tumor's origin is close to urethra or urinary bladder, impaired miction may occur. Table 1 shows hystopathological classification of primary retroperitoneal tumors published in literature (4-11).

Objective

To show diagnostic-therapeutic procedures and the results of surgical treatment of retroperitoneal tumors localized in female pelvis.

Table 1. Classification of primary retroperitoneal tumors

Histological type	Histogenetic origin %
• Lipoma • Fibroma • Liposarcoma • Leiomyoma • Leiomyosarcoma • Rhabdomyosarcoma • Neuroblastoma • Neurinoma • Malignant and benign schwannoma • Granular cell tumor • Fibrosarcoma • Anaplastic and undifferentiated sarcoma • Hemangiopericytoma • Lymphangioma • Hemangioma • Benign and malignant teratoma • Chordoma • Benign and malignant mesenchymoma • Mixoma • Benign and malignant paraganglioma • Malignant fibrous histiocyoma	• Fat tissue 22.2 % • Muscle tissue 22.2 % • Nervous tissue 18.6 % • Fibrous tissue 16.4 % • Blood vessels 6.2 % • Embrional tissue 4.7 % • Mesenchymal tissue 4.5 % • Epithelial tissue 2.5 % • Undefined origin 2.7 %

In : Cassidy J, Bissett D, Spence RAJ, Payne. *Oxford Handbook of Oncology*, Oxford University press, sec.eds. 2006 (Ref. 11)

Method

Eight (8) patients with different histological types of retroperitoneal tumors were operated at Clinic for Gynecology and Obstetrics in Novi Sad in the period from 2001 to 2010. Patients' age ranged from 32 to 68 years ($x = 59.3$). In all cases, after gynecological rectovaginal and ultrasound examination with endovaginal probe (*Medison – Sonoace X6, 5 MHz probe*), CT examination of abdomen and pelvis (*CT scan – Somatom Sensation Cardiac 64*), as well as cystoscopy and colonoscopy were performed. All patients were operated after the routine preoperative preparation, which included intern and ECG examination, chest X-ray and standard blood and urine analyses. Staging of soft tissue pelvic sarcoma was determined according to current classification for soft tissue sarcoma staging, and for retroperitoneal sarcoma of cervix uteri according to current FIGO classification (*Federation International Gynecologist Obstetritian*) (11). All patients were administered prophylactic dose of antibiotics preoperatively (Cephalosporin 1g i.v.), as well as heparin anticoagulant protection. "Bandage" of lower extremities was performed as well. Patients

were informed in detail about risks of surgical treatment, possible intra and postoperative complications and eventual involvement of other specialists (abdominal surgeon, urologist) during the operation, which they agreed with by signing informed consent. Regarding surgical approach, at 7 patients lower middle laparotomy was performed, which was extended upwards to *processus xyphoideus* in 2 cases, while at only one patient transverse laparotomy sec. *Pfannenstiel* was employed. After the incision of anterior abdominal wall and access to pelvic organs, a careful inspection and palpation of all pelvic organs (uterus, ovaries, fallopian tubes, urinary bladder, small and large intestine) was performed. Depending of tumor localization, peritoneal incision above tumor in the region of lig. Rotunda and laterally to ovaries and tubes was performed. After accessing retroperitoneal space, identification of retroperitoneal elements and organs: ureters, blood vessels-external and internal i.e. common iliac arteries and veins, psoas muscle, genitofemoral and obturator nerve, was done. Following identification of mentioned elements, sharp surgical preparation of tumor with safety margins was performed, paying special attention to avoiding injuries of abo-

ve mentioned organs. After tumor removal, in all cases retroperitoneal space was drained by vacuum drain number 16 (*Redon drain, Synergu USA*) minimally for 48 hours, or until secretion was below 30 ml/24 h. Definite diagnosis was made after the surgery, based on histopathological examination of tumor tissue. Only in 4 (50 %) cases, diagnostic imaging methods definitely confirmed retroperitoneal tumor localization on pelvis, while in remaining 4 (50 %) cases, diagnosis was made intraoperatively.

Results

During a ten year long period from 2001 to 2010, at Clinic for Gynecology and Obstetrics in Novi Sad, 7354 patient were operated, out of which 4015 women due to different pelvic tumors, and 8 (0.19%) patients with retroperitoneal tumors. Characteristics of surgical treatment at these patients (histopathological findings, type and length of surgical treatment and complications) are shown in Table 2. 5 (62.5 %) patients had different malignant tumors of mesenchymal origin (sarcomas), while 3 (37.5%) patients had benign tumors. In all cases, tumors were completely removed. The length of operation ranged from 60 to

240 minutes ($x=189$ min.), and blood loss during the operation ranged from 150 to 700 ml ($x = 360$ ml). Adjuvant irradiation of tumor site was performed at 3 (37.5 %) patients (2 cases of sarcoma and 1 malignant schwannoma). At 2 (25 %) patients with malignant retroperitoneal schwannoma, early in postoperative period, bleeding from presacral veins and arteries of greater omentum occurred, which required repeated surgical exploration, hemostasis and administration of blood products. In patient with fibrohistiocytoma of Retzius space, left leg edema occurred in postoperative period due to ligation of venous branches of external iliac vein, which was cured by anticoagulant therapy, physical treatment and wearing compressive stocking 3 months after the operation. The total of 6 (75 %) patients is alive and without clinical signs of recurrence. Two (25 %) patients passed away, one 4 years after the first operation due to recurrence of malignant schwannoma, and another one 12 months after the surgery due to pulmonary edema, which was not related to surgical treatment. Picture 1 (A-D) shows images of pelvic retroperitoneal tumors.

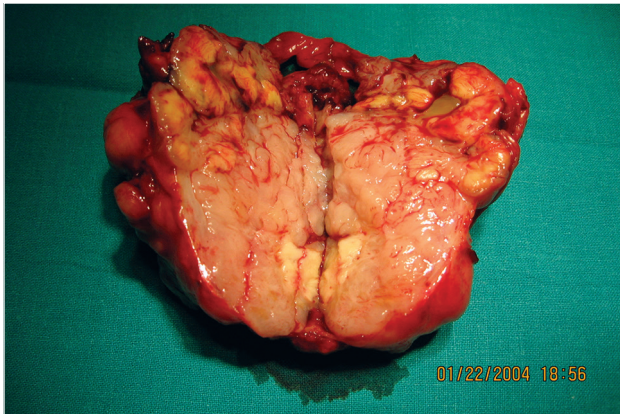
Table 2. Characteristics of surgical treatment at patients

Number of patient	Histopathological findings	Surgery	Complications	Recurrence	Outcome
1	Malignant schwannoma	Tumor removal, HTA, adnex.bil., omentectomy	Postoperative bleeding, reoperation	Without	Without adjuvant Th Alive for 3 y.
2	Malignant schwannoma	Tumor removal, HTA, adnex.bil., omentectomy	Postoperative bleeding, reoperation	2 years later, reoperation	Adjuvant chemo-irradiation Th, died after 4 y.
3	Benign schwannoma	Tumor removal	Without	Without	Alive for 5 y.
4	Fibrohistiocytoma	Tumor removal	Left leg edema	Without	Adjuvant irradiation, alive for 5 y.
5	Leiomyosarcoma of cervix	HTA, adnex.bil.	Without	Without	Died after 1 y. due to pulmonary edema
6	Benign teratoma	Tumor removal	Without	Without	Alive for 8 y.
7	Rhabdomyosarcoma	Tumor removal	Without	Without	Adjuvant irradiation Alive for 2 y.
8	Retroperitoneal leiomyomatosis	Tumor removal	Without	Without	Alive for 7 y.

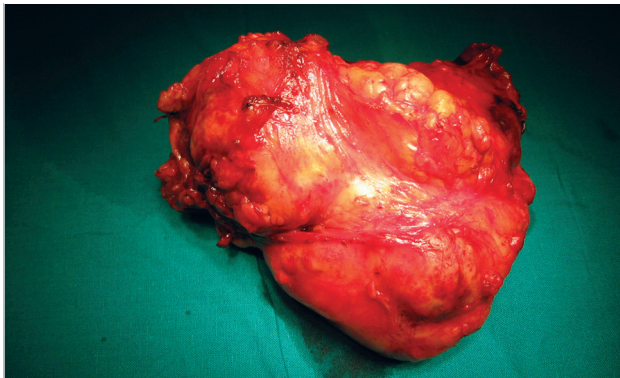
Abbreviations : HTA – total abdominal hysterectomy, bil – bilateral, Th – therapy, y – years



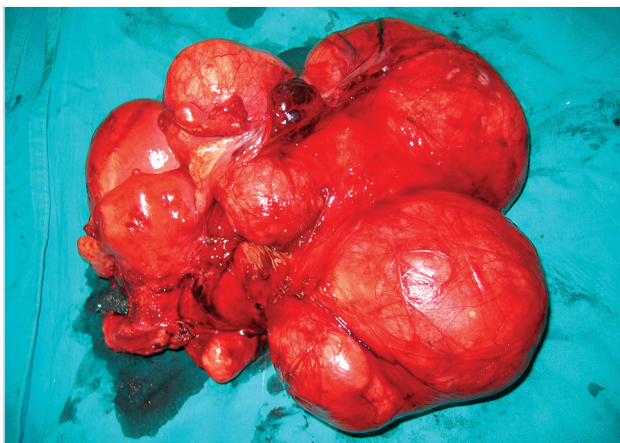
A



B



C



D

Picture 1. Different histological types of pelvic retroperitoneal tumors:

A – malignant schwannoma, B – benign schwannoma, C – pleomorphic fibrous histiocytoma, D – retroperitoneal leiomyomatosis

Discussion

Clinical diagnosis of retroperitoneal tumors is not always simple, and it requires pelvic and abdominal imaging either by computed tomography (CT) or magnetic resonance imaging (MRI) (7, 11, 12). However, examination should be performed by experienced radiologist, as mistakes and replacement with other types of tumors are possible. Therefore, definite diagnosis is in about 50% of cases is made intraoperatively and after histopathological examination (13). Treatment of retroperitoneal tumors is surgical and consists of complete removal of tumor mass. The most important prognostic factor is histopathological classification of tumor and whether the tumor is completely removed without residual tumor tissue. All malignant forms of retroperitoneal pelvic tumors have a tendency of recurrence, thus adjuvant irradiation of tumor site or surrounding can be performed after the surgery, which yields positive effect in certain cases (1,5,7,9). Use of adequate chemotherapeutic protocols for certain types of sarcomas (*doxorubicin* and *ifosfamide*, positive response 10-30 %) can also be applied (11,14). Best prognosis is for benign retroperitoneal tumors and malignant tumors with small volume and low oncogenetic potential (*Low grade sarcomas*) which do not infiltrate surrounding organs and are completely surgically removed (15). Infiltration of surrounding organs or vicinity of blood vessels can require involvement of different specialists in operation (abdominal, vascular surgeon or urologist). It is very important to assess technical possibility of complete tumor removal or refer the patient to the referent medical center with better prospects of successful treatment. Malignant forms of retroperitoneal tumors (sarcomas) require careful surveillance and follow up which should be performed 3-4 times a year during the first two postoperative years (16).

Conclusion

In our study, retroperitoneal tumors make up 0.19 % of all patients operated for pelvic tumors. In 50 % of cases, diagnosis was made intraoperatively and after definite histopathological examination of tumor tissue. The most common pelvic retroperitoneal tumors were schwannomas (3 or 37.5 %) followed by different pelvic soft tissue sarcomas. In all cases, complete surgical removal of tumors was performed, while second look surgery due to hemorrhage was performed in 2 (25 %) cases. Recurrence was detected in only 1 (12.5 %) patient, who died 4 years after primary surgical intervention. The total of 6 (75 %) patients are alive, while lethal outcome occurred in 2 (25 %) patients. Results of our study show that successful treatment of retroperitoneal tumors require prompt and multidisciplinary approach, in both making diagnosis and surgical treatment, and depending on histopathological type of tumor use of radio and chemotherapeutic treatment protocols.

References

1. Isaacs JH, Dolan Jr. Nongynecologic conditions encountered by the gynecologic surgeon. In : Rock JA, Thompson JD eds. *The Linde,s operative Gynecology*. Philadelphia - Tokyo: Lippincott, Williams&Wilkins; 1996. p. 1305-28.
2. Chan YM, Hon E, Ngai SW et al. Aggressive angiomyxoma in females : is radical resection the only option ? *Acta Obstet Gynecol Scand* 2000; 79: 216-20.
3. Dilek TUK, Dilek S, Pata O et al. Malignant fibrous histiocytoma of the ovary: a case report. *Int J Gynecol cancer* 2006; 16 (Suppl.1): 352-6.
4. Kentopp K, Jones MA, DeCain M, Tarraza HM. Pelvic retroperitoneal schwannoma mimicking an ovarian neoplasm : report of case and review of the literature. *Eur J Gynecol Oncol* 1998 ; Vol.XIX, N.1: 57-9.
5. Mandić A, Đurđević S, Popov M, Krnojelac D, Kukić B. Retroperitoneal malignant schwannoma and peritoneal malignant mesothelioma : a case report. *Journal of BUON* 2004; 9: 91-4.
6. Wagner S, Greco F, Hamza A et al. Retroperitoneal malignant solitary fibrous tumor of the small pelvis causing recurrent hypoglycemia by secretion of insulin-like growth factor 2. *European Urology* 2009; 55: 739-42.
7. Magtibay PM, Salmon Z, Keeney GL. Et al. Aggressive angiomyxoma of the female pelvis and perineum : a case series. *Int J Gynecol Cancer* 2006 ; 16 : 396-401
8. Guzin K, Afsar S, Yigit A et al. Pelvic ganglioneuroma. *Int J Gynecol Cancer* 2008 ; 18 : 553-6.
9. Tauro LF, George C, Kamath A, Lobo G, Shetty P, Hegde BR. Giant schwannoma in the pelvic retroperitoneum. *J Clin Diagn Res* 2008; 2: 1210-4.
10. Korkontzelos I, Tsimoyiannis E, Zagaliki A, Demou A, Karabina E, Antoniou N. Pelvic retroperitoneal schwannoma presenting as a gynecologic mass: case report. *Eur J Gynaecol Oncol*. 2005; 26(1): 117-9.
11. Cassidy J, Bissett D, Spence RAJ. Payne. *Oxford Handbook of Oncology*, Oxford University press, sec.eds. 2006 .
12. Dursun P, Salman MC, Taskiran C et al. Retroperitoneal leiomyomatosis : a case report. *Int J Gynecol Cancer* 2005; 15: 1222-5.
13. Fink D, Marsden DE, Edwards L. Malignant perivascular epitheloid cell tumor (PEComa) arising in the broad ligament. *Int J Gynecol Cancer* 2004; 14: 1036-9.
14. Jeremic D, Vojinov S, Levakov I, Marusic G. Retroperitoneal lymphadenectomy following chemotherapy for testicular cancer – analysis of postoperative complications according to Clavien-Dindo classification. *HealthMED Vol.5 No 6 – Suppl.1*, 2011 : 2186-89.
15. Menenakos C, Braumann C, Hartmann J, Christoph AJ. Retroperitoneal Castleman's tumor and paraneoplastic pemphigus: report of a case and review of the literature. *World Journal of surgical oncology* 2007 ; 5 : 45-9.
16. Hui Wen L, Wei Chih S, Ming Song T, Mei Leng C. Pelvic retroperitoneal leiomyoma. *American Journal of Surgery* 2010; vol. 199 (4) : 36-38.

Corresponding Author

Ljiljana Ivanovic,
Clinic for Gynecology and Obstetrics,
Novi Sad,
Republic of Serbia,
E mail : ljiljana.ivanovic1@gmail.com

Serum homocysteine, folate and B₁₂ concentration in patients with coronary artery disease: A case-control study

Seyyed Farzad Jalali¹, Amir Saeed Hosseini², Zeinab Shirvani Farsani³, Ali Bijani⁴

¹ Department of Cardiology, Babol University of Medical Sciences, Babol, Iran,

² Mazandaran University of Medical Sciences, Sari, Iran,

³ Department of Genetics, Tarbiat Modares University, Tehran, Iran,

⁴ Babol University of Medical Sciences, Babol, Iran.

Abstract

Background: Coronary artery disease is one of the most common causes of hospitalization. In addition to the known coronary risk factors, many important factors like high serum levels of homocysteine, low levels of antioxidants and folic acid have been suggested recently. The aim of this study was to assess the association between serum concentration of homocysteine, folate and B₁₂ with coronary artery disease in Iranian patients.

Methods and patients: We compared 60 patients with CAD to 60 matched normal subjects in Shahid Beheshti Hospital. The serum levels of homocystein, folic acid and vitamin B₁₂ were measured in each group.

Finding: The mean level of serum homocystein among cases and controls were 12.28±9.44 µmol/l and 9.1±4.39 µmol/l, respectively (p=0.02). This was obviously significantly different between the healthy men (8±3.1 µmol/lit) and the CAD patients (15.1±11 µmol/lit) (P=0.002), but there was no difference among the healthy women (10.18±5.2 µmol/lit) and the CAD patients (9.42±6.18µmol/lit) (p= 0.620).

Conclusion: In summary, we found one significant statistic difference between the cases and the controls about the serum levels of homocystein. Homocysteine levels were also higher in male patients than the healthy ones. But this relationship was not found in females. Serum vitamin B₁₂ and folate levels were not significantly different between the two groups statistically.

Key words: Coronary artery disease; Homocysteine; folate and vitamin B₁₂.

Introduction

Coronary artery disease (CAD) is a complex degenerative disease that causes reduced or absent blood flow in one or more of the arteries that encircle and supply the heart. Coronary artery atherosclerosis is the principal cause of CAD and is the single largest killer of both men and women. In spite of the fact that most of the CAD patients contain at least one of cardiovascular risk factors, 20% of patients with CAD no formal risk factors (1). The role of novel biofactors involving homocysteine in atherothrombotic vascular disease and prediction of risk of CAD is being more and more identified. Many studies found high serum homocysteine concentration to be associated to atherosclerotic disease including CAD (2–6).

Additionally, some reports showed hyperhomocysteinemia may have prognostic value in mortality of patients with CAD (7).

Some studies demonstrated that there is difference in prevalence and importance of homocysteine in CAD in different ethnic populations (8-10).

A few studies in Iran were done about the association of homocysteine with coronary artery disease (11-13).

Homocysteine is an intermediate formed by the catabolism of methionine to cysteine. It is metabolized by two pathways: trans-sulfuration and remethylation. Vitamin B as a cofactor and Folate as substrate are required for this process. Therefore the nutritional deficiency of these two vitamins is associated with high serum homocysteine (14-17).

The aim of the present study was to examine the relationship between the serum concentration of homocysteine as a risk factor and coronary artery disease.

Materials and Methods

This study was designed as a case-control study. Sixty patients (30 males and 30 females mean age 60.13 ± 9.44 yr) with CAD were recruited in the Cardiology Clinic at Shahid Beheshti Hospital, Babol, Iran. Healthy subjects or controls (30 males and 30 females mean age 59.30 ± 10.84 yr) had no history of cardiovascular disease, hypertension, hyperlipidemia, liver and renal disease, diabetes, cancer, alcoholism or other metabolic diseases. A fasting blood sample was taken from all the patients and controls for the estimation of homocysteine, folic acid and B12 vitamin. The samples were refrigerated immediately after collecting and storing them at -20°C .

Homocysteine was assayed by axis Kit (IBL, German). Serum Vitamin B₁₂ and Folate were determined using a radio-Immunoassay kit (ICN, USA).

Statistical analysis

Mean and standard deviation (SD) were calculated. The results from the different group of subjects were compared with SPSS 13.0 (SPSS, Inc., Chicago, Illinois), Student t-test, the Chi-square test and Pearson correlation coefficients and the level of significance was set at $p < 0.05$.

Results

The mean and standard deviation (SD) age in CAD patients' were 60.13 ± 9.44 and in controls were 59.30 ± 10.84 that have no significant difference ($p = 0.654$). The mean and standard deviation (SD) age in CAD men were 59.60 ± 9.32 , in men healthy were 58.47 ± 12.71 , in CAD women were 60.67 ± 9.68 and in healthy women were 60.13 ± 8.72 that were in same range.

tion (SD) age in CAD men were 59.60 ± 9.32 , in men healthy were 58.47 ± 12.71 , in CAD women were 60.67 ± 9.68 and in healthy women were 60.13 ± 8.72 that were in same range.

Serum homocysteine concentrations were $12.28 \pm 9.44 \mu\text{mol/l}$ in patients and $9.1 \pm 4.39 \mu\text{mol/l}$ among the controls there was a significant relation ($p = 0.02$). This difference was more obvious between the patients and healthy men ($p = 0.002$) whereas no significant difference was observed between serum homocysteine concentrations in patient and healthy women ($p = 0.62$). Also the levels of folate and vitamin B₁₂ in two group patients and control had no difference (table 1 & 2).

A positive correlation between age and serum homocysteine concentrations ($p = 0.024$ & Pearson correlation coefficients = 0.206) was observed. This correlation was presented between the patients and the controls between the men and the women but there was no significant correlation between serum homocysteine concentrations, folate and vitamin B₁₂ (table 3).

Discussion

In the present study the serum homocysteine concentrations were $12.28 \pm 9.44 \mu\text{mol/l}$ in patients and $9.1 \pm 4.39 \mu\text{mol/l}$ among controls that showed a correlation between the CAD persons with hyperhomocysteine.

Despite many studies, the role of hyperhomocysteinemia as a risk factor of CAD is contro-

Table 1. Comparison of Homocysteine, folic acid, B12 vitamin serum Levels in patients with CAD and controls

	CAD (mean $\pm$ SD)	CONTROLS (mean $\pm$ SD)	P value
Homocysteine Level($\mu\text{mol/L}$)	12.28 ± 9.44	9.1 ± 4.39	0.020
Folic acid level($\mu\text{mol/L}$)	10.7 ± 3.94	9.73 ± 3.93	0.182
B12 vitamin level($\mu\text{mol/L}$)	383.63 ± 141.78	434.87 ± 206.56	0.116

Table 2. Comparison of Homocysteine, folic acid, B₁₂ vitamin serum Levels in patients with CAD and controls according to gender

gender		CAD(mean $\pm$ SD)	CONTROLS (mean $\pm$ SD)	P value
male	Homocysteine Level($\mu\text{mol/L}$)	15.14 ± 11	8.02 ± 3.13	0.002
	Folic acid level($\mu\text{mol/L}$)	10.96 ± 3.68	9.33 ± 3.01	0.065
	B12 vitamin level($\mu\text{mol/L}$)	379.13 ± 140.2	448.2 ± 208.24	0.137
female	Homocysteine Level($\mu\text{mol/L}$)	9.42 ± 6.58	10.18 ± 5.2	0.62
	Folic acid level($\mu\text{mol/L}$)	10.43 ± 4.22	10.14 ± 4.69	0.798
	B12 vitamin level($\mu\text{mol/L}$)	388.13 ± 145.6	421.53 ± 207.53	0.474

Table 3. Correlation between age and homocysteine, folic acid, vitamin B₁₂ serum Levels

	Index	B12 vitamin Level(μ mol/L)	Folic acid Level(μ mol/L)	Homocysteine Level(μ mol/L)
age	Pearson correlation coefficients	0.056	0.146	0.206
	P value	0.541	0.111	0.024
Homocysteine Level(μ mol/L)	Pearson correlation coefficients	0.036	0.148	
	P value	0.697	0.107	
Folic acid level(μ mol/L)	Pearson correlation coefficients	0.039		
	P value	0.669		

versial. Boushey et al. discovered that a 5- μ mol/lit addition in homocysteine increases odds ratio for CAD as great as 1.6 for men and 1.8 for women. They showed that 10% of general population CAD risk is associated with homocysteine (18).

Also some investigations displayed that hyperhomocysteinemia is a causal risk factor for CAD (19-20). In other words, the increased level of homocysteine interacts with other routine risk factors and in combination with these factors increases the risk of CAD. Our results are comparable to the earlier studies done in Iran (11-13).

Also, these data is concordant the investigators (21-28). Moreover, Wu et al. reported that high homocysteine plus decreased Trx is strongly related to CAD severity, but high homocysteine alone is only weakly related to CAD severity (29).

However, Sastry et al (30) and Deepa et al. (31) in Indian population and Bunout et al. (32) and Vivona et al. (33) demonstrated that increased homocysteine level do not have direct correlation with atherosclerotic vascular disease and CAD. Although, the following years, other investigators in India displayed which the mean homocysteine levels in CAD patient were significantly higher than the controls (34-35).

In the present study, there is no correlation between serum folic acid and vitamin B12 level in CAD patients and controls (table 1 & 2). Similar results acquired from investigations of Dzielinska et al. (36), Moleerergpoom et al. (8), Lonn et al. (37), EL Oudi et al (27). Also Bunout et al reported that there was no difference in vitamin B12 levels between the CAD patients and the control subjects, but lower serum folate levels were remarked when compared to patients with atherosclerotic vascular disease and healthy control subjects (32). On the contrary, Nussier et al. in 2007 indicated a significant association

between the decreased folic acid and vitamin B12 with elevated CAD (38). In other analysis it was described that Folateh as significant inverse association with coronary heart disease in men (10).

Although there are several investigations which displays higher homocysteine levels with low intake of vitamin B12 and folic acid (34, 39-40), but in our study it was observed that there was no significance correlation between the serum level of homocysteine, folic acid and vitamin B12. This might be because of the effects of genetics background on regulation of enzymes in homocysteine metabolism (41-42).

We also analyzed the serum homocysteine level in sick males and females separately that there it was in men ($15.14 \pm 11 \mu$ mol/lit) more than women ($9.42 \pm 6.58 \mu$ mol/lit) ($p < 0.018$).

This difference could be due to larger muscle mass and greater creatine phosphate synthesis in men, the lowering effect of estrogen in women, and a homocysteine synthesis rate between genders (43).

In addition, our report denoted positive associations of elevated homocysteine levels with age (P value = 0.024 & Pearson correlation coefficients = 0.206) (table 2 & 3), in other word serum homocysteine levels in both males and females increase with age. Same results were observed in other papers (44 -45). Therefore, this study underscores the consequence of age and sex-associated disagreement in the serum homocysteine levels.

However there are several other factors that relate to the serum level of homocysteine such as smoking (19) anti-hypertensive drugs, Diuretics and fibrates (46), and Vegetarianism (47).

Also Elshorbagy and et al suggest that decreased homocysteine may explain the thinness, low Body mass index (BMI), and decreased subcutaneous fat seen in patients with homocystinuria (48).

Another factor is gene polymorphisms that is indicated by the fact that individuals having polymorphism in the homocysteine metabolism pathway genes including Solute Carrier family 19 (SLC19A1 & SLC19A3), FormImino Transferase Cyclodeaminase (FTCD), methylenetetrahydrofolate reductase (MTHFR) genes (46, 49) and Glutamate carboxypeptidase II (GCP II) gene (50). Hence, single nucleotide polymorphism (SNPs) in homocysteine-pathway genes act as markers of disease predisposition in case-control and population studies.

Since homocysteine concentration plays a role in CAD, Thus, future studies should be multifactorial to examine the levels of homocysteine in Iranian and other populations.

References

1. Smith SC. Current and future directions of cardiovascular risk prediction. *Am J Cardiol* 2006; 97(2A): 28A-32A.
2. Yan ZQ, Hansson GK. Innate immunity, macrophage activation, and atherosclerosis. *Immunol Rev* 2007; 219: 187-203.
3. Helfand M, Buckley DI, Freeman M, et al. Emerging risk factors for coronary heart disease: a summary of systematic reviews conducted for the US Preventive Services Task Force. *Ann Intern Med* 2009; 151: 496-507.
4. Wald DS, Law M, Morris JK. The dose-response relation between serum homocysteine and cardiovascular disease: implications for treatment and screening. *Eur J Cardiovasc Prev Rehabil* 2004; 11: 250-253.
5. Daly C, Fitzgerald AP, O'Callaghan P, Collins P, Cooney MT, Graham IM, et al. on behalf of the COMAC Group: homocysteine increases the risk associated with hyperlipidaemia. *Eur J Cardiovasc Prev Rehabil* 2009; 16: 150-155.
6. Virtanen JK, Voutilainen S, Happonen P, Alfthan G, Kaikkonen J, Mursu J, et al. Serum homocysteine, folate and risk of stroke: Kuopio Ischaemic Heart Disease Risk Factor (KIHD) Study. *Eur J Cardiovasc Prev Rehabil* 2005; 12: 369-375.
7. Nygard O, Nordrehaug JE, Refsum H, Ueland PM, Farstad M, Vollset SE. Plasma homocysteine level and mortality in patients with coronary artery disease. *N Engl J Med* 1997; 337(4): 230-6.
8. Moleerergpoom W, Sura T, Sritara P. Association between Serum Homocysteine, Folate and B12 Concentration with Coronary Artery Disease in Thai Patients. *J Med Assoc Thai* 2004; 87(6): 674-8.
9. Ni M, Zhang XH, Jiang SL, and Zhang Y. Homocystinemia as an Independent Risk Factor in the Chinese Population at a High Risk of Coronary Artery Disease. *Am J Cardiol* 2007; 100: 455-458.
10. Onat A, Hergenc G, Kucukdurmaz Z, Can G, Ayhan E, Bulur S. Serum folate is associated with coronary heart disease independently of homocysteine in Turkish men. *Clin Nutr* 2008; 27(5): 732-9.
11. Golbahar J, Rezaian GR. Association of Hyperhomocystinemia with Coronary Artery Disease in Southern Iran. *IJMS* 2004; 29(3): 116.
12. Hajimoradi B, Bahrami GR, Kiani A, Kazerani H, Moloudi A, Rai A, et al. Homocysteine level in patients with premature coronary artery disease. *Hakim Research Journal* 2007; 9(4): 31-6.
13. Mirdamadi SA, Farzamnia H, Varzandeh P, Almasi N, Arasteh M. Association Between Serum Homocysteine Concentration With Coronary Artery Disease In Iranian Patients, *ARYA Atherosclerosis Journal* 2011; 7(2): 1-5.
14. Weiss N, Keller C, Hoffmann U, Loscalzo J. Endothelial dysfunction and atherothrombosis in mild hyperhomocysteinemia. *Vasc Med* 2002; 7: 227-39.
15. Mager A, Orvin K, Koren-Morag N, et al. Impact of homocysteine lowering vitamin therapy on long-term outcome of patients with coronary artery disease. *Am J Cardiol* 2009; 104: 745-749.
16. Armitage JM, Bowman L, Clarke RJ, et al. Effects of homocysteine-lowering with folic acid plus vitamin B12 vs placebo on mortality and major morbidity in myocardial infarction survivors: a randomized trial. *JAMA* 2010; 303: 2486-2494.
17. Austin RC, Lentz SR, Werstuck GH. Role of hyperhomocystinemia in endothelial dysfunction and atherothrombotic disease. *Cell Death Differ* 2004; 11(1): 56-64.
18. Boushey CJ, Beresford SA, Omenn GS, Motulsky AG. A quantitative assessment of plasma homocysteine as a risk factor for vascular disease. Probable benefits of increasing folic acid intakes. *JAMA* 1995; 274(13): 1049-57.
19. Syed S Ahmed S, Ahmed SI, Effect of Smoking on The Levels Of Folic Acid, Vitamin B12 And Total Homocysteine In Patients With Coronary Artery Disease. *Pakistan Journal of Pharmacology* 2007; 24(2): 47-54.
20. Chaudhari V, Hyperhomocystinemia and Coronary Artery Disease in the Asian Indian Population. *Nutrition Noteworthy* 2003; 6(1): 1-5.

21. Rogers JD, Sanchez saffon A, Frol AB, Diaz Arrastia R. Elevated plasma homocysteine levels in patients treated with levodopa: associated with vascular disease. *Arch Neural* 2003; 60 (1): 59-64.
22. Yilmaz N, Cicek HK, CelikI.Meram, Kocabas R and Davutoglu.Diagnostic value of homocysteine, C-reactive proteinand bilirubin for coronary artery disease. *EMHJ* 2007; 13(3): 522-535.
23. Agoston-Coldea L, Mocan T, Seicean A, Gatfossé M, RosenstinglS.The Plasma Homocysteine Concentrations and Prior Myocardial Infarction, ROM. *J. INTERN. MED.*, 2010; 48(1): 65-72.
24. Xiao Y, Zhang Y, Lv X, Su D, Li D, Xia M, Qiu J, Ling W, MaJ.Relationship between lipid profiles and plasma total homocysteine, cysteine andthe risk of coronary artery disease in coronary angiographic subjects.*Lipids in Health and Disease* 2011; 10: 137 doi: 10.1186/1476-511X-10-137.
25. Aparna P, BetigeriAM ,Pasupathi P. Homocysteine and oxidative stress markers and inflammation in patients withcoronary artery disease. *Int J Biol Med Res* 2010; 1(4): 125-129.
26. Priya VV, Surapaneni KM. Erythrocyte lipid peroxidation, glutathione,ascorbic acid, vitamin E, antioxidant enzymes and serum homocysteinelevels in patients with coronary artery disease. *JCDR* 2008; 8: 338-384.
27. EL Oudi M, AouniZ, MazighC, KhochkarR,Gazoueni E, Haouela H, MachghoulS. Homocysteine and markers of inflammation inacute coronary syndrome. *Exp Clin Cardiol* 2010; 15(2): e25-e28.
28. Sun Y, Chien KL, Hsu HC, Su TC, Chen MF, Lee YT. Use of Serum Homocysteine to Predict Stroke, Coronary Heart Disease and Death in Ethnic Chinese. *Circ J* 2009; 73: 1423-1430.
29. Wu Y, Yang L, Zhong L. Decreased serum levels of thioredoxin in patients with coronary artery disease plus hyperhomocysteinemia is strongly associated with the disease severity. *Atherosclerosis* 2010; 212: 351-355.
30. Sastry BK, Indira N, Anand B, Kedarnath B; Prabha BS,Raju BS. A case-control study of plasma homocysteine levels in South Indians with and without coronary artery disease.*Indianheart J*2001; 53(6): 749-53.
31. Deepa R, Velmurugan K, Saravana G, Karkuzhali K, Dwarakanath V, Mohan V. Absence of associati-on between serum homocysteine levels and coronary artery disease in south Indian males. *Indian Heart J* 2001; 53 (1): 44-7.
32. Bunout D, Petermann M, Hirsch S, de la Maza P, Suazo M, Barrera G, Kauffman R. Low serum folate but normal homocysteine levels in patients with atherosclerotic vascular disease and matched healthy controls. *Nutrition*. 2000; 16(6): 434-8.
33. Vivona N, Bivona G, Noto D, Lo Sasso B, B. Cefalù A,Chiarello G, Falletta A, Ciaccio M, R. Averna M.C-reactive protein but not soluble CD40 ligand and homocysteineisassociated to common atherosclerotic risk factors in a cohort ofcoronary artery disease patients.*Clinical Biochemistry* 2009; 42: 1713-1718.
34. Abraham R, Joseph John M, Calton R, Dhanoa J. Raised Serum Homocysteine Levels In Patients Of CoronaryArtery Disease And The Effect Of Vitamin B12 And Folate On Its Concentration. *Indian Journal of Clinical Biochemistry* 2006; 21 (1) 95-100.
35. Anand P, Awasthi S, Mahdi A, Tiwari M, Agarwal-GG. SerumHomocysteine in Indian Adolescents. *Indian Journal of Pediatrics* 2009; 76: 705-709.
36. Dzielinska Z, Kadziela J, Sitkiewicz D, et al.elevated Levels of homocysteine in plasma as a risk factor for coronary artery disease. *Pol Arch Med Wewn* 2000; 104 (1): 345-53.
37. Lonn E, Yusuf S, Arnold MJ, Sheridan P, Pogue J, Micks M, McQueen MJ,Probstfeld J, Fodor G, Held C et al.Homocysteine lowering with folicacid and B vitamins in vascular disease. *The New England journal ofmedicine* 2006; 354(15): 1567-1577.
38. Nusier MK, El-DwairiQA.effects of vitamin B12 and folic acid on hyperhomocysteinemia in patients with acute myocardial infarction. *Journal of Health Science* 2007; 53(1): 16-22.
39. Misra A, Vikram NK, Pandey RM, DwivediM, Ahmad FU, Luthra K, Jain K, KhannaN,Devi JR, Sharana R. and GuleriaR.Hyperhomocysteinaemia, and low intakes of folicacid and vitamin B12 in urban North India. *EurJ Nutr*2002; 41(2): 68-77.
40. Ortega RM, Jemenez A, Andres P, FaciM,Lollo JM, Lozano MC, Bermejo LM, Lopez-Sobaler AM. andRequejoAM.Homocysteine levels in elderly Spanish people: Influence of pyridoxine, Vitamin B12 and folic acidintakes. *J Nutr Health Ageing* 2002; 6(1): 69-71.
41. Lin PT, Huang MC, Lee BJ, Cheng CH, Tsai TP, Huang YC. High plasma homocysteine is associated with the risk of coronary artery disease independent of methylenetetrahydrofolatereductase 677C→T genotypes. *Asia Pac J ClinNutr* 2008; 17 (2): 330-338.

42. Messika AH, Kaluski DN, Lev E, Iakobishvili Z, Shohat M, Hasdai D, Mager A. Nutrigenetic impact of daily folate intake on plasma homocysteine and folate levels in patients with different methylenetetrahydrofolate reductase genotypes. *European Journal of Cardiovascular Prevention and Rehabilitation* 2010; 17(6): 701-705.
43. Gharaibeh MY, Gahtan RA, Khabour OF, Alomari MA. Hyperhomocysteinemia, Low Folate, and Vitamin B12 Deficiency in Elderly Living at Home and Care Residences: A Comparative Study. *LABMEDICINE* 2010; 41(7): 410-414.
44. Dominguez LJ, Galioto A, Pineo A, Ferlisi A, Ciaccio M, Putignano E, et al. Age, homocysteine, and oxidative stress: relation to hypertension and type 2 diabetes mellitus. *J Am Coll Nutr* 2010; 29(1): 1-6.
45. Matetzky S, Freimark D, Ben-Ami S, et al. Association of elevated homocysteine levels with a higher risk of recurrent coronary events and mortality in patients with acute myocardial infarction. *Arch Intern Med* 2003; 163(16): 1933-7.
46. Ghassibe-Sabbagha M, Platt DE, Youhanna S, Abchee AB, Stewart K, Badro DA, Haber M, Salloom AK. Genetic and environmental influences on total plasma homocysteine and its role in coronary artery disease risk. *Atherosclerosis* 2012; : xxx-xxx.
47. Yves Ingenbleek M.D, Kilmer S, McCully M.D. Vegetarianism produces subclinical malnutrition, hyperhomocysteinemia and atherogenesis. *Nutrition* 2012; 28: 148-153.
48. Elshorbagy AK, Nurk E, Gjesdal CG, Tell GS, Ueland PM, Nygård O, Tverdal A, Vollset SE, Refsum H. Homocysteine, cysteine, and body composition in the Hordaland Homocysteine Study: does cysteine link amino acid and lipid metabolism? *Am J Clin Nutr* 2008; 88: 738-46.
49. Wernimont SM, Clark AG, Stover PJ, Wells MT, Litonjua AA, Weiss ST, Gaziano JM, Tucker KL, Bacca-relli A, Schwartz J, Bollati V and Cassano PA. Folate network genetic variation, plasma homocysteine, and global genomic methylation content: a genetic association study. *BMC Medical Genetics* 2011; 12(150): 1-11.
50. Divyia S, Naushad SM, Addlagatta A, Murthy PVLN, Reddy CR, Digumarti RR, Gottumukkala SR, Kumar A, Rammurti S, Kutala VK, Paradoxical role of C1561T glutamate carboxypeptidase II (GCP II) genetic polymorphism in altering disease susceptibility. *Gene* 2012; 497: 273-279.

Corresponding Author

Amir Saeed Hosseini,
Mazandaran University of Medical Sciences,
Sari,
Mazandaran Province,
Iran,
E-mail: ASHosseini@Mail.Mazums.ac.ir

Radiographic interpretation of the abnormalities of the follicles of impacted teeth

Branko Mihailovic¹, Milan Miladinovic¹, Milos Duka², Zoran Vlahovic¹, Nebojsa Mitic³, Dejan Dubovina¹

¹ Faculty of Medicine in Priština, Dentistry Clinic, Oral Surgery Department, Serbia,

² Military Medical Academy, Belgrade, Dentistry Clinic, Oral Surgery Department, Serbia,

³ Faculty of Medicine in Priština, Institute of Pathology, Serbia.

Abstract

Introduction: It is still an unresolved issue whether asymptomatic impacted teeth should be extracted or left in place. Verification of their asymptomatic status is based on the radiographic analysis, but it is not known for sure if radiologically normal follicles can produce valid histologic verification.

Material and methods: The study involved 80 impacted teeth; radiographic analysis was done on all of them using digital panoramic radiography. The finding of pathologic degeneration was based on the presence of 3 mm pericoronal radiolucence. Pathohistologic verification was done afterwards, using the hematoxylin eosin staining method.

Results: In 30 cases, positive radiographic and histopathologic analysis was obtained. In 50 cases, radiographs were negative, out of which in 31 cases associated with positive histopathology and in 19 cases with negative histopathology.

Conclusion: The results of histopathologic analysis showed that around impacted teeth follicular cysts are much more common than supposed based on radiographic imaging. Prophylactic extraction of clinically and radiographically dormant impacted teeth thus seems to be justified.

Key words: Impacted teeth, dental follicle, odontogenous cyst, histologic verification, panoramic radiography

Introduction

The question whether to extract asymptomatic impacted or retained wisdom teeth, and other teeth in a lesser degree, or to leave them in place, has not been clearly answered. These teeth may be extracted if there is a benefit in the domain of oral surgery or orthodontics; however, if we reconsider the issue in the light of long-term lack of space, their prophylactic extraction cannot reduce or prevent

possible lack of space even a couple of years later¹. On the other hand, the verification of asymptomatic status of these teeth is usually based on the clinical examination and radiographic analysis. These teeth are associated with appropriate physiologic dental follicle. In that regard, using radiologic analysis, an oral surgeon is able to obtain the information about the possible development of a follicular cyst around the crown of ungrown tooth and its relationship with physiologic dental follicle, often associated with cystic degeneration clearly confirmed by histopathologic verification²⁻⁴. However, it is still unknown whether radiographically sound and healthy follicles necessarily imply healthy histologic verification. The aim of this paper is to examine the presence of pathologic changes even in radiographically normal dental follicle (negative for cystic formations) and to assess possible histologic abnormalities in the follicle surrounding an impacted tooth in cases in which pathologic changes are not radiographically visible.

Material and methods

The study involved 80 impacted permanent teeth in 62 individuals (34 women and 28 men), aged 11 to 68 years. Radiographic analysis, performed on all teeth, consisted of digital panoramic imaging. Pathologic degeneration of a dental follicle was defined as a 3 mm pericoronal radiolucence, where the distance of less than 3 mm between the external follicle envelope and enamel surface of the impacted tooth was considered non-pathologic⁵. The tissue for histologic processing was fixated in 10% formaldehyde, embedded in paraffin blocks, microtomed in multiple sections, and hematoxylin-eosin stained, with some of the preparations specially stained as well (Mallory, Van-Gieson). Histologic analysis tried to detect epithelial elements in the dental follicle tissue and the beginnings of cystic

change. Some preparations with insufficiently clear epithelial elements were immunohistochemically processed for cytokeratins.

Results

In 30 cases, the analysis of radiographic images indicated cystic degeneration of dental follicles – the follicular space was larger than 3 mm and the presence of epithelial elements and cystic degeneration in the follicle were histologically verified (Table 1). In 50 cases there was no radiologic suspicion of cystic degeneration (Figure 1), i.e. the follicular space was larger than 3 mm. Out of these, in 31 cases histopathologic findings nevertheless verified the presence of epithelial elements and dental follicle cystic degeneration. Histologic picture of a group of follicles in which epithelial elements were found demonstrated the nests of epithelium captured in the soft tissue (Figure 2), but also small calcifications in the captured epithelial foci in the soft tissue (Figure 3). Some sections demonstrated dense inflammatory infiltrate and fresh hemorrhage in the center, with transversally or longitudinally sectioned papillas of the squamous-stratified epithelium (Figure 4). Non-specific granulation tissue and markedly hyperemic blood vessels, with superficial epithelial destruction, dominated the histological picture of some of the preparations (Figure 5). A common histologic picture of dental follicle cystic degeneration involved the cyst filled with keratine and cholesterol crystals, coated with squamous-stratified epithelium (Figure 6).

Table 1. Distribution of radiologic and histopathologic findings of extracted dental follicles

Radiologic finding (RF)	Histopathologic finding				Total
	With epithelial elements		Without epithelial elements		
	No.	%	No.	%	
RF positive	30	100.00	0	0.00	30
RF negative	31	62.00	19	38.00	50
Total	61		19		80



Figure 1. Negative radiologic finding – follicular space smaller than 3 mm

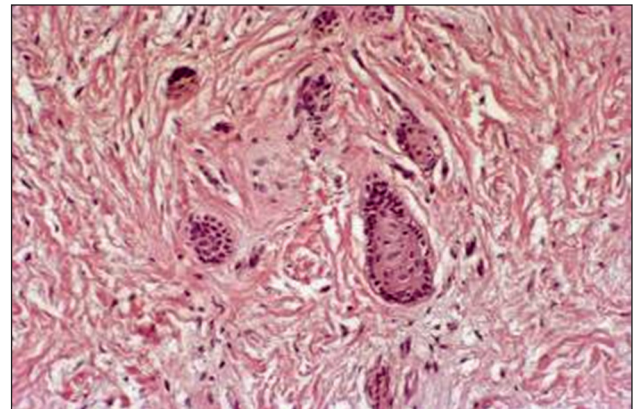


Figure 2. Histologic image of the follicle preparation with epithelial elements. Nests of captured epithelium in the soft tissue

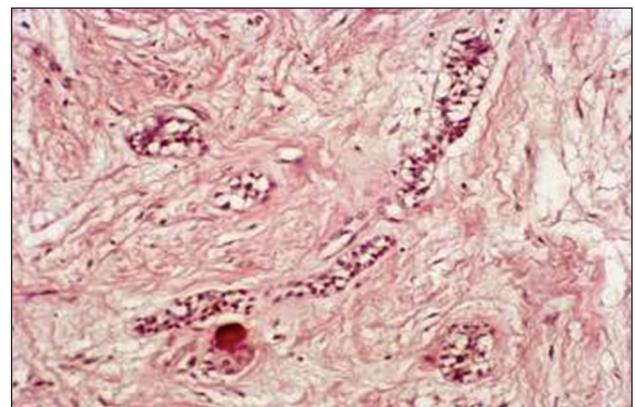


Figure 3. Histologic image of the follicle preparation with epithelial elements. Small calcifications in the foci of captured epithelium in the soft tissue

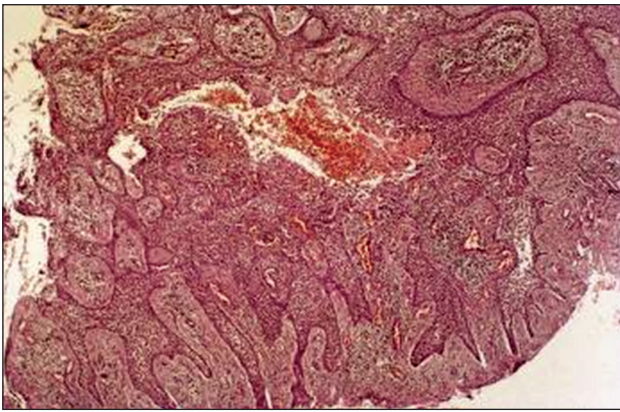


Figure 4. Dense inflammatory infiltration and fresh bleeding in the center; with transversally and longitudinally sectioned papillas of squamous-stratified epithelium

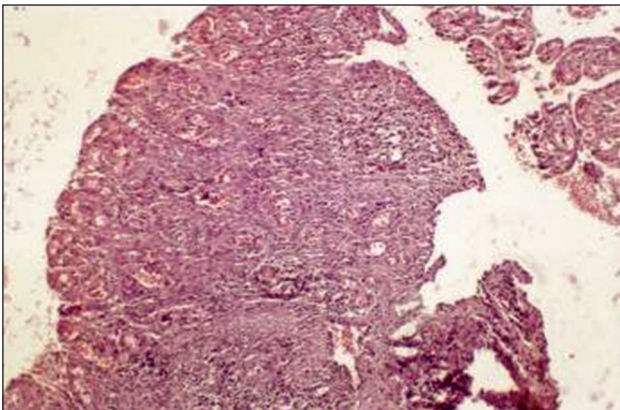


Figure 5. Predominance of non-specific granulation tissue and presence of strongly hyperemic blood vessels with destruction of superficial epithelium

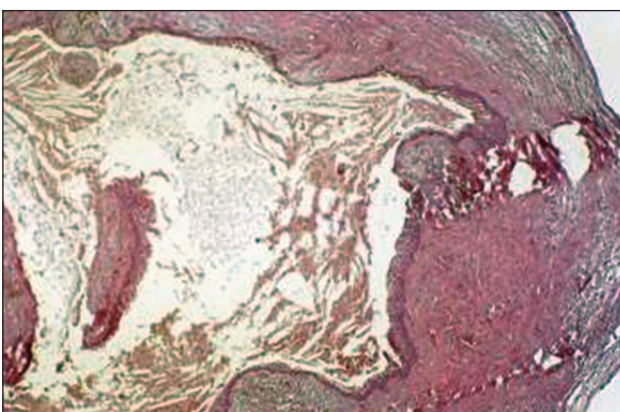


Figure 6. Degeneration of dental follicle involves a cyst filled with keratin and cholesterol crystals, coated with squamous-stratified epithelium

In the remaining 19 cases, with both radiologic and histopathologic findings negative, i.e., without epithelial elements as a reliable verification

sign, radiologic and histologic assessment correlated with each other. Histologic preparations of this group of follicles demonstrated uniform histologic picture with predominant soft tissue and lymphocytic infiltrations (Figure 7) within which the fragments of calcified bone could be seen without any epithelial elements (Figure 8).

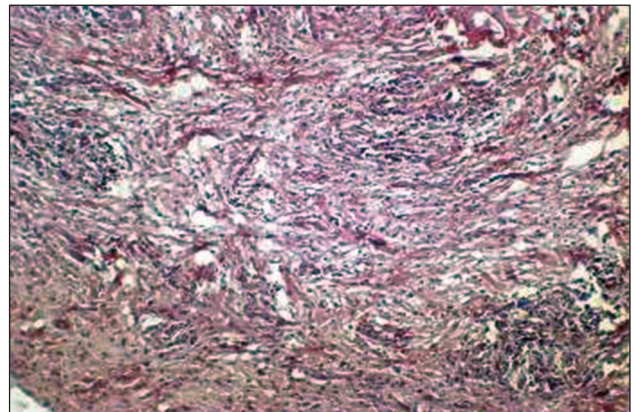


Figure 7. Follicles without radiologic and histopathologic findings, with conspicuous lymphocytic infiltrations.

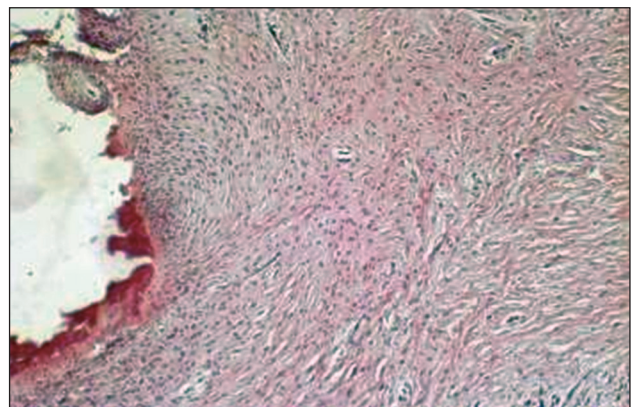


Figure 8. Follicles without radiologic and histopathologic findings, with fragments of calcified bone, without epithelial cells.

Discussion

The mainstay of diagnosis and decision-making related to the extraction of impacted teeth are based on radiographic evaluation and clinical examination. Although these two diagnostic approaches can be reliable methods for short-term solutions, potential dental follicle degeneration, unintelligible radiologically, can lead to subsequent problems caused by the teeth which have not been prophylactically extracted.

Our findings indicated a surprisingly common presence of cystic changes with impacted teeth the radiographic findings of which had been in order. We found that radiography produced reliable results if positive; it was then always accompanied by identical histopathologic verification. In cases of negative radiography, in less than half, i.e. in 19 cases (38%), dental follicles were in fact healthy, and in 31 cases (62%) dental follicles were involved with cystic degeneration, as shown by histopathologic verification.

The difference in incidence of cystic degeneration of dental follicles between the radiographic and histologic methodology has been observed by other authors as well⁶. Whether this is the question of insufficiently precise measurement of the follicular space with two-dimensional digital radiography (usually characterized by a 25% distortion), or the space of 3 mm is not an appropriate measure of absence of dentogenous cysts, will be shown by the studies using three-dimensional radiography without distortion and with measurement precision to the order of a tenth of a millimeter⁷. *Stephens et al.* have therefore suggested that the magnitude of the pericoronal space indicating a cyst should not exceed 2.5 mm⁸.

Baykul et al. have found more than 50% of cystic changes in a histologic preparation compared to asymptomatic radiography, stressing that the number was predominant in persons over 20 years of age, which agreed with 62% in our study⁹. *Adelsperger et al.*⁶ have found 34%, and *Rakprasitkul et al.* 35%¹⁰.

*Saravana and Subhashraj*¹¹ have found an increased number of cystic degenerations of 46%, suggesting continued both histopathologic evaluation and radiographic diagnosis in the management of impacted third molars.

Although there has been a general agreement that impacted teeth which cause pathologic changes of either general or local nature should be removed, prophylactic extraction is still disputed. The body of evidence is still insufficient to support routine removal of impacted teeth to prevent disease. This study supports this notion. On the other hand, there have been reports describing common complications caused by impacted teeth left intact^{12,13}. The risk of missed radiologic diagnosis, according to the reported results, exceeds 50%; if not spotted in time,

dental follicle cystic degeneration leads to follicular cyst with asymptomatic, expansive growth, causing the resorption of adjacent bone tissue; associated with upper lateral teeth, a follicular cyst can collide with the sinus; with impacted upper canines, it can collide with the sinus and nasal cavity, and bone destruction caused by the third lower molar in the region of angulus and ramus of the mandible can often produce pathologic fractures.

We believe that the incidence of these changes is even higher, given the fact that a large number of impacted teeth (without radiographic suspicion of dental follicle cystic changes) are extracted for some other reason.

Conclusion

Analyzing the results of histologic studies we came to a surprising conclusion that the appearance of a follicular cyst around the impacted teeth was much more common than it could have been supposed based on radiography. Focusing the attention to the nature of these lesions and their possible negative effects, the results of our histologic study justified the prophylactic removal of clinically and radiographically dormant impacted teeth.

Acknowledgement

This paper has been created and published in the name of our Lord and our Savior Jesus Christ.

References

1. Mettes TG, Nienhuijs ME, van der Sanden WJ, Verdonchot EH, Plasschaert AJ. Interventions for treating asymptomatic impacted wisdom teeth in adolescents and adults. *Cochrane Database Syst Rev.* 2005 Apr 18; (2): CD003879.
2. Macdonald-Jankowski DS. Orthokeratinized odontogenic cyst: a systematic review. *Dentomaxillofac Radiol.* 2010 Dec; 39(8): 455-67.
3. Sun CX, Ririe C, Henkin JM. Hyperplastic dental follicle - review of literature and report of two cases in one family. *Chin J Dent Res.* 2010; 13(1): 71-5.
4. Eichhorn W, Wehrmann M, Blessmann M, Pohlenz P, Blake F, Schmelzle R, et al. Metastases in odontogenic cysts: literature review and case presentation. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2010 Apr; 109(4): 582-6.

5. Kotrashetti VS, Kale AD, Bhalaerao SS, Hallikeremath SR. *Histopathologic changes in soft tissue associated with radiographically normal impacted third molars. Indian J Dent Res. 2010 Jul-Sep; 21(3): 385-90.*
6. Adelsperger J, Campbell J, Coates D, Summerlin DJ, Tomich J. *Early soft tissue pathosis associated with impacted third molars without pericoronal radiolucency. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000; 89: 402-6.*
7. Mihailović B, Miladinović M, Mladenović D, Lazić Z, Janković A, Živković D, et al. *Computerized dentistry. (Serbian). Belgrade: Obeležja; 2009.*
8. Stephens RG, Kogon SL, Reid JA. *The unerupted or impacted third molar: a critical appraisal of its pathologic potential. J Can Dent Assoc 1989; 55: 201-7.*
9. Baykul T, Sağlam AA, Aydın U, Başak K. *Incidence of cystic changes in radiographically normal impacted lower third molar follicles. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2005 May; 99(5): 542-5.*
10. Rakprasitkul S. *Pathologic changes in the pericoronal tissues of unerupted third molars. Quintessence Int 2001; 23: 633-8.*
11. Saravana GH, Subhashraj K. *Cystic changes in dental follicle associated with radiographically normal impacted mandibular third molar. Br J Oral Maxillofac Surg. 2008 Oct; 46(7): 552-3. Epub 2008 Apr 10.*
12. Leung YY, Cheung LK. *Does staged removal of lower third molars pose unnecessary re-operations to patients? Leung YY, Cheung LK.*
13. Adeyemo WL, Ogunlewe MO, Ladeinde AL, Hassan OO, Taiwo OA. *A comparative study of surgical morbidity associated with mandibular third-molar surgery in young and aging populations. J Contemp Dent Pract. 2010 Jul 1; 11(4): E001-8.*

Corresponding Author

Milan Miladinovic,
Faculty of Medicine in Pristina – Kosovska Mitrovica,
Kosovska Mitrovica,
Serbia,
E-mail: milanbetter@gmail.com

Psychic vulnerability and the increase of crack addiction in Brazil

Jose Cezario de Almeida¹, Alberto Olavo Advincula Reis², Luiz Carlos de Abreu², Modesto Leite Rolim Neto³

¹ Curso de Medicina, Universidade Federal de Campina Grande - UFCG, Cajazeiras, PB, Brasil,

² Faculdade de Saude Publica, Universidade de Sao Paulo- USP, Sao Paulo, SP, Brasil,

³ Curso de Medicina, Universidade Federal do Ceara – UFC, Barbalha, CE, Brasil.

The crack cocaine is a drug in the form of stones or granules obtained by mixing the base paste of coca or refined cocaine (made of *Erythroxylum coca* plant leaves), sodium bicarbonate and water. Due to its obvious clandestine production, without any kind of control, there are differences in the purity of crack, which can also contain other types of toxic substances such as lime, cement, kerosene, sulfuric acid, acetone, ammonia and sodium hydroxide. The designation 'crack' is probably due to the noise that the stones make when were burned during use¹.

Typically, the crack cocaine is smoked with makeshift pipes made of aluminum cans and PVC pipe (polyvinyl chloride), which allow the aspiration of large amounts of smoke. The stone is heated, melts and turns into gas, which after being inhaled is absorbed by the pulmonary alveoli and quickly reach the bloodstream². While cocaine hydrochloride in its typical form takes about 15 minutes to reach the brain and take effect after aspiration, the arrival of crack to the central nervous system is almost immediate: 8-15 seconds on average¹. The effect of crack in the brain lasts between five and ten minutes, during which it is boosted the release of neurotransmitters, especially dopamine, serotonin and norepinephrine. The immediate effect includes symptoms such as euphoria, restlessness, feeling of pleasure, irritability, changes in perception and thinking, as well as cardiovascular and motor changes such as tachycardia and tremor³.

While the spread of cocaine date from the 1970s and 1980s, when the drug was associated with the richer strata of the population, the stars of music and movie, the crack became more popular in the mid-1990s, when it became to represent a cheaper way to achieve the effects of cocaine. In Brazil, this first wave of popularity reached its peak in Sao Paulo, in the transition between the

1990s and the 2000s, having as its symbol an emblematic region in the downtown area, known as 'crackland'^{4,5}.

In recent years, however, especially since the end of the last decade, there has been a new wave of proliferation of crack users in Brazil, but this time, dispersed throughout the territory, deserving special attention the situation of medium-sized cities of the interior, with less than 500,000 inhabitants, and the states of Northern and Northeastern regions. The number of young, not infrequently between childhood and adolescence, addicted to crack has grown in epidemic form, invalidating, temporarily or permanently, a significant number of Brazilians in full capacity to study, work and produce^{6,7}.

This geographical distribution coincides with foci of recent development in Brazil. Regions with bad socioeconomic conditions until a few years ago, or that received major investments grew significantly, causing a large volume of financial resources without proper social counterpart, resulting in brutal levels of income concentration, population growth and lack of essential public services, such as health, education and security, which were not supplied at the same rate of demand. Children and young people within this context are vulnerable to various psychopathologies, depending on their predispositions, and substance abuse is the most common of them⁶.

Dependent on crack cocaine often have neurocognitive damages, which are related to the frequency and amount of use. Tests of attention, verbal fluency, visual memory, learning ability and executive functions reveal, in these patients, changes similar to those of patients with demential disorders, probably due to severe involvement of prefrontal areas and the temporal cortex⁸. According to some researches, users of cocaine, in moderate to heavy use, even in abstinence at the time

of the examination, showed delays in the following areas: mental flexibility and ability to control, visual-motor skills, memory and learning⁹.

The state of psychological distress that is established in these patients is the result, in addition to actions of the substance itself, the consequences of that use in daily life, such as loss of opportunities and social isolation¹⁰. Symptoms of depression and anxiety can manifest as comorbidity or develop due to the consumption of crack. In both cases, represent barriers to treatment adherence and affect the user's motivation to change¹¹.

Crack users expend a part of their productive lives in search of the substance or recovering from its effects. This keeps them apart from the prevailing social parameters with respect to the interests, behavior patterns and vocabulary. They form an extremely stigmatized population, leading certain sectors of society to propose inhuman and ineffective solutions regarding to public health, such as compulsory internment¹². Even those who embark on rehabilitation face contempt, disgust and disapproval, clearly expressed by some people. Such feelings tend to weaken further the user who tries to quit, already battered by the chemical action of the drug for long periods.

References

1. Laposata EA, Mayo GL. A review of pulmonary pathology and mechanisms associated with inhalation of freebase cocaine ("crack"). *Am J Forensic Med Pathol.* 1993; 14(1): 1-9.
2. Ferri CP, Laranjeira RR, Silveira DX, Dunn J, Formigoni ML. Aumento da procura de tratamento por usuários de crack em dois ambulatórios na cidade de São Paulo, nos anos de 1990 a 1993. *Rev Ass Med Brasil.* 1997; 43(1): 25-8.
3. Carlini EA, Notto AR, Galduroz JCF, Nappo AS. Visão histórica sobre o uso de drogas: passado e presente; Rio de Janeiro e São Paulo. *J Bras Psiquiatr.* 1996; 45: 227-236.
4. Ribeiro M, Dunn J, Laranjeira R, Sesso R. High mortality among young crack cocaine users in Brazil: a 5-year follow-up study. *Addiction.* 2004; 99: 1133-1135.
5. Dualibi LB, Ribeiro M, Laranjeira R. Profile of cocaine and crack users in Brazil. *Cad Saúde Pública.* 2008; 24(4 Suppl.): 545-557.
6. Carlini EA, Galduroz JCF, Silva AAB, Notto AR, Fonseca AM, et al. *II Levantamento domiciliar sobre o uso de drogas psicotrópicas no Brasil: estudo envolvendo as 108 maiores cidades do Brasil, 2005.* São Paulo: Centro Brasileiro de Informações Sobre Drogas Psicotrópicas / Secretaria Nacional Antidrogas, 2007.
7. Chaves TV, Sanchez ZM, Ribeiro LA, Nappo SA. Crack cocaine craving: behavior and coping strategies among current and former users. *Rev Saúde Pública.* 2011; 45(6): 1-6.
8. Gawin FH, Kleber HD. Abstinence symptomatology and psychiatric diagnosis in cocaine abusers. *Arch-GenPsychiatry.* 1986; 43(2): 107-113.
9. Rodrigues VS, Caminha RM, Horta RL. Déficits cognitivos em pacientes usuários de crack. *Rev Bras TerCogn.* 2006; 2: 67-72.
10. Horta RL, Horta BL, Rosset AP, Horta CL. Crack cocaine users who attend outpatient services. *Cad Saúde Pública.* 2011; 27(11): 2263-2270.
11. Teichner G, Horner MD, Harvey RT. Neuropsychological predictors of the attainment of treatment objectives in substance abuse patients. *Int J Neurosci.* 2001; 106(3): 253-263.
12. Cunha PJ, Nicastrí S, Gomes LP, Moino RM, et al. Neuropsychological impairments in crack cocaine-dependent inpatients preliminary findings. *Rev Bras Psiquiatr.* 2004; 26(2): 103-106.

Corresponding Author
Modesto Leite Rolim Neto,
Universidade Federal do Ceara,
Juazeiro do Norte – CE,
Brazil,
E-mail: modestorolim@yahoo.com.br

Endoscopic management of non-variceal upper gastrointestinal bleeding

Praveen Kumar Yadav, Zhan-Ju Liu

Department of Gastroenterology, the Shanghai Tenth People's Hospital, Tongji University, Shanghai, China

Abstract

Non-variceal upper gastrointestinal bleeding (NVUGIB) is common, with a high rate of recurrent bleeding and substantial mortality rate. Endoscopy done within the first 24 hours of bleeding has been shown to be the most reliable means of establishing the source of upper gastrointestinal haemorrhage. Endoscopic management of NVUGIB has been expanded from a purely diagnostic role to a therapeutic role in many patients. In addition to controlling active bleeding, it is an option in a patient who is clinically at a high risk of re-bleeding, or in patients who have peptic ulcers with visible vessels or stigmata indicating high risk. For the NVUGIB, early upper GI endoscopy provides important information to aid in risk prediction efforts. Administration of PPIs is important for NVUGIB. Endoscopy therapy has emerged as the initial diagnostic and therapeutic tool in the evaluation and treatment of severe gastrointestinal hemorrhage. Research continues in improving technologies as well as outcomes research to determine optimal timing of endoscopy and criteria for hospitalization. Therapeutic endoscopy will continue to have a pivotal role in high-risk gastrointestinal bleeding in the future. Diagnostic accuracy is related to the time interval between the bleeding episode and endoscopy, and to clinical presentation.

Key words: Endoscopic sclerotherapy; Electrocoagulation; Haemorrhage; Haemostasis; Upper Gastrointestinal bleeding

Introduction

Non-variceal upper gastrointestinal bleeding (NVUGIB) remains a common and challenging emergency for gastroenterologists and general physicians. The annual incidence is 48 to 160 per 100,000 of the population and mortality generally from 10% to 14%.^[1] Even though, there

have been significant improvement in endoscopic and supportive therapies. The overall mortality stubbornly remains around 10%, and may even reach 35% in hospitalized patients with serious co-morbidity. Some data suggest a decreasing annual incidence of NVUGIB amid an unchanging or decreasing incidence of peptic ulcer bleeding, which is increasingly related to the use of nonsteroidal anti-inflammatory drugs (NSAIDs) or low-dose acetylsalicylic acid (ASA). Mortality from NVUGIB has decreased by 23% in the United States (1998 to 2006) and by 40% in the United Kingdom (1993 to 2007), but has remained unchanged in Canada (1993 to 2003) and the Netherlands (1993 to 2003).^[1]

Patients aged over 80 yr now account for around 25% of all UGIB and 33% of UGIB occurring in hospitalized patients and therefore tend to account for much of the poor outcome of this condition. The causes of NVUGIB are shown in Table 1, although the commonly quoted figure of 50% for peptic ulcer bleeding may be overestimated. In a recent large CORI (Clinical Outcome Research Initiative) study of UGIB, peptic ulcer was the probable cause of UGIB in only 20% of cases.^[2,3] The incidence of peptic ulcer disease is expected to continue to decline with more widespread helicobacter pylori eradication and proton pump inhibitor (PPI) usage.

Table 1. Causes of non-variceal UGIB

Diagnosis	Incidence (%)
Peptic ulcer	20–50
Mallory-Weiss tear	15–20
Erosive gastritis/duodenitis	10–15
Esophagitis/esophageal ulcer	5–10
Malignancy	1–2
Angiodysplasia/vascular malformations	5
Other	5

Resuscitation, risk assessment and management of pre-endoscopy for UGIB

Patients should be stratified into low and high risk by using prognostic scales, on the basis of clinical, laboratory, and endoscopic criteria.^[4] Early identification of high-risk patients allows appropriate intervention, which can minimize morbidity and mortality. The clinical predictors for high risks of bleeding or mortality are poor healthy condition, low haemoglobin level, shock, melaena, transfusion requirement, comorbid illness, fresh red blood in rectal examination, emesis, or in nasogastric aspirate, increased urea, creatinine, and serum aminotransferase levels.^[4] Shock occurs when blood loss approaches more than 40% of the total blood volume. Close monitoring of patients' blood pressure, pulse and gross evidence of ongoing bleeding is mandatory. Agitation, pallor, hypotension and tachycardia may indicate shock requiring immediate volume replacement. A drowsy or comatose patient is at high risk of aspiration if vomiting or haematemesis continue. If necessary, a cuffed endotracheal tube may be inserted to protect the airway.

Resuscitation must be commenced immediately with the insertion of at least two large bore intravenous cannulae, which should be inserted into larger peripheral veins. Supplemental oxygen may be helping a confused, agitated elderly patient. Central venous pressure (CVP) monitoring is advisable in patients with profound shock or multiple organ dysfunctions and in elderly patients with significant comorbidity. Fluid resuscitation can be commenced with isotonic crystalloid solutions. Blood sample must be drawn for urgent full blood count, typing and cross matching, coagulation screen, blood urea and electrolytes and liver function tests.

According to the American Society of Anesthesiologists,^[5] preoperative blood transfusion should be based on the patient's risk for complications from inadequate oxygenation rather than by a fixed haemoglobin level. Red blood cell transfusion is rarely indicated when haemoglobin level is greater than 100 g/L and is almost always indicated when the level is less than 60 g/L. A meta-analysis of observational studies, including studies in trauma, surgery, and intensive care,^[6] found that transfusion is associated with a higher risk for death, nosocomial infection, multiorgan dysfunction,

and acute respiratory distress syndromes than no exposure in multivariate analyses.

The actual transfusion requirement and the threshold of haemoglobin levels for transfusion in patients with acute UGIB may be higher than usual. It is because of haemodynamic instability, inaccurate haemoglobin measures, or the presence of continued or recurrent bleeding. In a prospective cohort study,^[7] haemoglobin levels less than 82 g/L in patients with NVUGIB predicted elevated cardiac troponin I levels. Because patients with NVUGIB are often elderly or have comorbid cardiovascular conditions, they may have poor tolerance to anemia. The hemoglobin levels of 60 to 100 g/L may warrant transfusion in patients with underlying cardiac disease (ischemic heart disease, peripheral vascular surgery, or heart failure).^[5]

When a patient presents with gastrointestinal bleeding, risk assessment and resuscitation proceed simultaneously. Such assessment aids in rational decision-making regarding treatment options. At the initial assessment, it is important to define the factors with prognostic importance. Patients who developed NVUGIB after hospitalization for other serious illnesses have a much worse prognosis than those who are admitted because of bleeding, with a mortality of about 30%.

Early upper gastrointestinal endoscopy (within 12 to 24 hours) treatment is the cornerstone of management of NVUGIB. Early endoscopy has 3 major roles including diagnosis, treatment and risk stratification. It is the most accurate method available for identifying the source of bleeding. Recently, a number of studies have indicated that systematic assessment of clinical and endoscopic risk factors (endoscopic triage) may obviate hospitalization in some patients and may help in determining the appropriate length of hospital stay in others.^[8]

In patients receiving anticoagulants, correction of coagulopathy is recommended but should not be delayed endoscopic examination.^[1] One retrospective cohort study^[9] including 233 patients with NVUGIB found that 95% of the patients who received anticoagulants had an international normalized ratio (INR) between 1.3 and 2.7, suggesting not delaying endoscopic therapy in patients with mild to moderate coagulation defects. Furthermore, an exploratory analysis of 1869 patients in the RUGBE (Registry on Non-variceal Upper Gastro-

intestinal Bleeding and Endoscopy) Canadian cohort study^[10] found that neither INR nor platelet count predicted re-bleeding. A study in patients with any NVUGIB found that intensive measures to correct INR can reduce mortality.^[11]

Promotility agents should not be used routinely before endoscopy to increase the diagnostic yield.^[1] In selected patients with suspected blood in the stomach, the use of pre-endoscopy promotility agents may improve diagnostic yield, but they are not warranted for routine use in all patients who present with NVUGIB. A meta-analysis^[12] evaluated erythromycin and metoclopramide and found that use of a prokinetic agent significantly reduced the need for repeated endoscopy (odds ratio [OR], 0.51 [95% CI, 0.30 to 0.88]) in patients suspected of having blood in their stomach, compared with placebo or no treatment. The groups did not differ in length of stay, units of blood transfused, or need for surgery. An analysis of data from erythromycin trials^[13] found that pre-endoscopic erythromycin resulted in a cost-effective outcome in most of the trials.

Selected patients with acute ulcer bleeding who are at low risk for re-bleeding on the basis of clinical and endoscopic criteria may be discharged promptly after endoscopy.^[1] Patients having serious comorbid conditions such as heart failure, recent cardiovascular or cerebrovascular event or chronic alcoholism, are not suitable for early discharge if they having an endoscopic finding of high-risk stigmata (active bleeding, NBVV, or adherent clot), or having unsuitable socio-family conditions.^[14] Patient location (distance to nearest emergency care center), local legal regulations, and social support should also be considered.

Although pre-endoscopic PPI therapy has not been shown to affect re-bleeding, surgery, or mortality, the beneficial effects on the need for intervention, supportive cost effectiveness analyses, and excellent safety profile suggest that these agents may be useful, particularly in those suspected of having high-risk stigmata. Pre-endoscopic PPI treatment significantly reduced the proportion of patients with high risk stigmata and the need for endoscopic therapy compared with patients in the control group who received placebo or a histamine-2 receptor antagonist.^[15]

A North American analysis found that pre-endoscopic PPI therapy was more effective and more

costly in the United States, while it became more effective and less costly in Canada as the duration of hospitalization for high-risk patients increased or that of low-risk patients decreased.^[16]

PNED score: The PNED score indicates that ulcers are by far the most common cause of NVUGIB, accounting for 66% of all diagnoses. An important feature of the PNED study is that it represents a consortium of practice sites that use a structured endoscopy reporting system to collect information in a centralized endoscopic database. Such data are useful because they reflect “real world” endoscopic practice from a wide range of practice settings and minimize patient selection or potential referral bias.^[17]

In an earlier multicenter investigation (Progetto Nazionale Emorragia Digestiva (PNED), prospectively studied a cohort of 1,020 patients hospitalized with acute NVUGIB and identified risk factors associated with mortality^[18]. The PNED score showed a high discriminant capability and was significantly superior to the Rockall score in predicting the risk of death (AUC 0.81 (0.72-0.90) vs. 0.66 (0.60-0.72), $P < 0.000$). Positive likelihood ratio for mortality in patients with a PNED risks score > 8 were 16.05.^[19] This score is accurate and superior to the Rockall score in predicting death in patients with NVUGIB. Further external validation at the international level is needed.

A dedicated software including an endoscopic reporting system (Cartella Clinica Endoscopia Digestiva, Bracco, Italy) linked to a project-specific research database was developed. A network of centers in Italy that received emergency admissions was established—the PNED study group. Details of the network, source data collection, and management have been explained in details elsewhere^[18].

Early endoscopic examination

Early endoscopy (within 24 hours of presentation) is recommended for most patients with acute UGIB^[1] and is associated with significant reduction during hospital stay in patients at low risk,^[20] high risk, and combined patient groups,^[21] in comparison with delayed endoscopy. Recent administrative data found that the performance of early endoscopy was associated with a decreased need for surgery in elderly patients.^[22] And those patients with NVUGIB who were admitted on

weekends had higher adjusted in-hospital mortality and were less possibility for going early endoscopy within 1 day of hospitalization.^[21] The Blatchford and pre-endoscopic Rockall scores^[23] use only clinical and laboratory data (before endoscopy) to identify patients who require intervention, whereas the complete The Blatchford score includes haemoglobin level, blood urea level, pulse, systolic blood pressure, the presence of syncope or melaena, and evidence of hepatic disease or cardiac failure and accurately identifies patients at low risk for clinical intervention. Schacher et al.^[24] compared the clinical outcomes of patients who received either endoscopy within two to three hours or within 48 hours. They did not find that very early endoscopy reduces incidence of recurrent bleeding, mortality or need for surgery. The only benefit may be early discharge for low-risk patients. In fact, early endoscopy exposes more cases of active bleeding and hence, increases the use of therapeutic endoscopy. Although early endoscopy is encouraged for most patients, endoscopy can be delayed or deferred in selected high-risk patients like active acute coronary syndrome or suspected perforation. Also, a very low Blatchford score can identify very low-risk patients who are unlikely to have high-risk stigmata or benefit from endoscopic therapy.^[25]

The definition of early endoscopy ranges from 2 to 24 hours after initial presentation. Among the 1869 patients of the RUGBE cohort, 76% received their first endoscopy within 24 hours of presentation.^[10] Early endoscopy (within the first 24 hours), with risk classification by clinical and endoscopic criteria, allows for safe and prompt discharge of patients classified as low risk, improves patient outcomes for patients classified as high risk, and reduces use of resources for patients classified as either low or high risk.^[4]

In a subgroup of patients with a bloody gastric aspirate, blood transfusions and hospital stay were significantly decreased with urgent (>12 hours vs. <12 hours) endoscopy.^[26] Retrospective analyses that assessed urgent (0 to 8 hours) versus early (6 or 8 to 24 hours) endoscopy^[27] reported no between-group differences in clinical outcomes; however, these studies did not control for other endoscopist-related factors, type of therapeutic interventions, or co-interventions. A study identified

4 independent predictors (i.e. fresh blood in the nasogastric tube, haemodynamic instability, a haemoglobin level less than 80 g/L, and a leukocyte count greater than 12×10^9 cells/L) of active bleeding and the need for very early endoscopy (<12 hours).^[28] Of note, indirect findings from recent administrative data suggest that early endoscopy may be associated with lower mortality.^[21] On the basis of available data, the participants are recommended a target time to endoscopy of within 24 hours of presentation.

Endoscopic therapy

Endoscopy is undertaken either as a semi elective procedure in patients who have had relatively minor bleeding or it is done urgently in patients who have sustained major bleeding. It must be emphasized that endoscopy should only be done when resuscitation has been achieved. Ideally blood pressure and central venous pressure should be stable. Endoscopy therapy has been shown to improve outcome in non-variceal haemorrhage. The optimal timing of endoscopy remains a balance between clinical need and resources, but endoscopy performed within 24 hours of hospital admission has been shown to reduce the length of hospital stay and may reduce the likelihood of re-bleeding or surgical intervention in the highest risk patients.^[29] After resuscitation, endoscopy is undertaken. Only minority of profusely bleeding patients need immediate emergency endoscopy. On-call endoscopists must be well trained who can be able to apply a range of endoscopic treatments. Patients with an adherent clot may also constitute a high risk group. Current opinion favors the displacement of the clot by irrigation or mechanical removal, followed by endoscopic haemostasis of any underlying visible vessel. The various modalities of endoscopic haemostasis are outlined as follows (Table 2).^[30]

1. Injection therapy

1.1 Adrenaline

Endoscopic injection of fluid around and into the bleeding point reduces the rate of bleeding from approximately 50% to 20% in patients with non-bleeding visible vessels. Adrenaline is the injection agent of choice because it is non-ti-

Table 2. Various modalities of endoscopic haemostasis

Thermal therapy	Heater probe
	Multipolar electrocoagulation (BICAP, Gold Probe)
	Argon plasma coagulation (APC)
Injection therapy	Adrenaline (1:10000 to 1:100000)
	Procoagulants (fibrin glue, human thrombin)
	Sclerosants (ethanolamine, 1% polidocanol)
	Alcohol (98%)
Mechanical therapy	Clips
	Band Ligation
	Staples
	Sutures
Combination therapy	Injection plus thermal therapy
	Injection plus mechanical Therapy

ssue damaging. In experimental animal studies, mucosal injection fluid at 1:10,000 adrenaline (epinephrine) causes prolonged vasoconstriction for up to 2 hours. A total volume of 4-16 ml (1:10000) may be injected safely,^[31] as most of the adrenaline will undergo first-pass metabolism in the liver. Adrenaline injection has reduced hospital stay, transfusion requirement and operative intervention (41% to 15%).

In one randomized controlled trial (RCT)^[32] comparing the effect of different volumes 20, 30 and 40 ml epinephrine, each groups' initial haemostasis was achieved in 97.4%, 98.7% and 100% of patients respectively. There were no significant differences in the rate of initial haemostasis between the three groups. The rate of peptic ulcer perforation was significantly higher in the 40 ml epinephrine group than in the 20 and 30 ml epinephrine groups ($P<0.05$). The rate of recurrent bleeding was significantly higher in the 20 ml epinephrine group (20.3%) than in the 30 ml (5.3%) and 40 ml (2.8 %) epinephrine groups ($P<0.01$). There were no significant differences in the rates of mortality, surgical intervention, the amount of transfusion requirements, or the days of hospitalization between the three groups. The number of patients who developed epigastric pain due to endoscopic injection, was significantly higher in the 40 ml epinephrine group (51/76, 67%) than in the 20ml (2/76, 2.63%) and 30 ml (5/76, 6.57%) epinephrine groups ($P<0.001$). This study concludes that the optimal injection volume of epinephrine for endoscopic treatment of an actively bleeding ulcer (spurting or oozing) is 30 ml.

Another RCT demonstrated that the mean volume of epinephrine injected was 16.5 ml (95% CI [15.7, 17.3 ml]) in the large-volume group and 8.0 ml (95% CI [7.5, 8.4 ml]) in the small-volume group.^[33] The number of episodes of recurrent bleeding was smaller in the large-volume group (12/78, 15.4%) compared with the small-volume group (24/78, 30.8%, $P=0.037$). The volume of blood transfused after entry into the study, duration of hospital stay, numbers of patients requiring urgent surgery, and mortality rates were not statistically different between the 2 groups. It showed that injection of a large volume (>13 ml) of epinephrine can reduce the rate of recurrent bleeding in patients with high-risk peptic ulcer and is superior to injection of lesser volumes of epinephrine when used to achieve sustained haemostasis.

1.2 Sclerosants

Sclerosants such as ethanol, polidocanol (1%) and ethanolamine are used in ulcer haemostasis which are equally effective as adrenaline but carry more risk. Some sclerosants, such as ethanolamine, are drawn up using a filter. Sclerosants are irritants that cause acute tissue inflammation, acute chemical fixation, and acute edema, which tamponades the bleeding lesion and promotes thrombogenesis.^[34] They subsequently produce necrosis and fibrosis. The amount of sclerosant injected should be limited to minimize tissue injury. For example, ethanol injection is limited to 1 ml, and should not be subsequently repeated at the same bleeding site.^[34] Combined therapy with thermocoagulation using contact probes may, moreover, extend tissue injury

after ethanol injection.^[34,35] Sterile hypertonic saline is also injected for mechanical tamponade, but it is less effective than epinephrine because it does not cause vasospasm or platelet aggregation and is generally considered only in patients with severe coronary artery disease.^[36]

In one study,^[37] ethanol injection alone was shown to have a re-bleeding rate as low as 4%; however, most other published studies have achieved similar haemostasis to adrenaline alone. Several comparative studies that involved the use of sclerosants as treatment for acutely bleeding peptic ulcers are reported. In one randomized prospective trial^[38] that involved 208 patients, absolute ethanol was found to be as safe and as effective as multipolar electrocoagulation and neodymium-yttrium aluminium garnet laser in the endoscopic therapy of acute bleeding peptic ulcers. Another study^[39] found injection with absolute ethanol to be as effective and safe as haemoclips in controlling bleeding from gastric ulcers. Similar results^[40] were also found in randomized prospective trials that compared absolute polidocanol with haemoclips.

1.3 Procoagulants (thrombogenic agents)

Human thrombin and fibrin sealant are procoagulants that have been investigated in ulcers haemostasis. Human thrombin after epinephrine injection has been compared with epinephrine injection alone. Fibrin glue is a formulation of fibrinogen and thrombin which when combined instantly forms a fibrin network. The two substances are injected via a double-lumen needle. Fibrin sealant significantly reduced recurrent bleeding only if injected daily. There is concern regarding viral transmission with the use of fibrin glue.

A separate class of injectable agents includes thrombin, fibrin, and cyanoacrylate glues, which are used to create a primary tissue seal at a bleeding site.^[41] Thrombin has been used in several studies in conjunction with heat probe therapy and epinephrine injection; but, only one of these studies (by using thrombin combined with epinephrine) showed any additional benefit conferred by the addition of thrombin. No prospective randomized trials of thrombin monotherapy have been performed. The evidence for thrombin injection is mixed with differing reports of effect on clinical outcomes.^[42] Repeated daily injection of fibrin

glue following treatment with diluted adrenaline in patients with active bleeding or Non Bleeding Visible Vessel until the ulcer base is clean or covered is expensive, however it reduces re-bleeding but not mortality rates.

2. Thermal modalities

This can be achieved by either of non-contact thermal modalities such as argon plasma coagulation (APC) and laser photocoagulation, or contact thermal modalities, heater probe coagulation, monopolar coagulation, bipolar coagulation.

2.1 Non-contact thermal modalities

APC as a non-contact thermoblative technique is now available at many endoscopic units where it is frequently used to treat chronic, actively bleeding lesions of gastrointestinal tract. Nonetheless, APC carry little the risk of perforation because it only coagulates superficial layer of mucosa. Although validated data regarding the rates of perforation are lacking, it is estimated that it is below 1%.^[43] Typically it is used APC for ablation of solitary or multiple vascular ectasias and telangiectasias seen as a clinical spectrum of angiodysplasias, watermelon stomach and post-irradiation injury of the colon. The operated distance between the probe and the targeted tissues depends on the power setting. Complications of laser therapy include perforation, bleeding, fistula formation and stenosis. Laser therapy is currently not recommended.^[31]

2.2 Contact thermal modalities

The heater probe and bipolar electrocoagulation are the most commonly used devices for contact coagulation of bleeding and non-bleeding visible vessels. All thermal devices generate heat either directly (heater probe) or by passage of electrical current through tissue (multipolar probes). The heater probe consists of a Teflon-coated hollow aluminium cylinder with an inner heating coil. Coagulation depth is similar to that in bipolar coagulation. Monopolar electrocoagulation requires the placement of neutral electrode on the patient's body and the electrical current flows from the probe through the patient's body. Coagulation depth is greater than that in bipolar electrocoagulation. In bipolar electrocoagulation an electrical current pa-

sses through the tissue between the two electrodes on the probe tip. In contrast to monopolar electrocoagulation, the circuit is completed locally.

3. Mechanical therapies

Mechanical therapy refers to the implantation of a device that causes physical tamponade of a bleeding site. Devices for potentially permanent mechanical treatment of bleeding include metal clips, rubber band ligation, endoloops, and sewing devices. However, currently the widely available mechanical therapies are endoscopically placed clips and band ligation devices.

3.1 Endoscopic clips

The terms 'endoclip' and 'haemoclip' have been used for this device interchangeably in the literature. Current available haemoclips are (i) QuickClip 2 (opening width of 8 or 12 mm), (ii) Resolution Clip (opening width of 11 mm), (iii) TriClip (opening width of 12 mm) and (iv) Inscope multiclip applicator with four endoclips (opening width of 14 mm). Jensen et al.^[44] studied the haemostatic capability of the three aforementioned clips in a randomized canine model for bleeding ulcers and showed that all had an initial success rate of 100% with long-term retention rate higher in the resolution clip group. Endoscopic clips usually are placed over a bleeding site (e.g., visible vessel) and left in place. This process is safe and effective for haemostatic therapy of bleeding peptic ulcers, Mallory-Weiss tears, and other bleeding lesions.

Endoscopic placement of metal clips has recently been advocated for haemostasis. One prospective randomized trial compared haemoclips with a thermal modality. Acute re-bleeding occurred in 1.8% of the haemoclip patients compared with 21% of heater probe patients ($P < 0.05$). The median number of blood units transfused and hospital days was also significantly lower for haemoclips. There was no difference in emergency surgery rate or 30-day mortality.^[45] Haemoclips may be particularly useful for actively bleeding large vessels but may be difficult to apply in awkwardly placed ulcers (e.g. high lesser curve or posterior duodenal ulcers).^[31]

A meta-analysis^[46] compared the efficacy of endoscopic clipping versus injection or thermo-

coagulation in the control of NVUGIB. Definitive haemostasis was higher with clipping (86.5%) than injection (75.4%; RR 1.14, 95% CI 1.00 to 1.30). Use of clips significantly reduced re-bleeding (9.5%) compared with injection (19.6%; RR 0.49, 95% CI 0.30 to 0.79) and the need for surgery (2.3% vs 7.4%; RR 0.37, 95% CI 0.15 to 0.90). Clipping and thermocoagulation had comparable efficacy (81.5% and 81.3%; RR 1.00). No difference in mortality was reported between any interventions. One randomized comparative study^[47] of combination epinephrine-polidocanol injection and Haemoclip versus Haemoclip alone for bleeding peptic ulcers showed clipping to be inferior to combination therapy.

3.2 Endoscopic band ligation (EBL)

Other means of mechanical ligation include rubber band ligation, which is commonly performed for haemorrhoid and variceal ligation, have also been used to treat non-variceal causes of bleeding and involve the placement of elastic bands over tissue to produce mechanical compression and tamponade. Band ligation and endoloops are useful to treat varices but are difficult to apply to a fibrotic ulcer base. EBL is currently technically easier to use than endoclips and has been shown to be safe and effective for control of small lesions in a small series of acute peptic ulcer bleeding^[48] and with bleeding due to Dieulafoy's lesions.

4. Endoscopic combination therapies

Endoscopic therapy using a combination of the above-discussed methods is favored to monotherapy alone considering the theoretical additive effect of each modality and given the different mechanisms of action of each technique. One meta-analysis^[46] showed that definitive haemostasis was higher with injection combined with clipping (86.5%) compared with injection alone, leading to a reduction in re-bleeding and reduced requirement for surgery. There was no difference in mortality between single and combination therapies. Another meta-analysis^[49] of 16 RCTs reported that adding a second endoscopic intervention thermal, mechanical or injection following and endoscopic adrenaline injection reduced the further bleeding rate from 18.4% to 10.6% (OR 0.53, 95% CI 0.40

to 0.69) and emergency surgery from 11.3% to 7.6% (OR 0.64, 95% CI, 0.46 to 0.90). Mortality fell from 5.1% to 2.6% (OR 0.51, 95%, CI 0.31 to 0.84). Above mentioned two meta-analyses have demonstrated that combinations of endoscopic therapy are superior to use of a single modality therapy and combination treatment does not increase the risk of complications.

Hence Clips, thermocoagulation, or sclerosant injection should be used in patients with high-risk lesions, alone or in combination with epinephrine injection.^[1] Several recent meta-analyses have better quantified the efficacy of endoscopic therapies.^[46,50-53] Although monotherapy with epinephrine injection is more effective than medical therapy in patients with high-risk stigmata, it is inferior to other monotherapies or to combination therapy that uses 2 or more methods.^[46,50-53] Numerous meta-analyses indicate that adding a second procedure, such as a second injectate (for example, alcohol, thrombin, or fibrin glue), thermal contact, or clips, is superior to epinephrine injection alone.^[46,50,51]

Monotherapy with thermal devices, sclerosants, clips, thrombin, or fibrin glue provides more effective endoscopic haemostasis than epinephrine alone.^[50] Clips were superior to injection monotherapy in 4,^[46,50,51,53] of 5 meta-analyses.^[46,50-53] Clips with injection were superior to injection alone but not to clips alone.^[46,53] Combination therapy (injection plus second injectate, thermal, or clips) was superior to injection therapy alone, but not to clips or thermal therapy alone.^[51,53] Although the data showed that it strongly supported the use of thermal devices, clips, or combination treatments, nevertheless, the participants felt that the data were insufficient to show superiority or equivalence of the recommended treatments. Complications with dual versus single endoscopic therapy included induction of bleeding (1.7% in each group) and perforation (0.6% vs. 0%; $P = 0.003$) (102); however, perforation has also been reported with monotherapy in some RCTs.^[47]

Management after endoscopy

After the initial endoscopy and the institution of endoscopic therapeutic measures where necessary, the key point in the aftercare is the recognition of patients at high risk of re-bleeding and death who would require careful monitoring in an intensive care or high dependency setting. Patients who

have major upper gastrointestinal haemorrhage must be closely monitored following endoscopy with continual observation of pulse, blood pressure, and urine output. Identification of re-bleeding or of continuing haemorrhage is essential. Patients who are haemodynamically stable 4–6 hours after endoscopy with or without endoscopy therapy should be allowed to drink and start a light diet; there are no data suggesting that prolonged fasting is necessary in this group of patients.^[54]

Predictors of an increased risk of re-bleeding and death (as well as failure of endoscopic therapy) include (i) clinical factors such as shock at the time of presentation, advanced age, co-existing illnesses, (ii) endoscopic features such as ulcer location (posterior duodenal ulcer), size of the ulcer (>2 cm), stigmata of recent haemorrhage and the presence of blood at the time of endoscopy as well as (iii) laboratory features such as haemoglobin (<10 g/dl) and elevated blood urea levels.^[55]

'Second-look' endoscopy and endoscopic re-treatment

Second look endoscopy (repeat endoscopy) should be considered in the following circumstances: (i) if there is clinical evidence of active re-bleeding, suggested by the passage of fresh melaena or haematemesis, fall in blood pressure, rise in pulse, or fall in central venous pressure. In some patients major re-bleeding is an indication for surgical intervention without repeating endoscopy, but in most patients it is wise to endoscopically confirm re-bleeding; (ii) if there are concerns regarding optimal initial endoscopic therapy. Accurate injection or thermal therapy is sometimes extremely difficult in actively bleeding patients and suboptimal therapy may be all that is possible. In this group of patients repeat intervention 12–24 hours later is worthy of consideration. Currently however it is not recommended that routine endoscopy is undertaken in all patients following initial endoscopic treatment.

If there is clinical evidence of re-bleeding or if the initial therapeutic procedure was unsuccessful or partially successful repeat therapeutic endoscopy may be indicated (depending on local endoscopic and surgical expertise).

Patients with recurrent bleeding respond favorably to repeat endoscopic therapy. Scheduled repeat endoscopy (e.g., at 24 hours) has been ad-

vocated for patients with high-risk stigmata that were treated at the time of the initial bleed. Retrospective and prospective studies have suggested that scheduled repeat endoscopy reduces recurrent bleeding rates and may be cost effective in these patients.^[56] The precise role of scheduled repeat endoscopy has yet to be defined.

A more recent meta-analysis^[57] found that routine second-look endoscopy, with heater probe therapy when appropriate, significantly reduced the risk for re-bleeding (RR, 0.29 [CI, 0.11 to 0.73]) compared with single endoscopy. However, performing second-look endoscopy with injection monotherapy conferred no advantage. In a meta-analysis, Marmo et al.^[58] comparing systematic second-look endoscopy involving 785 patients and re-treatment versus expectant treatment, showed that the risk of recurrent bleeding with the former approach was reduced by 6.2% (12% vs 18.2%; OR 0.64, 95% CI 0.44 to 0.95, $P < 0.001$), but risk reductions for surgery and mortality were not significant. A second meta-analysis^[46] studies, including 1,202 patients, also showed reduction of re-bleeding in patients undergoing second look endoscopy (11.4% vs 15.7%; OR 0.69; 95% CI 0.49 to 0.96).

The recently published trial and the only one with a control group that received high-dose intravenous PPI therapy does not found benefit with second-look endoscopy.^[59] An U.S. cost-effectiveness analysis^[60] found that the strategy of selective (not routine) second-look endoscopy at 24 hours only in patients at high risk for re-bleeding was more effective and less expensive than repeated endoscopy in patients with re-bleeding (with or without intravenous PPIs) or routine repeated endoscopy in all patients, although extrapolations were made from trials that did not actually use high-dose intravenous PPI therapy. In the only study that fully reported risks,^[61] no complications directly attributable to the second-look endoscopy were reported. Although the role of second-look endoscopy is unclear and published studies consist of inadequate numbers but those findings show that repeat endoscopy has significant advantages in terms of reducing re-bleeding but does not confer survival benefit. Repeat endoscopy is safe and complications are rare.

In conclusion, although older data supported a second-look approach, these trials did not use contemporary management strategies associated with

decreased re-bleeding, such as initial endoscopic haemostasis with haemoclips or combination therapy,^[56] or post-endoscopic haemostasis high-dose PPI therapy.^[62] Furthermore, the few existing contemporary data do not favor the use of routine second-look endoscopy at this time.

Recurrent bleeding after endoscopic treatment

Despite adequate initial endoscopic therapy, recurrent bleeding in patients with UGIB can occur in up to 24% of high-risk patients, although more recent studies that emphasize the use of PPI therapy in addition to combination endoscopic therapy show recurrent bleeding rates of approximately 10%.^[60]

Management of rebleeding

Recurrent bleeding remains the single most important adverse prognostic factor. Morbidity and mortality are higher in those with re-bleeding and 95% of re-bleeding occurs within the first 72 hours of hospitalization.^[51] The major challenge in applying endoscopic therapy for bleeding is that haemostasis is not permanent and re-bleeding occurs in about 15%-20% of the cases. Patients having re-bleed after endoscopic therapy have increased mortality and require urgent intervention.^[63] Endoscopic treatment would avoid the surgical risk. However, delay in establishing haemostasis may result in hypotension and adversely affect the survival. In patients with peptic ulcers and recurrent bleeding after initial endoscopic control of bleeding, endoscopic retreatment reduces the need for surgery without increasing the risk of death and is associated with fewer complications than is surgery.

Single retrospective comparison between embolism and surgery showed no difference in re-bleeding or mortality despite the more advanced age and greater prevalence of heart disease in the embolism group.^[64] Embolization has been used for a wider variety of causes of NVUGIB, such as esophageal haemorrhage, GI surgery, Pancreatitis and haemobilia. A respective review of 163 patients with acute upper GI haemorrhage and transcatheter embolization reviewed factors associated with clinical success and concluded such treatment had a positive impact on survival independent of clinical condition^[65] while a further review indicated early

re-bleeding was associated with abnormal coagulation and use of coils alone.^[66]

Limitation and complications

Complications of endoscopic therapy are limited including perforation in the esophagus, stomach or small intestine and heart or lung problems such as pneumonia, irregular heart rhythms. Lung or heart failure is the very uncommon. There are some minor complications as nausea and vomiting, allergic skin reaction; reactions to the sedative medications are possible. A pooled analysis for all these modalities revealed a complication rate of 0.5% (95% CI 0.4–0.8).^[50] Clips and epinephrine had the lowest rates of perforations while the Heater Probe group had the highest. Endoscopic therapy is limited by factors such as an unstable patient, poor sedation, inadequate visualization due to blood, difficult areas of reach such as the posterior wall of duodenum, junction between the first and second part of duodenum, and lesser curve.

Conclusions

Upper gastrointestinal haemorrhage is a life threatening emergency and initial evaluation involves fluid resuscitation and optimisation of haemodynamic status. Patients requiring hospitalization should be observed in a monitored area depending on the severity of bleeding. NVUGIB remains a significant cause of morbidity and mortality. By risk assessment scoring systems patients at high risk can be identified including clinical and endoscopic variables. However, the effect on mortality is that low aggressive endoscopic therapy, adequate resuscitation, and PPI therapies are effective for achieving haemostasis and preventing adverse clinical outcomes. Non-variceal upper gastrointestinal hemorrhage not controlled by endoscopic therapy should be treated by repeat endoscopic treatment, selective arterial embolization or surgery. Multi-disciplinary care, including endoscopists, surgeons, intensivists and radiologists early involved in the assessment and decision stages, is vital to optimistic care.

Funding

This work was supported by the grants from the National Natural Science Foundation of China (No. 30971358)

Abbreviations

NVUGIB, Non-variceal upper gastrointestinal bleeding;

APC, Argon plasma coagulation;
CORI, Clinical outcome research initiative;
EBL, Endoscopic band ligation;
GIT, Gastrointestinal tract;
NSAID, Nonsteroidal anti-inflammatory drugs;
PPI, Proton pump inhibitor;
RCT, Randomized controlled trial;
SRH, Stigmata of recent hemorrhage;
UGIB, Upper gastrointestinal bleeding;
NBVV, Non Bleeding Visible Vessel.

References

1. Barkun A, Bardou M, Kuipers E, Sung J, Hunt RH, Martel M, et al. International Consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding. *Ann Intern Med* 2010; 152: 101-13.
2. Boonpongmanee S, Fleischer DE, Pezzullo JC, Collier K, Mayoral W, Al-Kawas F, et al. The frequency of peptic ulcer as a cause of upper-GI bleeding is exaggerated. *Gastrointest Endosc* 2004; 59: 788-94.
3. Ferguson CB, Mitchell RM. Non-variceal upper gastrointestinal bleeding. *Ulster Med J* 2006; 75: 32-39.
4. Barkun A, Bardou M, Marshall JK. Nonvariceal upper GI bleeding consensus conference group. Consensus recommendations for managing patients with nonvariceal upper gastrointestinal bleeding. *Ann Intern Med* 2003; 139: 843-57.
5. American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. Practice guidelines for perioperative blood transfusion and adjuvant therapies: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. *Anesthesiology* 2006; 105:198-8.
6. Marik PE, Corwin HL. Efficacy of red blood cell transfusion in the critically ill: a systematic review of the literature. *Crit Care Med* 2008; 36: 2667-74.

7. Bellotto F, Fagioli S, Pavei A, Gregory SA, Cati A, Silveri E, et al. Anemia and ischemia: myocardial injury in patients with gastrointestinal bleeding. *Am J Med* 2005; 118: 548-51.
8. Brullet E, Campo R, Calvet X, Guell M, Garcia-Monforte N, Cabrol J. A randomized study of the safety of outpatient care for patients with bleeding peptic ulcer treated by endoscopic injection. *Gastrointest Endosc* 2004; 60: 15-21.
9. Wolf AT, Wasan SK, Saltzman JR. Impact of anticoagulation on rebleeding following endoscopic therapy for nonvariceal upper gastrointestinal hemorrhage. *Am J Gastroenterol* 2007; 102: 290-96.
10. Barkun A, Sabbah S, Enns R, Armstrong D, Gregor J, Fedorak RN, et al. The Canadian Registry on Nonvariceal Upper Gastrointestinal Bleeding and Endoscopy (RUGBE): Endoscopic hemostasis and proton pump inhibition are associated with improved outcomes in a real-life setting. *Am J Gastroenterol* 2004; 99: 1238-46.
11. Baradarian R, Ramdhaney S, Chapalamadugu R, Skoczylas L, Wang K, Rivilis S, Remus K, et al. Early intensive resuscitation of patients with upper gastrointestinal bleeding decreases mortality. *Am J Gastroenterol* 2004; 99: 619-22.
12. Barkun A, Bardou M, Gralnek I. Erythromycin and other prokinetics in acute upper gastrointestinal bleeding? A meta-analysis. *Fund Clin Pharmacol* 2009; 23(suppl): 56.
13. Winstead NS, Wilcox CM. Erythromycin prior to endoscopy for acute upper gastrointestinal haemorrhage: a cost-effectiveness analysis. *Aliment Pharmacol Ther* 2007; 26: 1371-7.
14. Gralnek IM, Barkun AN, Bardou M. Management of acute bleeding from a peptic ulcer. *N Engl J Med* 2008; 359: 928-37.
15. Keyvani L, Murthy S, Leeson S, Targownik LE. Pre-endoscopic proton pump inhibitor therapy reduces recurrent adverse gastrointestinal outcomes in patients with acute non-variceal upper gastrointestinal bleeding. *Aliment Pharmacol Ther* 2006; 24: 1247-55.
16. Al-Sabah S, Barkun AN, Herba K, Adam V, Fallone C, Mayrand S, et al. Cost-effectiveness of proton-pump inhibition before endoscopy in upper gastrointestinal bleeding. *Clin Gastroenterol Hepatol* 2008; 6: 418-25.
17. Grossi E, Marmo R, Intraligi M, Buscema M. Artificial Neural Networks for Early Prediction of Mortality in Patients with Non Variceal Upper GI Bleeding (UGIB). *Biomedical Informatics Insights* 2008; 1: 7-19.
18. Marmo R, Koch M, Cipolletta L, Capurso L, Pera A, Bianco MA, et al. Predictive factors of mortality from non variceal upper gastrointestinal hemorrhage: a multicenter study. *Am J Gastroenterol* 2008; 103: 1639-47.
19. Marmo R, Koch M, Cipolletta L, Capurso L, Grossi E, Cestari R, et al. Predicting mortality in non-variceal upper gastrointestinal bleeders: validation of the Italian PNED Score and Prospective Comparison with the Rockall Score. *Am J Gastroenterol* 2010; 105: 1284-91.
20. Lee JG, Turnipseed S, Romano PS, Vigil H, Azari R, Melnikoff N, et al. Endoscopy-based triage significantly reduces hospitalization rates and costs of treating upper GI bleeding: a randomized controlled trial. *Gastrointest Endosc* 1999; 50: 755-61.
21. Ananthakrishnan AN, McGinley EL, Saeian K. Outcomes of weekend admissions for upper gastrointestinal hemorrhage: a nationwide analysis. *Clin Gastroenterol Hepatol* 2009; 7: 257-58.
22. Cooper GS, Kou TD, Wong RC. Use and impact of early endoscopy in elderly patients with peptic ulcer hemorrhage: a population-based analysis. *Gastrointest Endosc* 2009; 70: 229-35.
23. Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. *Lancet* 2000; 356: 1318-21.
24. Schacher GM, Lesbros-Pantoflickova D, Ortner MA, Wasserfallen JB, Blum AL, Dorta G. Is early endoscopy in the emergency room beneficial in patients with bleeding peptic ulcer? A "fortuitously controlled" study. *Endoscopy* 2005; 37: 324-8.
25. Stanley AJ, Ashley D, Dalton HR, Mowal C, Gaya DR, Thompson E, et al. Outpatient management of patients with low-risk upper-gastrointestinal haemorrhage: multicentre validation and prospective evaluation. *Lancet* 2009; 373: 5-7.
26. Lin HJ, Wang K, Perng CL, Chua RT, Lee FY, Lee CH, et al. Early or delayed endoscopy for patients with peptic ulcer bleeding. A prospective randomized study. *J Clin Gastroenterol* 1996; 22: 267-71.
27. Tai CM, Huang SP, Wang HP, Lee TC, Chang CY, Tu CH, et al. High-risk ED patients with nonvariceal upper gastrointestinal hemorrhage undergoing emergency or urgent endoscopy: a retrospective analysis. *Am J Emerg Med* 2007; 25: 273-78.
28. Adamopoulos AB, Baibas NM, Efstathiou SP, Tsioulos DI, Mitromaras Tsami A, Mountokalakis TD. Differentiation between patients with acute upper

- gastrointestinal bleeding who need early urgent upper gastrointestinal endoscopy and those who do not. *A prospective study. Eur J Gastroenterol Hepatol* 2003; 15: 381-87.
29. Spiegel BMR, Vakil NB, Ofman JJ. Endoscopy for acute non-variceal upper gastrointestinal tract hemorrhage: is sooner better? A systematic review. *Arch Intern Med* 2001; 161: 1393-04.
 30. Ghosh S, Watts D, Kinnear M. Management of gastrointestinal haemorrhage. *Postgrad Med J* 2002; 78: 4-14.
 31. Church NI, Palmer KR. Injection therapy for endoscopic haemostasis. *Baillieres Best Prac Res Clin Gastroenterol* 2000; 14: 427-41.
 32. Liou TC, Lin SC, Wang HY, Chang WH. Optimal injection volume of epinephrine for endoscopic treatment of peptic ulcer bleeding. *World J Gastroenterol* 2006; 12: 3108-13.
 33. Lin HJ, Hsieh YH, Tseng GY, Perng CL, Chang FY, Lee SD. A prospective, randomized trial of large-versus small-volume endoscopic injection of epinephrine for peptic ulcer bleeding. *Gastrointest Endosc* 2002; 55: 615-19.
 34. Jensen DM, Machicado GA. Endoscopic hemostasis of ulcer hemorrhage with injection, thermal, and combination methods. *Tech. Gastrointest. Endosc.* 2005;7, 124-31.
 35. Monkewich GJ, Haber GB. In, *Advanced Therapy in Gastroenterology and Liver Disease 5th edn* (eds Bayless, T. M. & Diehl, A. M.) 167-177 (BC Decker, Hamilton, Ontario, 2005).
 36. Liou TC, Chang WH, Wang HY, Lin SC, Shih SC. Large-volume endoscopic injection of epinephrine plus normal saline for peptic ulcer bleeding. *J. Gastroenterol. Hepatol.* 2007;22, 996-2.
 37. Asaki S. Efficacy of endoscopic pure ethanol injection method for gastrointestinal ulcer bleeding. *World J Surg* 2000; 24: 294-98.
 38. Sofia C, Portela F, Gregório C, Rosa A, Camacho E, Tomé L, et al. Endoscopic injection therapy vs. multipolar electrocoagulation vs. laser vs. injection + octreotide vs. injection + omeprazole in the treatment of bleeding peptic ulcers. *A prospective randomized study. Hepatogastroenterology* 2000; 47: 1332-6.
 39. Shimoda R, Iwakiri R, Sakata H, Ogata S, Kikkawa A, Ootani H, et al. Evaluation of endoscopic hemostasis with metallic hemoclips for bleeding gastric ulcer: comparison with endoscopic injection of absolute ethanol in a prospective, randomized study. *Am J Gastroenterol* 2003; 98: 2198-2.
 40. Ljubicic N, Supanc V, Vrsalovic M. Efficacy of endoscopic clipping for actively bleeding peptic ulcer: comparison with polidocanol injection therapy. *Hepatogastroenterology* 2004; 51: 408-12.
 41. Church NI, Dallal HJ, Masson J, Mowat NA, Johnston DA, Radin E, et al. A randomized trial comparing heater probe plus thrombin with heater probe plus placebo for bleeding peptic ulcer. *Gastroenterology* 2003; 125: 396-3.
 42. Pescatore P, Jornod P, Borovicka J, Pantoflickova D, Suter W, Meyenberger C, et al. Epinephrine versus epinephrine plus fibrin glue injection in peptic ulcer bleeding: a prospective randomized trial. *Gastrointest Endosc* 2002; 55: 348-53.
 43. Manner H, Plum N, Pech O, Ell C, Enderte MD. Colon explosion during plasma coagulation. *Gastrointest Endosc* 2008; 67: 1123-27.
 44. Jensen DM, Machicado GA, Hirabayashi K. Randomized controlled study of three different types of hemoclips for hemostasis of bleeding canine acute gastric ulcers. *Gastrointest Endosc* 2006; 64: 768-73.
 45. Cipolletta L, Bianco MA, Marmo R, Rotondano G, Piscopo R, Vingiani AM, et al. Endoclips versus heater probe in preventing early recurrent bleeding from peptic ulcer: a prospective and randomised trial. *Gastrointest Endosc* 2001; 53: 147-51.
 46. Sung JJ, Soi KK, Lai LH, Wu JC, Lau JY. Endoscopic clipping versus injection and thermocoagulation in the treatment of non-variceal upper gastrointestinal bleeding, a meta-analysis. *Gut* 2007; 56: 1364-73.
 47. Gevers AM, De Goede E, Simoons M, Hiele M, Rutgeerts PA randomized trial comparing injection therapy with hemoclip and with injection combined with hemoclip for bleeding ulcers. *Gastrointest Endosc* 2002; 55: 466-69.
 48. Park CH, Lee WS, Joo YE, Choi SK, Rew JS, Kim SJ. Endoscopic band ligation for control of acute peptic ulcer bleeding. *Endoscopy* 2004; 36: 79-82.
 49. Calvet X, Vergara M, Brullet E, Gisbert JP, Campo R. Addition of a second endoscopic treatment following epinephrine injection improves outcome in high risk bleeding ulcers. *Gastroenterology* 2004; 126: 441-50.
 50. Laine L, McQuaid KR. Endoscopic therapy for bleeding ulcers: an evidence based approach based on meta-analyses of randomized controlled trials. *Clin Gastroenterol Hepatol* 2009; 7: 33-47.

51. Marmo R, Rotondano G, Piscopo R, Bianco MA, D'Angella R, Cipolletta L. Dual therapy versus monotherapy in the endoscopic treatment of high-risk bleeding ulcers: a meta-analysis of controlled trials. *Am J Gastroenterol* 2007; 102: 279-89.
52. Yuan Y, Wang C, Hunt RH. Endoscopic clipping for acute nonvariceal upper-GI bleeding: a meta-analysis and critical appraisal of randomized controlled trials. *Gastrointest Endosc* 2008; 68: 339-51.
53. Barkun AN, Martel M, Toubouti Y, Rahme E, Bardou M. Endoscopic hemostasis in peptic ulcer bleeding for patients with high-risk lesions: a series of meta-analyses. *Gastrointest Endosc* 2009; 69: 786-99.
54. British Society of Gastroenterology Endoscopy Committee. Non-variceal upper gastrointestinal haemorrhage: guidelines. *Gut* 2002; 51(suppl IV): iv1-iv6.
55. Wong SK, Yu LM, Lau JY, Lam YH, Chan AC, Ng EK, et al. Prediction of therapeutic failure after adrenaline injection plus heater probe treatment in patients with bleeding peptic ulcer. *Gut* 2002; 50: 322-5.
56. Romagnuolo J. Routine second look endoscopy: ineffective, costly and potentially misleading. *Can J Gastroenterol* 2004; 18: 401-4.
57. Tsoi K, Chan H, Pao C, Chiu P, Sung J. Is second-look endoscopy with heater probe or injection for peptic ulcer bleeding necessary [Abstract]? *Gut* 2008; 57: A355.
58. Marmo R, Rotondano G, Bianco M, Piscopo R, Prisco A, Cipolletta L. Outcome of endoscopic treatment for peptic ulcer bleeding: is a second look necessary? A meta-analysis. *Gastrointest Endosc* 2003; 57: 62-7.
59. Chiu PW, Joeng HK, Choi CL, Kwong KH, Ng EK, Lam SH. Predictors of peptic ulcer rebleeding after scheduled second endoscopy: clinical or endoscopic factors? *Endoscopy* 2006; 38: 726-9.
60. Spiegel BM, Ofman JJ, Woods K, Vakil NB. Minimizing recurrent peptic ulcer hemorrhage after endoscopic hemostasis: the cost-effectiveness of competing strategies. *Am J Gastroenterol* 2003; 98: 86-97.
61. Chiu PW, Lam CY, Lee SW, Kwong KH, Lam SH, Lee DT, et al. Effect of scheduled second therapeutic endoscopy on peptic ulcer rebleeding: a prospective randomised trial. *Gut* 2003; 52: 1403-7.
62. Leontiadis G, Howden CW. The role of proton pump inhibitors in the management of upper gastrointestinal bleeding. *Gastroenterol Clin North Am* 2009; 38: 199-213.
63. Cameron EA, Pratap JN, Sims TJ, Inman S, Boyd D, Ward M, et al. Three-year prospective validation of a pre-endoscopic risk stratification in patients with acute upper-gastrointestinal haemorrhage. *Eur J Gastroenterol Hepatol* 2002; 14: 497-1.
64. Ripoll C, Bañares R, Beceiro I, Menchen P, Catalina MV, Echenagusia A, et al. Comparison of transcatheter arterial embolization and surgery for treatment of bleeding peptic ulcer after endoscopic treatment failure. *J Vasc Interv Radiol* 2004; 15: 447-50.
65. Schenker MP, Duszak R Jr, Soulen MC, Smith KP, Baum RA, Cope C, et al. Upper gastrointestinal hemorrhage and transcatheter embolotherapy: clinical and technical factors impacting success and survival. *J Vasc Interv Radiol* 2001; 12: 1263-71.
66. Aina R, Oliva VL, Therasse E, Perreault P, Bui BT, Dufresne MP, et al. Arterial embolotherapy for upper gastrointestinal hemorrhage: outcome assessment. *J Vasc Interv Radiol* 2001; 12: 195-200.

Corresponding Author

Zhan-Ju Liu,
 Department of Gastroenterology,
 The Shanghai Tenth People's Hospital,
 Tongji University,
 Shanghai,
 China,
 E-mail: zhanjuliui@yahoo.com

Evaluation of computer workstation ergonomics and prevalence of the musculoskeletal symptoms - A cross sectional study of Macedonian office workers

Viktorija Prodanovska-Stojcevska¹, Jovica Jovanovic², Tanja Jovanovska¹, Rozalinda Isjanovska³

¹ Medical College, University St.Kliment Ohridski Bitola, R.Macedonia,

² Faculty of Medicine, University of Nis, Serbia,

³ Medical Faculty, SS Cyril and Methodius University Skopje, R. Macedonia.

Abstract

The aim of this paper is to evaluate a computer workstation in an office environment and to identify the ergonomic deficiencies in typical offices and prevalence of the musculoskeletal symptoms for employees at a computer work stations. A cross-section study was conducted during the period of May and June in 2010 in Bitola, Republic of Macedonia. This study included 100 employees with computer workstations from 3 companies with a separate primary function. The criterion was that the employee has to perform at least 1 hour working at the computer during their working hours. The instruments for the study were display questionnaire and Nordic questionnaire for musculoskeletal symptoms. Most of the workstations fulfilled the criteria of the checklist. The deficiency in the postures at the workplace was registered in few questions: 28% of the employees had a monitor reflection, 65% replied that the electrical line were not secured and 62% of the employees do not have a copy holder. As with the usage of Nordic Questionnaires, musculoskeletal problems were identified for the computer employees in duration of 12 months in the last 7 days. As of this period, the most prevalent were the symptoms in the neck area 48%, upper back in 48% and the lower part of the back in 42%. Computer workstations in offices should be laid out following ergonomics standards, guidelines, and recommendations. Employees must be trained in ergonomic layout and organization of their workstations. With regard to musculoskeletal symptoms, preventive measures should focus on neck and shoulder disorders.

Key words: Computer workers, workstation, musculoskeletal symptoms

Introduction

Computer availability has made workers work faster, easier, neater and less frustrating to the one that are using (1). Computers (video display terminals) have become increasingly common in both workplace and homes over the past 20 years (2).

Visual and musculoskeletal symptoms and disorders are the most common occupational health problems among computer users (3). These problems include sustained pain in the neck and upper extremities, such as wrist tendonitis, epicondylitis and trapezius muscle strain (4). The risk factors in the workplace include hours of computer use, sustained awkward head and arm postures, poor lighting conditions and work organizational factors (5-13).

Ergonomics is the science and technology of fitting the activities and environment to the abilities, dimensions and needs of people to improve performance while enhancing comfort, health and safety (14). By applying ergonomic principles the efficiency of human-computer interaction, health and the user's safety can be improved (15). Eason (16) developed a classical ergonomic framework and identified factors that affect human performance. These factors include task characteristic, user issues, environmental factors and human-computer interaction (16).

The position of the head of the computer user is to put the minimum stress on the neck muscle and the recommended viewing angle is 15°-30° (17). The position of a video display terminal relative to eyes can influence visual strain and the two main parameters are the viewing distance from the eyes to the screen and the height of the visual target relative to the eyes (18).

The common devices of the computer are keyboard and mouse. While using these devices the optimal posture of the wrist is to keep the wrist straight and free from extension or flexion and ulnar deviation so can minimize stress (17). Different layouts of a VDT workstation were studied like Sotoyama, Jonai, and Saito(19). They recommended desk height to be adjustable to the user's height and the monitor to be set closer to the keyboard to provide a smaller ocular surface area.

The positive effect in reducing computer workstation symptoms has shown ergonomics training (15). Proper training to computer operators are needed on how to maintain a correct posture and adjust their workstations (20,21). Ivergard (22) provided some ground rules in the design of an education and training program for a computer workstation.

Effective training programs and producing positive changes in workstation configuration and posture have reducing the severity of symptoms and making the improvement in productivity (23).

A lot of research has been conducted in this area; it is believed implementation of ergonomics in the office environment is somewhat limited, especially in developing countries like Republic of Macedonia. The objective of this research was to study and identify ergonomic deficiencies in computer workstations in typical offices, prevalence of the musculoskeletal symptoms at the computer employees and their possible association with the workplace; and suggest strategies to reduce or eliminate these deficiencies to improve occupational health and safety.

Material and methods

There was a cross-section study conducted during the period of May and June in 2010 in Bitola, Republic of Macedonia. This study included 100 employees with computer workstations from 3 companies with a separate primary function. Employees that were involved in the study had to perform at least 1 hour working at the computer during their working hours. After the notification for consent, the employees fulfilled the questionnaire regarding ergonomic features at their workplace and a standardized questionnaire for possible musculoskeletal symptoms. The time needed to answer the questionnaire was limited for 30-

40 min. In order to improve the condition at the workplace for this group of employees, they were advised with recommended safe and comfortable work positioning. Within the same context, there was a guidelines suggested by OSHA (*Occupational Safety and Health Administration*) where many suggestion for diminishing and eliminating of the identified issues were given as well as a possibility to create own "adjusted position" during the computer work performance.

Workstation checklist

The checklist was based on a German VDT questionnaire (BiFra), which has been used since 1995 to evaluate various VDT workstations throughout Germany, and is also available in French and English(24). The checklist used in this survey contains 32 items regarding display (e.g. size, reflections; 5 items), keyboard/mouse (e.g. area in front of the keyboard or for mouse movement; 6 items), desk and arrangement of the VDT and accessories (e.g. adjustability of height, space for legs; 7 items), chair (e.g. adjustability of height; possibility of changing working postures; 4 items), ambient and environmental conditions (e.g. lighting of office and desk; 10 items).

Standardized Nordic questionnaires for the analysis of musculoskeletal symptoms

The questionnaire consists of structured, forced, binary or multiple choices and was used as self-administered questionnaire (25). The purpose of the questionnaires is to serve as instrument in the screening of musculoskeletal symptoms in an ergonomics context. The general questionnaire is designed to answer the following question: , Do musculoskeletal troubles occur in a given population, and if so in what parts of the body are they located?,,

The questionnaire is composed of two sections. First basic part is composed of questions that refer the appearance of the musculoskeletal symptoms according the anatomic area (neck, shoulders, elbow, wrist and hand and finally the upper and the lower part of the back). An additional classification of the symptoms according the period of the appearance within last 12 months and during last 7 days was done as well.

Second part of the questionnaire includes additional questions regarding the symptoms for each

anatomic localization, functional influence, and durability as well as the musculoskeletal symptoms during last 7 days.

Statistical analysis

Data bases were formed by using specific software intended for this purpose. The data collected are presented in charts. This study includes percentage of the structure in order to present the prevalence (in percentage as well). The attributive statistical series are analyzed by determining the percentage of structure. Confirmation of the statistical significance among the detected differences using Chi-square test for two attributive variables and a statistical significance for $p < 0,05$.

Results

Demographic characteristics of the study population

100 employees out of whom 70% are females and 30% males fulfilled the questionnaire. The mean age was 40.06 (± 10.8) years. All of them were full-time employed, 8 hours per day, 5 days a week. 75% of them are performing computer work more than 4 hours per day and 25% do 1-4 hours per day.

Workstation characteristics

The VDT workstations were checked with regard to the ergonomic and spatial features given on the checklist (BiFra). Most of the workstations fulfilled the criteria of the checklist. Occasionally, reflections on the visual displays due to shortcomings in the lighting equipment were documented. With regard to the 100 workstations, for which the employees' questionnaires were available, many of the ergonomic features of VDT workstations were fulfilled: At 94% of them the monitor screen is not flickering, 90% the monitor could be easily positioned; 91% have an adequate space in front of the keyboards to lean the thumbs and the forearms, 87% the keyboard is not sliding on the work desk, 88% have an adequate space for the mouse movement, 79% have an adequate volume of the desk space, 82% enough space for their feet and 96% the height of the desk is sufficient to their needs.

As of the analysis of the question regarding the chair 75% of the examined have replied not having

a comfortable body posture during the work performance, 64% cannot change the body posture during their work and 52% from the employees do not have an ergonomic designed chair. (Figure 1).

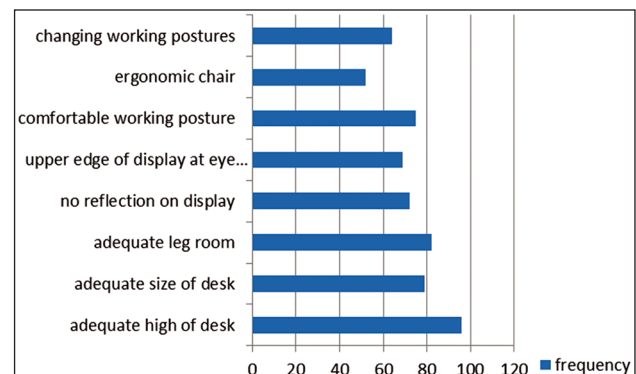


Figure 1. Characteristics of evaluated computer station $n=100$

The deficiency in the postures at the workplace was registered in few questions: 28% of the employees had a monitor reflection, 65% replied that the electrical line were not secured and 62% of the employees do not have a copy holder.

Symptoms appearance

As with the usage of Nordic Questionnaires, musculoskeletal problems were identified for the computer employees in duration of 12 months in the last 7 days. As of this period of 12 months, the most prevalent were the symptoms in the neck area 48%, upper beek in 48% and the lower part of the beek in 42%. 17% have registered symptoms in the right shoulder, right wrists/ hands, and 15% was registered in the elbow. Within the recent 7 days, 22% of them have registered a neck problems and 16% pain in the upper part of the beek (Figure 3).

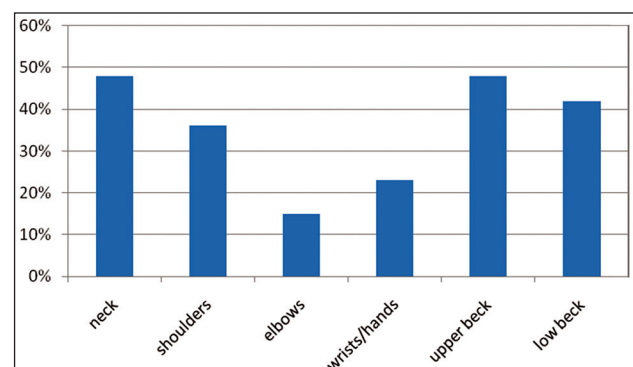


Figure2. Prevalence percentage of the musculoskeletal symptoms separated in areas for the examined in the last 12 months

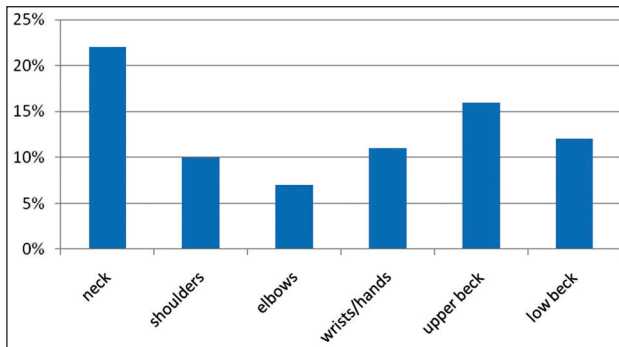


Figure 3. Prevalence percentage of the musculoskeletal symptoms separated in areas for the examined in the last 7 days

Regarding the time for performing computer work during daily working hours 5% of the responders who work 1-4 hours per day have musculoskeletal symptoms of the upper extremities. 30% of the workers who spend more than 4 hours at the computer during working hours reported musculoskeletal symptoms at the given anatomic area. As for sex distribution 95 % of the employees who reported symptoms of the upper extremities are female.

The statistical significance is registered between the symptoms of the neck and gender (Pearson Chi Square=84,005; $df=3$; $p=0,0001$), odds ratio 3,67 (95% Confidence Interval from 1,4359 to 9,3632) respectively the high risk of getting symptoms in female population.

Association is registered between the question for safe and rhythmical stroke technique of the keyboard and pain in the wrist/hand during last 7 days Pearson Chi-square: 5,18407, $df=1$, $p=0,022797$. Seemingly, there is a association registered between safe and rhythmical stroke technique of the keyboard and pain in the hand ankle during last 7 days among the employees that spend more than 1 hour at the computer Pearson Chi-square: 5,10500, $df=1$, $p=0,023859$.

Discussion

The primary aim of this study was to depict and assess the computer workstation and the period prevalence for the appearance of the musculoskeletal symptoms especially in the area of the upper extremities among those employees within the Macedonian offices and administration workplaces.

As for the examination, the study included 100 office workstations with an office employee in

each of them. Even though that the sample was with an insignificant amount yet it represented a typical computer workstation setting. The outcome received is dully applicable for computer employees respectively.

The evaluation results have shown that most of the criteria for posture at the workplace are satisfied. This refers especially to the questions that include the monitor (setting, legibility, screen flickering and positioning), setting of the keyboard and mouse (safe and rhythmical stroke, sufficient amount of space for movement of the mouse and mouse pad), the volume of the work space and the height positioning of the desk.

The research conducted in Germany regarding the features at the workplace considering the computer work has shown that generally, the ergonomic conditions at the investigated workstations can be considered as good or very good. The majority of the working places fulfilled all criteria of the checklist (26).

As of the deficiencies in the postures at the workplace the following could be mentioned: screen reflection, unsecured electrical lines, shortage in copy holders, no possession of ergonomic designed chair and not sufficient space for work that might allow a change of the body posture during the working hours. Those deficiencies are due to the fact that such workstations are not specialized for computer workers but they represent a regular workstations adapted with the necessities for the institutions with an additional supplying with computer equipment.

Similar to those results i.e. deficiencies were identified in the study that was conducted in Oman where computer workstation facilities and furniture were inadequate, which may have contributed to ergonomic deficiencies in terms of layout and workstation organization (15) most employees did not have document holders that are important for minimizing back and neck bending, especially for those who spend a lot of time on data entry.

The researches have shown that the percentage of the registered musculoskeletal symptoms is increased in the period on 12 months than the one that shows the results from the last 7 days. As of the anatomic localization of symptoms, most of them are registered in the area of the neck, upper and lower part of the back. The appearance of the

musculoskeletal symptoms in the neck area probably comes up because of the deficiencies in the position of the chair such as: not sufficient work space, absence of document holder as well as not having an ergonomic designed chair.

The results from the conducted Norwegian study (27) regarding the prevalence of the musculoskeletal symptoms showed higher prevalence of neck and shoulder complaints in the study population compared to arm, elbow and hand complaints.

Similar results are received from the research done with the Nordic questionnaires. As with the 12-month symptom prevalence, 1-week prevalence results revealed that the neck and shoulder symptoms were clearly more prevalent than the hand/ wrist and elbow/forearm symptoms (26). With regard to the 12-month prevalence of the whole sample, the highest values were found in the neck (55%) and shoulder (38%) region. The least pronounced prevalence was found in the hand/wrist and elbow/forearm, with values of 21% and 15%, respectively.

Positive association is registered between the safe and the rhythmical stroke technique of the keyboard with the symptoms in the wrist/hand that appeared within the last 7 days, especially to those employees that work for more than 1 hour at the computer.

A similar exposure ("keying") was reported by Gerr et al. to be positively associated with hand/arm symptoms and disorders (28, 10). In two Japanese studies, effects of the duration of daily VDT work on physical symptoms (29) on the general health status (30) were documented.

Conclusion

The computer workstation mainly fulfills the conditions especially those related to setting of the monitor, keyboard, mouse then, the adequate space and height of the desk and the comfort of the feet. The deficiencies in terms of the setting of the workplace appear in the body posture and the possibility of its change during the work, lack of an ergonomic chair, reflection of the monitor and the lack of a copy holder. The most prevalent musculoskeletal symptoms are in the neck, the upper and the lower part of the back and neck during the period of 12 months. As for the prevalence of the symptoms within last 7 days, the most present

were those on the neck and the upper back. The musculoskeletal symptoms are more prevalent in the computer workers that work more than 4 hours per day than the employees that work 1-4 hours per day. Regarding the sex distribution symptoms are registered mainly in the female employees. An association is registered between the techniques of the keyboard punch and the appearance of symptoms in the wrist/hand for the period of last 7 days.

Computer workstations in offices should be laid out following ergonomics standards, guidelines and recommendations. Employees must be trained in ergonomic layout and organization of their workstations. With regard to musculoskeletal symptoms, preventive measures should focus on neck and shoulder disorders. The data gathered in this survey can be used as a reference for further studies with comparable outcomes and in occupational safety and health campaigns addressing the ergonomic characteristics of VDT workstations.

References

1. Ayanniyi et al.: Differences in prevalence of self-reported musculoskeletal symptoms among computer and non-computer users in a Nigerian population: a cross-sectional study. *BMC Musculoskeletal Disorders*, 2010, 11: 177.
2. Gerr F, Marcus M, Monteilh C, Hannan L, Ortiz D, Kleinbaum D: A randomised controlled trial of postural interventions for prevention of musculoskeletal symptoms among computer users. *Occup Environ Med* 2005, 62: 478-487.
3. Hagberg M, Rempel D.: Work-related disorders and the operation of computer VDT's. Chapter 58 in *Handbook of Human-Computer Interaction*, 2nd Edition. M. Helander, T.K. Landauer, P. Prabhu (eds.), Elsevier Science BV; 1997.
4. Brewer S, Van Eerd D, Amick B, Irvin E, Daum K, Gerr F, Moore S, Cullen K, Rempel D.: Workplace interventions to prevent musculoskeletal and visual symptoms and disorders among computer users: A systematic review. *J Occup Rehabil* (2006) 16: 325-358.
5. Cole BL.: Do video display units cause visual problems? A bedside story about the processes of public health decision-making. *Clin Exp Optom* 2003; 86: 205-20.
6. Daum KM, Clore KA, Simms SS, Wilczek DD, Vesely JW, Spittle BM, Good GW.: Productivity Associated with visual status of computer users. *Optometry* 2004; 75: 33-47.

7. Hales TR, Sauter SL, Peterson MR.: Musculoskeletal disorders among visual display terminal users in a telecommunications company. *Ergonomics* 1994; 37: 1603–21.
8. Kryger AI, Andersen JH, Lassen CF.: Does computer use pose an occupational hazard for forearm pain; from the NUDATA study. *Occup Environ Med* 2003; 60: e14.
9. Lassen CF, Mikkelsen S, Kryger AI, Brandt L, Overgaard E, Thomsen JF, Vilstrup I, Andersen JH.: Elbow and wrist/hand symptoms among 6943 computer operators: a 1-year follow-up study (the NUDATA study). *Am J Ind Med* 2004; 46: 521–33.
10. Marcus M, Gerr F, Monteilh C.: A prospective study of computer users: II. Postural risk factors for musculoskeletal symptoms and disorders. *Am J Ind Med* 2002; 41: 236–49.
11. Palmer KT, Cooper C, Walker-Bone K, Syddall H, Coggon D.: Use of keyboards and symptoms in the neck and arm: evidence from a national survey. *Occup Med* 2001; 51: 392–5.
12. Punnett L, Bergqvist U.: Visual display unit work and upper extremity musculoskeletal disorders, A review of epidemiological findings. National Institute for Working Life – Ergonomic Expert Committee Document 1997; 1: 1–173.
13. Sheedy JE, Shaw-McMinn PG.: Diagnosing and treating computer-related vision problems. Philadelphia: Butterworth-Heinemann; 2003, p. 288.
14. Salvendy G, editor. Handbook of industrial engineering: technology and operations management. 3rd ed. New York, NY, USA: Wiley Interscience; 2001.
15. Shikdar AA, Al-Kindi MA.: Office ergonomics: deficiencies in computer workstation design. *Int J Occup Saf Ergon.* 2007; 13(2): 215–23.
16. Eason KD.: Ergonomic perspectives on advances in human–computer interaction. *Ergonomics.* 1991; 34(6): 721–41.
17. Springer TJ.: VDT workstations: a comparative evaluation of alternative. *Appl Ergon.* 1982; 13: 211–2.
18. Jaschinski W, Heuer H, Kylian, H.: Preferred position of visual displays relative to the eyes: a field study of visual strain and individual differences. *Ergonomics.* 1998; 41(7): 1034–49.
19. Sotoyama M, Jonai H, Saito S.: Analysis of ocular surface area for comfortable VDT workstation layout. *Ergonomics.* 1996; 39(6): 877–84.
20. Chung MK, Choi K.: Ergonomic analysis of musculoskeletal discomforts among conversational VDT operators. *Computers & Industrial Engineering.* 1997; 33(3–4): 521–4.
21. Sanders MS, McCormick EJ.: Human factors in engineering and design. 7th ed. New York, NY, USA: McGraw Hill International Editions; 1993.
22. Ivergård T. Handbook of control room design and ergonomics. London, UK: Taylor & Francis; 1989.
23. Lewis RJ, Fogleman M, Deeb J, Crandall E, Agopowicz, D.: Effectiveness of a VDT ergonomics training program. *Int J Ind Ergon.* 2001; 27: 119–131.
24. BiFraMitarbeiterbefragung[http://www.institut-aser.de/out.php?idart=485&lang=en]. 08/03/2008
25. Kuorinka I, Jonsson B, Kilbom A, Vinterberg H, Biering-Sorensen F, Andersson G, Jorgensen K: Standardised Nordic questionnaires for the analysis of musculoskeletal symptoms. *Appl Ergon* 1987, 18(3): 233–237.
26. Klusmann A, Gebhardt H, Falk Liebers, Rieger A.M.: Musculoskeletal symptoms of the upper extremities and the neck: A cross-sectional study on prevalence and symptom-predicting factors at visual display terminal (VDT) workstations. *BMC Musculoskeletal Disorders* 2008, 9: 96 doi: 10.1186/1471-2474-9-96
27. Eltayeb S, Bart JS, Kennes J, Lamberts HG P, Rob A de Bie. Prevalence of complaints of arm, neck and shoulder among computer office workers and psychometric evaluation of a risk factor questionnaire. *BMC Musculoskeletal Disorders* 2007, 8: 68 doi: 10.1186/1471-2474-8-68.
28. Gerr F, Marcus M, Ensor C, Kleinbaum D, Cohen S, Edwards A, Gentry Ortiz DJ, Monteilh C: A prospective study of computer users: I. Study design and incidence of musculoskeletal symptoms and disorders. *Am J Ind Med* 2002, 41(4): 221–235.
29. Nakazawa T, Okubo Y, Suwazono Y, Kobayashi E, Komine S, Kato N, Nogawa K: Association between duration of daily VDT use and subjective symptoms. *Am J Ind Med* 2002, 42(5): 421–426.
30. Ye Z, Honda S, Abe Y, Kusano Y, Takamura N, Imamura Y, Eida K, Takemoto T, Aoyagi K: Influence of Work Duration or Physical Symptoms on Mental Health among Japanese Visual Display Terminal Users. *Industrial Health* 2007, 45(2): 328–333.

Corresponding Author
 Viktorija Prodanovska-Stojcevska,
 Lecturer in Medical College in Bitola,
 University St Kliment Ohridski,
 Bitola,
 R. Macedonia,
 E-mail: prodanovska@yahoo.com

Comparative analysis of three different short tandem repeat multiplex system approaches in fingerprint DNA analysis

Anida Causevic-Ramosevac¹, Lejla Kovacevic², Dzenisa Buljugic³, Mirela Dzehverovic³, Jasmina Cakar³, Damir Marjanovic³

¹ Bosnalijek, Pharmaceutical and Chemical Industry, Joint Stock Company, Sarajevo, Bosnia and Herzegovina,

² Faculty of Pharmacy, University of Sarajevo, Sarajevo, Bosnia and Herzegovina,

³ Institute for Genetic Engineering and Biotechnology, University of Sarajevo, Bosnia and Herzegovina.

Abstract

Aim: The aim of this study was to report on the efficacy of using miniSTR and STR markers in possible analysis of so called touch DNA samples which is representing “Low Copy Number” (LCN) DNA profiling.

Methods: The study included 30 personal fingerprint samples (by the standard collection methods) and 30 buccal swab samples (referent samples). The samples were processed using 3 commercial kits (*PowerPlex® S5*, *PowerPlex® ESI 17* and *PowerPlex® 16*). PCR amplification was carried out in PE GeneAmp 9700, PCR System Thermal Cycler. Detection of the amplified products was performed on ABI PRISM 310 Genetic analyser (ABI, Foster City, CA), while RT-PCR DNA quantification was performed using Quantifiler DNA Identification kit.

Results: Minimal concentrations of nuclear DNA were registered in 8 (27%) of 30 fingerprints, while they were undetectable in the other 22 (73%) of 30 fingerprints. Concentrations of detected isolated DNA ranged from $9,33 \times 10^{-3}$ pg/μl to $1,41 \times 10^{-2}$ pg/μl.

Conclusion: Results of this study confirmed the presence of artificial alleles after use of all of the three commercial kits (*PowerPlex® S5*, *PowerPlex® 16* and *PowerPlex® ESI 17*). This suggests possible contamination during sample collection, but also appearance of allele drop in and drop out. Allele drop in and allele drop out are expected while performing analysis of small amounts of DNA, especially during PCR protocol optimization.

Consequently, further studies should investigate the optimization of all steps of DNA analysis procedures.

Key words: Short Tandem Repeats, Low Copy Number, Fingerprint DNA analysis

Introduction

The multiplex detection and analysis of mini-STR and STR markers is a common tool used in the forensic DNA analysis (1, 2, 3).

Short tandem repeats (STRs), are microsatellites, consist of tandemly repeated units of short nucleotide motifs, 1–6 bp long (4). These regions occur frequently and randomly throughout the genomes and typically show extensive variation. STRs are widely considered the genetic marker of choice for studies and have been applied in a wide range of studies of human populations (5). MiniSTR markers can help recover information from degraded DNA samples that typically result in partial profiles and total loss of information from standard STR. They are based on the idea of moving primers closer to the hypervariable region, in order to create shorter amplicons (6). Use of miniSTR concept underwent its expansion in the last few years and several mini-STR commercial kits have been released since then.

Nowadays, available commercial kits sometimes are allowing analysis of extremely low amounts of DNA presented in biological samples. The study we describe extends the potential forensic applications of miniSTRs and STRs to LCN samples („touch samples“), such as the fingerprint.

In the last decade, fingerprints were a frequent biological trace in forensic cases. Consequently, efforts are being made in the context of selecting the most appropriate genetic markers, as well as in terms of modifying the procedures of DNA analysis of biological trace fingerprints, and all this in order to generate a complete DNA profile.

Low copy number (LCN) typing, refers to the analysis of any sample that contains less than 200 pg of template DNA (7). It is therefore a sensitive technique that allows a profile to be obtained from only a few cells, an amount that corresponds to just a few cells of skin or sweat left from a fingerprint. DNA profiling of LCN samples faces many problems and depends upon many factors. Two factors that impact the robustness of LCN typing are stochastic effects and sensitivity of detection. They collectively result in allele drop-out, exaggerated heterozygote peak height imbalance, exaggerated peak height difference between loci within a profile, exaggerated stutter and allele drop-in. All of those stochastic effects could cause errors of data interpretation. Due to the sensitivity of the assay and the types of samples analyzed (ie, touch samples), the LCN profile may not be relevant to a case (7, 8).

Experience gathered at the Laboratory of Forensic Genetics, Institute for Genetic Engineering and Biotechnology in Sarajevo, confirms the difficulties of generating a complete DNA profiles from biological trace-fingerprint. As can be concluded, analysis of LCN samples, especially those one that could be described as “touch” samples, is still very challenging. We present some of the obtained results.

Methods

The study included 30 personal fingerprint samples (by the standard collection methods) and 30 buccal swab samples (referent samples). Extraction of fingerprint and buccal swab samples was performed using Qiagen® protocol with Qiagen® kit for DNA extraction (9).

RT-PCR DNA quantification was performed using Quantifiler DNA Identification kit (10), which is modified according to TaqMan technology and used for simultaneously quantification of all human DNA.

PCR amplification was carried out in PE GeneAmp 9700, PCR System Thermal Cycler. The total volume of each reaction was 25µL. Three commercial kits were used for PCR analysis of samples (PowerPlex® S5, PowerPlex® ESI 17 and PowerPlex®).

Usage of miniSTR PowerPlex® S5 kit in PCR analysis

The PowerPlex S5 kit (11) was used to simultaneously amplify 5 miniSTR loci as follows: D18S51, D8S1179, TH01, FGA, as well as the gender determination locus Amelogenin.

Usage of combined PowerPlex® ESI 17 kit in PCR analysis

The PowerPlex ESI 17 kit (12) was used to simultaneously amplify 17 loci: 12 STR loci (D22S1045, D2S1338, D19S433, D3S1358, D2S441, D10S1248, D1S1656, D16S539, D12S391, D21S11, vWA, SE33), 4 miniSTR loci (TH01, FGA, D18S51, D8S1179), as well as the gender determination locus Amelogenin.

Usage of PowerPlex® 16 kit in PCR analysis

The PowerPlex 16 kit (13) was used to simultaneously amplify 16 STR loci as follows: D3S1358, TH01, D21S11, D18S51, Penta E, D5S818, D13S317, D7S820, D16S539, CSF1PO, Penta D, vWA, D8S1179, TPOX, FGA, as well as the gender determination locus Amelogenin.

Application of all of the 3 mentioned PowerPlex® kits was done according to the protocol recommended by the manufactured.

Detection of all of the amplified products was performed on ABI PRISM 310 Genetic analyser (14). In the detection process of STR loci, adequate softwares that can manipulate with ABI PRISM® 310 Genetic analyser were used. Primary results were compared and analysed by usage of 310 Data Collection Software v. 3.1.0. Further analysis of results was made by usage of GeneMapper R ID v.3.2 Software, in order to classify amplified fragments according to size. The numeration and final design of DNA profiles was done by application of GeneMapper R ID v.3.2 Software.

Results

Minimal concentrations of nuclear DNA were registered in only 8 (27%) of 30 fingerprints. DNA was not detected within the other 22 (73%) of 30 fingerprints. Concentrations of detected isolated DNA ranged from $9,33 \times 10^{-3}$ pg/µl to $1,41 \times 10^{-2}$ pg/µl.

The results of PCR analysis using combined miniSTR PowerPlex® S5 kit

The results of PCR analysis using combined miniSTR PowerPlex® S5 kit are presented on figure 1.

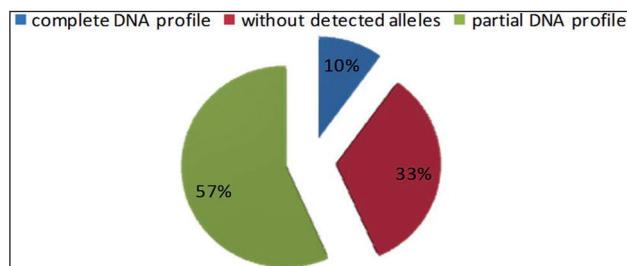


Figure 1. Results of detected miniSTR profiles after use of PowerPlex® S5 kit

Of 30 analysed samples, a potentially complete DNA profile was generated in 3 samples. However, the possibility of allele drop out cannot be ruled out in this case. The other DNA profiles were partial or without detected alleles on STR loci.

An example of a potentially complete miniSTR DNA profile detected from fingerprint 25 is presented on the figure below (Figure 2).

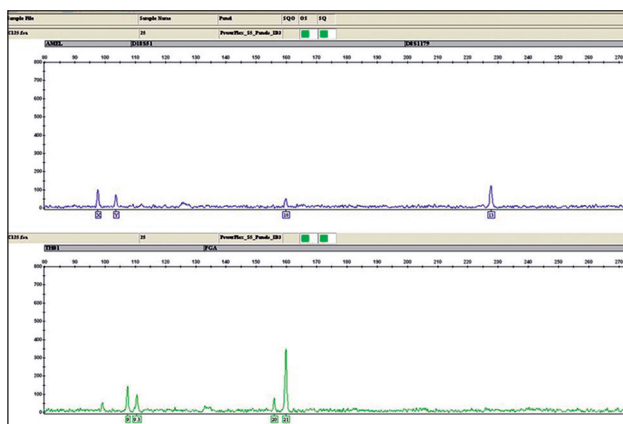


Figure 2. Complete miniSTR DNA profile detected from fingerprint 2

The results of PCR analysis using combined miniSTR and standard STR PowerPlex® ESI 17 kit

The results of PCR analysis using combined miniSTR and standard STR PowerPlex® ESI 17 kit from 30 fingerprints are shown on figure 3.

PCR analysis using multiplex STR PowerPlex® ESI 17 kit didn't result in any complete DNA profiles (Figure 3).

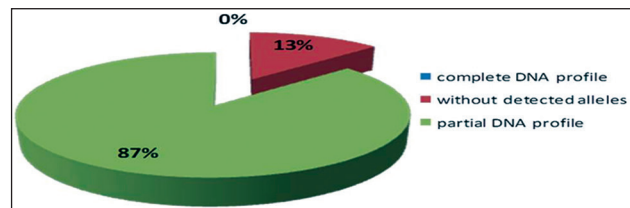


Figure 3. Results of detected STR DNA profiles after use of PowerPlex® ESI 17 kit

The results of PCR analysis using STR PowerPlex® 16 kit

The results of PCR analysis using multiplex STR PowerPlex® 16 kit (Promega, 2008) from 30 fingerprints are shown on figure 4. Of 30 fingerprint samples, 3 potentially complete DNA profiles were generated, while the others were partial or without detected alleles (Figure 4).

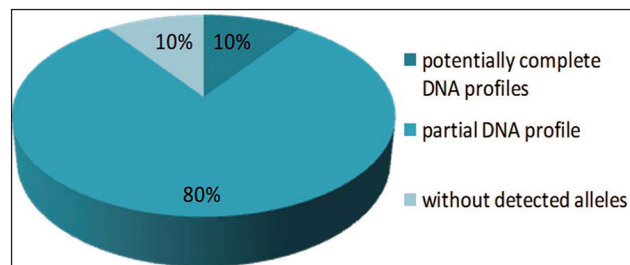


Figure 4. Results of detected STR profiles after use of PowerPlex® 16 kit

An example of a strong partial STR DNA profile detected from fingerprint 25 is presented on the figure below (Figure 5).

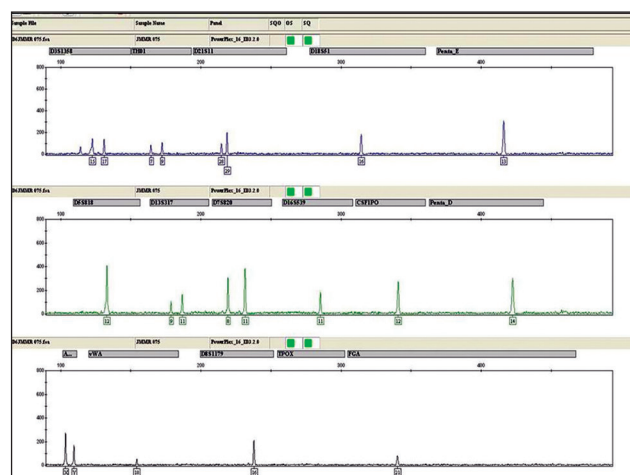


Figure 5. Strong partial pp16 STR DNA profile detected from fingerprint 25

In order to confirm the origin of DNA profiles generated from fingerprints, a comparison with

the DNA profiles generated from buccal swabs of the same person was made.

The results of comparative analysis from fingerprint samples after application of PowerPlex® S5 kit with DNA profiles of referent samples after application of PowerPlex® 16 kit

A total of 20 DNA profiles (10 samples did not provide DNA profiles) generated from fingerprint samples after application of *PowerPlex® S5* (11) kit were compared with DNA profiles of referent samples after application of *PowerPlex® 16* (13) kit. *PowerPlex® S5* and *PowerPlex® 16* match on 5 loci: AMEL, D18S51, D8S1179, TH01 and FGA.

A comparative analysis from fingerprint samples after application of *PowerPlex® S5* kit with DNA profiles of referent samples after application of *PowerPlex® 16* showed matching at all 5 STR loci in 1 (5%) sample. Matching alleles at 4 loci was reported in 1 (5%) sample, at 3 loci in 6 (30%) samples, at 2 loci in 6 (30%) samples and at 1 loci in 1 (5%) sample. No matching was detected in 5 (25%) samples (Figure 6).

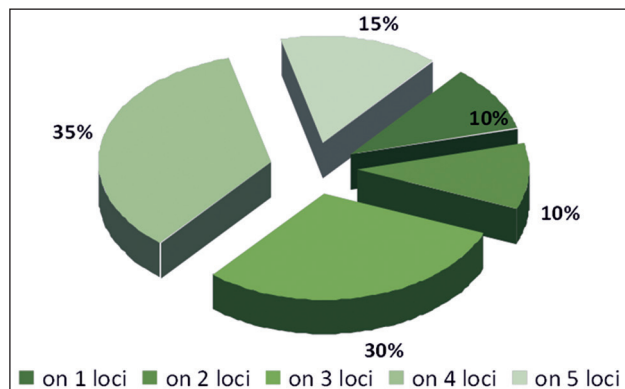


Figure 6. Matching of detected allelic variants between the fingerprint sample after application of *PowerPlex® S5* and the referent sample after application of *PowerPlex® 16* kit

The results of comparative analysis from fingerprint samples after application of PowerPlex® ESI17 kit with DNA profiles of referent samples after application of PowerPlex® 16 kit

A total of 22 DNA profiles (8 samples did not provide DNA profiles) generated from fingerprint samples after application of *PowerPlex® ESI 17* (12) kit were compared with DNA profiles of referent

samples after application of *PowerPlex® 16* (13) kit. *PowerPlex® ESI 17* and *PowerPlex® 16* match on 9 STR loci. Loci on which they match are: D3S1358, D16S539, vWA, D21S11, AMEL, D18S51, TH01, D8S1179 and FGA.

A comparative analysis from fingerprint samples after application of *PowerPlex® ESI 17* kit with DNA profiles of referent samples after application of *PowerPlex® 16* didn't report matching alleles (0%) at 9 STR loci. Matching alleles at 8 loci were reported in 4 (18%) samples, at 7 loci in 3 (14%) samples, at 6 loci in 0 (0%) samples, at 5 loci in 4 (18%) samples, at 4 loci in 3 (14%) samples, at 3 loci in 1 (4%) sample, at 2 loci in 3 (14%) samples, at 1 loci in 2 (9%) samples. No matching was detected in 2 (9%) samples (Figure 7).

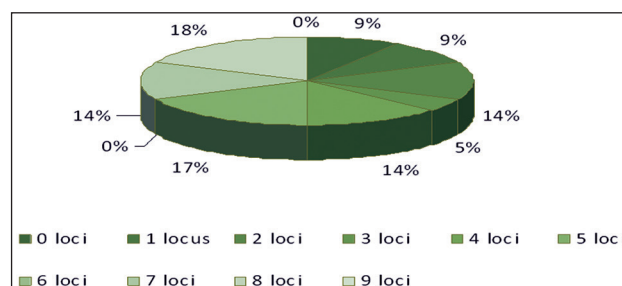


Figure 7. Matching of detected allelic variants between the fingerprint sample after application of *PowerPlex® ESI 17* and the referent sample after application of *PowerPlex® 16* kit

A total of 25 DNA profiles (5 samples did not provide DNA profiles) generated from fingerprint samples after application of *PowerPlex® 16* (13) kit were compared with DNA profiles of referent samples after application of *PowerPlex® 16* kit. A comparative analysis was made on all 16 matching loci.

A comparative analysis from fingerprint samples after application of *PowerPlex® 16* kit with DNA profiles of referent samples after application of *PowerPlex® 16* showed matching at all 16 STR loci in 1 (4%) sample. Matching allele variants at 15 loci was not reported (0%). Matching alleles were reported at 14 loci in 1 (4%) sample, at 13 loci in 2 (8%) samples, at 9 loci in 2 (8%) samples, at 8 loci in (8%) samples, at 7 loci in 1 (4%) sample, at 6 loci in 2 (8%) samples, at 5 loci in 2 (8%) samples, at 4 loci in 2 (8%) samples, at 3 loci in 3 (12%) samples, at 2 loci in 0 (0%) samples, and at 1 loci in 5 (20%) samples. Matching was not reported in 2 (8%) samples (Figure 8).

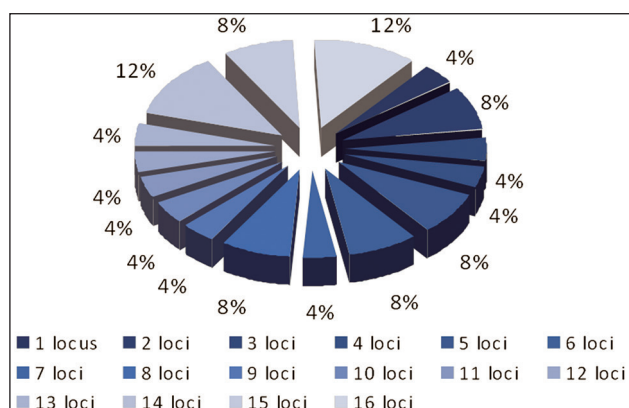


Figure 8. Matching of detected allelic variants between the fingerprint sample after application of PowerPlex® 16 and the referent sample after application of PowerPlex® 16 kit

Discussion

Previous experience has shown an increased incidence of stutter, heterozygous disequilibrium and allele drop-out in LCN samples (15, 8). However, besides allele drop-out, the authors of previous studies mentioned potential contamination of the samples as a limiting factor in generating an adequate DNA profile as well (16).

Results of this study confirmed the presence of artificial alleles after use of all of the three commercial kits (*PowerPlex® S5*, *PowerPlex® ESI 17* and *PowerPlex® 16*). Also, the results of this study indicated that we cannot exclude the possibility of fingerprint contamination during collection of samples, which could have potentially lead to the contamination of fingerprint with the biological trace of the person collecting the sample. However, due to the presence of a database with DNA profiles of people who were collecting samples, DNA profile of the person collecting the fingerprints was compared with the generated DNA profiles for the purpose of excluding contamination as a potential risk factor.

As well-known, miniSTRs are based on the idea of moving primers closer to the hypervariable region, in order to create shorter amplicons (2). Therefore, the percentage of success and accuracy of detection of allelic variants at analyzed loci of LCN samples is greater than after the use of standard or combined multiplex systems. MiniSTR markers have many advantages such as sensitivity and the possibility of detection of alleles even in

case of a small number of samples. However, their disadvantage lies in the fact that the possibility of artificial alleles is high. Unlike miniSTR multiplex systems, STR markers reduce the rate of artificial alleles and provide more stable results, but can lead to increased rates of allele drop-outs, and to non-detection of LCN DNA profiles.

As stated earlier, there are many problems in generating a successful DNA profile from the so-called LCN samples, such as the fingerprint. It is known that high quality DNA profiles from this type of sample can be generated from a larger number of collected cells (150-160 cells), which quantitatively correspond to 1 ng of DNA (17). However, the fingerprint as biological evidence does not contain a large number of cells, and therefore does not contain a large number of nuclei, from which it is possible to isolate nuclear DNA. Also, the amount of isolated DNA varies from person to person, and can even vary within the same person, depending on the time of taking fingerprint, perspiration, length of exposure of the finger to foil, limited transfers of cells on foil, etc., which further aggravates the success of generating DNA profiles.

The results of this study have pointed out the need to optimize the extraction methods and PCR technology in the analysis of fingerprint in general. One of the optimization ways is choosing the best DNA extraction protocol and its further optimization. Specifically, based on previous experience, for the purposes of this study DNA isolation procedure was performed by Qiagen® kit. Therefore, the possibility of application of other DNA isolation protocols should not be excluded in further investigations, since some of them has been shown to be very functional with some other type of samples, which also contain very small quantities of DNA (LCN) (18). Therefore, quantification phase should not be terminal, but only a guide in determining the best possible PCR protocol (19, 20).

Previous experience has proved that the PCR protocol optimization that includes either increase in number of cycles, in the amount of *Taq polymerase*, in the length of PCR elongation phase, or in recent times the use of “nested PCR”, ie the amplification of the entire genome, can improve the analysis of the LCN samples. By applying the techniques of “nested PCR” and potentially capillary electrophoresis (21), it will be possible to generate

a successful DNA profile from LCN samples containing quantities below 5 pg of DNA. The above experience could serve as a guide for optimizing the existing PCR protocols for the test samples in order to obtain better and cleaner results.

Also, besides the three applied kits in this study, we should bear in mind that there are more optimized kits for DNA amplification on the market currently, such as AmpF / STR® Minifiler™ System, which involves simultaneous amplification of eight target miniSTR loci. Future research in this area should be directed to the application of the above mentioned multiplex system for the purpose of generating a complete DNA profiles from biological trace of a fingerprint.

Conclusion

Taking in mind all of the above said, it can be concluded that further studies should investigate the optimization of all steps involved in DNA analysis procedures.

References

- Butler JM. *Forensic DNA Typing: Biology, Technology and Genetics of STR Markers* (2nd edition). London: Elsevier Academic Press; 2005.
- Coble M.D., Butler J.M. Characterization of new mini STR loci to aid analysis of degraded DNA. *J Forensic Sci* 2005; 50: 43-53.
- Marjanović D., Primorac D., *Molekularna forenzična genetika. Institut za genetičko inženjerstvo i biotehnologiju, Sarajevo, BiH*, 2009.
- Fan H, Chu JY. A brief review of short tandem repeat mutation. *Genomics Proteomics Bioinformatics*. 2007 Feb; 5(1): 7-14.
- Gilmore S, Peakall R, Robertson J. Short tandem repeat (STR) DNA markers are hypervariable and informative in *Cannabis sativa*: implications for forensic investigations. *Forensic Sci Int*. 2003 Jan 9; 131(1): 65-74.
- Butler JM et al. The development of reduced size STR amplicons as tools for analysis of degraded DNA. *J Forensic Sci*. 2003 Sep; 48(5): 1054-64.
- Budowle B, Eisenberg AJ, van Daal A. Validity of low copy number typing and applications to forensic science. *Croat Med J*. 2009 Jun; 50(3): 207-17.
- Leemans et al. Evaluation of methodology for the isolation and analysis of LCN-DNA before and after dactyloscopic enhancement of fingerprints. *International Congress Series*. 2006; 1288: 583-585
- Qiagen. *QIAGEN Genomic DNA Handbook*, Wiena: Qiagen Co; 2005.
- Applied Biosystems. *Quantifiler™ Human DNA Quantification Kit, User's Manual*. Applied Biosystems; 2003.
- Promega. *PowerPlex® S5 System – Technical Manual*. Madison: Promega Corporation; 2008.
- Promega. *PowerPlex® ES17 System – Technical Manual*. Madison: Promega Corporation; 2009.
- Promega. *PowerPlex® 16 System – Technical Manual*. Madison: Promega Corporation; 2008
- Applied Biosystems. *ABI Prism® 310 Genetic Analyzer, User's Manual*. Applied Biosystems; 2006.
- Gill P et al. An investigation of the rigor of interpretation rules for STRs derived from less than 100 pg of DNA. *Forensic Sci Int* 2000; 112(1): 17-40.
- Gill P. Application of Low Copy Number DNA Profiling. *Croat Med J* 2001; 42(3): 229-32.
- Kanable R. *DNA from Fingerprints?* 2005.
- Opel KL et al. Evaluation and quantification of nuclear DNA from human telogen hairs. *J Forensic Sci*. 2008 Jul; 53(4): 853-7.
- Primorac D et al. *Analiza DNA u sudskoj medicini i pravosuđu*. Medicinska naklada Zagreb, 2008; 2-50.
- Marjanović D, Primorac D. *Molekularna forenzična genetika. Institut za genetičko inženjerstvo i biotehnologiju, Sarajevo*, 2009.
- Smith PJ, Ballantyne J. Simplified low-copy-number DNA analysis by post-PCR purification. *J Forensic Sci*. 2007 Jul; 52(4): 820-9. Epub 2007 Jun 6.

Corresponding Author
Anida Causevic-Ramosevac,
Bosnalijek,
Pharmaceutical and Chemical Industry,
Joint Stock Company,
Sarajevo,
Bosnia and Herzegovina,
E-mail: anidac.01@gmail.com

Instructions for the authors

All papers need to be sent to e-mail: healthmedjournal@gmail.com

Every sent article gets its number, and author(s) will be notified if their paper is accepted and what is the number of paper. Every correspondence will use that number. The paper has to be typed on a standard size paper (format A4), leaving left margins to be at least 3 cm. All materials, including tables and references, have to be typed double-spaced, so one page has no more than 2000 alphanumeric characters (30 lines). Sent paper needs to be in the form of triplicate, considering that original one enclosure of the material can be photocopied. Presenting paper depends on its content, but usually it consists of a page title, summary, text references, legends for pictures and pictures. Type your paper in MS Word and send it on a diskette or a CD-ROM.

Title page

Every article has to have a title page with a title of no more than 10 words: name (s), last and first of the author (s), name of the institution the authors (s) belongs to, abstract with maximum of 45 letters (including space), footnote with acknowledgments, name of the first author or another person with whom correspondence will be maintained.

Abstract

Second page needs to contain paper abstract, 200 words at the most. Abstract needs to hold all essential facts of the work-purpose of work, used methods (with specific data, if possible) and basic facts. Abstract must have review of underlined data, ideas and conclusions from text. Abstract has no quoted references. For key words, at the most, need to be placed below the text.

Central part of the article

Authentic papers contain these parts: introduction, goal, methods, results, discussion and conclusion. Introduction is brief and clear review of a problem. Methods are shown so that interested reader is able to repeat described research. Known methods don't need to be identified, it is cited (referenced). Results need to be shown clearly and logically, and their significance proven by statistical analysis. In discussion, results are interpreted and compared to existing, previously published findings in the same field. Conclusions have to give an answer to author's goal.

References

Quoting references must be in a scale in which they are really used. Quoting most recent literature is recommended. Only published articles (or articles accepted for publishing) can be used as references. Not-published observations and personal notifications need to be in text in brackets. Showing references is as how they appear in text. References cited in tables or pictures are also numbered according to quoting order. Citing paper with six or less authors must have cited names of all authors; if seven or more authors wrote the paper, the name of the first three authors are cited with a note "et al". If the author is unknown, at the beginning of papers reference, the article is named as "unknown". Titles of the publications are abbreviated in accordance to Index Medicus, but if not listed in the index, whole title of the journal has to be written.

Footnote-comments, explanations, etc., cannot be used in the paper.

Statistical analysis

Tests used for statistical analysis need to be shown in text and in tables or pictures containing statistical analysis.

Tables and pictures

Tables have to be numbered and shown by their order, so they can be understood without having to read the paper. Every column needs to have title, every measuring unit (SI) has to be clearly marked, preferably in footnotes below the table, in Arabian numbers or symbols. Pictures also have to be numbered as they appear in text. Drawings need to be enclosed on a white paper or tracing paper, while black and white photo have to be printed on a radiant paper. Legends next to pictures and photos have to be written on a separate A4 format paper. All illustrations (pictures, drawings, diagrams) have to be original and on their backs contain illustration number, first author last name, abbreviated title of the paper and picture top. It is appreciated if author marks the place for table or picture. Preferable the pictures format is TIF, quality 300 DPI.

Use of abbreviations

Use of abbreviations has to be reduced to minimum. Conventional units can be used without their definitions.