



Acta Medica Academica

Journal of Department of Medical Sciences
of Academy of Sciences and Arts of Bosnia and Herzegovina



ISSN 1840-1848 (Print)

Volume 48 Number 3 December 2019

ISSN 1840-2879 (Online)

Online First www.ama.ba



Clinical Science

-
- | | | |
|-----|--|---|
| 255 | Occlusal Stress Distribution on the Mandibular First Premolar – FEM Analysis | Amra Ahmić Vuković, Selma Jakupović, Selma Zukić, Anita Bajzman, Alma Gavranović Glamoč, Sadeta Šečić |
| 262 | Qualitative Evaluation of the Bracket-Adhesive-Enamel Junction of Metal Orthodontic Brackets: A Preliminary Report | Fouad Salama, Malak Aldosari, Hessa Alrejaye, Mohammad Aldosari |
| 271 | Effects of Treating an Overactive Urinary Bladder in Patients with Multiple Sclerosis | Maida Zonić-Imamović, Semir Imamović, Amela Čičkušić, Azra Delalić, Renata Hodžić, Mirza Imamović |
-

Public Health

-
- | | | |
|-----|--|--|
| 278 | The Effects of a Workplace Health Promotion Program to Decrease Cadmium Exposure Levels in Nickel-Cadmium Battery Workers | Miroslava Sovičová, Hana Tomášková, Lenka Carbolová, Anna Šplíchalová, Tibor Baška, Henrieta Hudečková |
| 286 | Neuroenhancing Substances Use, Exam Anxiety and Academic Performance in Bosnian-Herzegovinian First-Year University Students | Jasna Kusturica, Ajša Hajdarević, Haris Nikšić, Amira Skopljak, Zana Tafi, Aida Kulo |
-

Stomatology

-
- | | | |
|-----|---|--|
| 294 | Maternal Dental Health Knowledge and Its Relation to the Dental Caries Experience of Their Children in Mamyzawa Camp of Refugees in Erbil, Iraq | Bushra Rashid Noaman, Rebwar Fadil Khalid, Lezan Dawood Fattah |
|-----|---|--|
-

Case Presentation

-
- | | | |
|-----|---|--|
| 303 | Degloving Injury of the Lower Extremity: Report of Two Cases | Alexandros Kyriakidis, Ioannis Katsaros, Evangelos Vafias, Loukas Agorgianitis, Vladimiro Kyriakidis, Athanasios Zacharopoulos |
| 307 | An Unusual Bilateral Duplication of the Suprascapular Vein and Its Relation to the Superior Transverse Scapular Ligament Revealed by <i>Anatomage Table</i> | Eleni Panagouli, Alexandra Tsirigoti, Georgia Kotsira, Theano Demesticha, Panagiotis Skandalakis, Theodore Troupis, Dimitrios Filippou |
| 312 | Eccentric Macular Hole Formation Following Successful Macular Hole Surgery | Jasmin Zvorničanin, Edita Zvorničanin, Damir Husić |
-

Historical Article

-
- | | | |
|-----|--|--|
| 317 | Teodora Krajewska, Official Female Doctor of Tuzla and Sarajevo: Medical Practitioner, Woman of Science, Polish Patriot and Feminist | Brigitte Fuchs, Husref Tahirović |
| 329 | To Save a Corpse from Decomposition – the Purpose of Petrification in the Second Half of the 19 th Century | Marta Licata, Chiara Rossetti, Chiara Tesi, Omar Larentis, Roberta Fusco, Rosagemma Ciliberti |
| 333 | Carl Ferdinand von Arlt, Ritter von Bergschmidt (1812-1887): A Pioneer in Ophthalmology | Konstantinos Laios, Antonis Charalampakis, Evangellos Mavrommatis, Konstantinos Manes, Efstathia Lagiou, Pavlos Lytsikas – Sarlis, Marilita M. Moschos |
-

Letter to the Editor

-
- | | | |
|-----|---|---------------------|
| 337 | Dr. Anna Bayerova: Female Pioneer of Medicine in Bosnia and Herzegovina | Omer Č. Ibrahimagić |
|-----|---|---------------------|
-

AIMS AND SCOPE

Acta Medica Academica is a triannual, peer-reviewed journal that publishes: (1) reports of original research, (2) original clinical observations accompanied by analysis and discussion, (3) analysis of philosophical, ethical, or social aspects of the health profession or biomedical sciences, (4) critical reviews, (5) statistical compilations, (6) descriptions of evaluation of methods or procedures, (7) case reports, and (8) images in clinical medicine. The fields covered include basic biomedical research, clinical and laboratory medicine, veterinary medicine, clinical research, epidemiology, pharmacology, public health, oral health, and medical information.

COPYRIGHT

© 2019 Department of Medical Sciences, Academy of Sciences and Arts of Bosnia and Herzegovina, Sarajevo, Bosnia and Herzegovina. All rights reserved. The full text of articles published in this journal can be used free of charge for personal and educational purposes while respecting authors and publishers' copyrights. For commercial purposes no part of this journal may be reproduced without the written permission of the publisher.

EDITORIAL CONTACT INFORMATION

Address of the Editorial Board: *Acta Medica Academica*, Academy of Sciences and Arts of Bosnia and Herzegovina, Bistrik 7, 71000 Sarajevo, Bosnia and Herzegovina, Tel.: 00 387 33 560 718, Fax.: 00 387 33 560 703. Contact person: Nerma Tanović, E-mail: amabih@anubih.ba

SUBSCRIPTION

Acta Medica Academica is published triannually. The annual subscription fee is € 50 outside of Bosnia and Herzegovina.

PUBLISHER CONTACT INFORMATION

Academy of Sciences and Arts of Bosnia and Herzegovina, Sarajevo, Bosnia and Herzegovina. Contact person: Husref Tahirović, E-mail: husref.tahirovic@untz.ba

COVER PHOTO PICTURE

Teodora Krajewska (1854-1935; one of the first female doctors in Bosnia and Herzegovina) by unknown author, created on 1 January 1896.

AUTHOR INFORMATION

Instructions to authors can be found at <http://www.ama.ba/forms/AMA-2019-instrukcija.pdf>. Home page of the Journal www.ama.ba offers free access to all articles.

EDITORIAL ASSISTANT

Nerma Tanović, Sarajevo, BA.

TECHNICAL EDITOR

Husref Tahirović, Tuzla, BA.

DTP

Narcis Pozderac, Sarajevo, BA.

PRINT

Dobra knjiga, Sarajevo, BA. Printed on acid-free paper.

CIRCULATION

500 copies.

EDITOR-IN-CHIEF

Husref Tahirović, Tuzla, BA

ADVISORY BOARD

Muhidin Hamamdžić, Sarajevo, BA
Mirsada Hukić, Sarajevo, BA
Lidija Lincender-Cvijetić, Sarajevo, BA
Slobodan Loga, Sarajevo, BA
Senka Mesihović-Dinarević, Sarajevo, BA
Ljerka Ostojić, Mostar, BA
Berislav Topić, Sarajevo, BA
Enver Zerem, Tuzla, BA

EDITORIAL BOARD

Adnan Čustović, Manchester, GB
Emir Festić, Jacksonville, US
Farrokh Habibzadeh, Shiraz, IR
Gordan Srkalović, Lansing, US

ASSOCIATE EDITORS FOR STATISTICS

Mojca Čížek Sajko, Maribor, SI
Zdenko Sonicki, Zagreb, HR
Dubravka Matanić, Zagreb, HR
Maja Popović, Turin, IT
Ervin Sejdic, PhD, D
Emir Veledar, Miami, US

EDITORIAL COUNCIL

Roberto Copetti, Latisana, IT
Zijad Duraković, Zagreb, HR
Suad Efendić, Stockholm, SE
Ognjen Gajić, Rochester, US
Amina Godinjak, Sarajevo, BA
Nedim Hadžić, London, GB
Faruk Hadžiselimović, Liestal, CH
Bojan Joksimović, Foča, BA
Eldin E. Karaiković, Evanston, US
Nina Marković, Sarajevo, BA
Muzafer Mujić, Sarajevo, BA
Livia Puljak, Split, HR
Ario Santini, Târgu Mures, RO
Norman Sartorius, Geneva, CH
Mihra Taljanović, Tucson, US
Ivana Tica Sedlar, Mostar, BA
Miloš Trifković, Sarajevo, BA
Semir Vranic, Doha, QA

ENGLISH LANGUAGE REVISION

Janet Tuškan, Zagreb, HR

THE JOURNAL IS INDEXED IN

Medline/PubMed; EBSCOhost; Index Copernicus; CAB Abstract/Global Health Databases; IndexScholar.com; DOAJ; CrossRef; InfoBase Index.

Print and electronic issues of AMA are covered in Scopus and Embase through Medline.

Occlusal Stress Distribution on the Mandibular First Premolar – FEM Analysis

Amra Ahmić Vuković¹, Selma Jakupović², Selma Zukić¹, Anita Bajzman¹,
Alma Gavranović Glamoč³, Sadeta Šečić⁴

¹Department of Dental Morphology with Dental Anthropology and Forensics, Faculty of Dentistry, University of Sarajevo, ²Department of Restorative Dentistry and Endodontics, Faculty of Dentistry, University of Sarajevo, ³Department of Prostodontics, Faculty of Dentistry, University of Sarajevo, ⁴Department of Oral Surgery, Faculty of Dentistry, University of Sarajevo

Correspondence:

avukovic@sf.unsa.ba
Tel.: + 387 33 442 083
Fax.: + 387 33 443 395

Received: 26 March 2019; Accepted: 17 November 2019

Abstract

Objective. The aim of this paper was to analyze the distribution of stress and deformation on the mandibular first premolar under two types of loading (axial and para-axial load of 200 N) using the FEM computer method. **Materials and Method.** For this research a μ CT scan of the first mandibular premolar was used, and the method used in this research was FEM analysis under two types of loading. **Results.** The values of the von Mises stress measured in the cervical part of an intact tooth under axial load were up to 12 MPa, and under paraaxial load over 50 MPa. The values of the stress measured on the bottom of the non-carious lesion are very high \approx 240 Mpa. Stress values in the cervical part of the intact tooth are higher in the zone of the sub-surface enamel. The deformation values of the tooth under para-axial loading were \approx 10 times higher than the value of the deformation under axial load. The greatest deformations were seen in the area of the tooth crown. **Conclusions.** Occlusal loading leads to significant stress in the cervical part of

teeth. The values of the measured stress are greater under the action of paraxial load. The values of stress in abfraction lesions measured under a paraxial load are extremely high. Exposing the lesion to further stress will lead to its deepening. The total deformation of the entire tooth under paraxial load was \approx 10 times higher compared to the deformation value of the tooth under axial load.

Key Words: Mandibular first premolar ■ Morphology ■ Abfraction ■ FEM ■ Stress ■ Deformation.

Introduction

Morphological Characteristics of the Mandibular First Premolar

The mandibular first premolar is a specific tooth in form and function. It could be considered as a transitional form between the lower canine and the mandibular second premolar because it has some characteristics of both. Although it has the morphological characteristics of the posterior teeth, the lower first premolar has a masticatory function similar to the canine (1). Due to the lingual inclination of its crown, its occlusal surface does not lie perpendicular to the long axis of the root (2). The mandibular first premolar has a large buccal cusp with the tip located near the center of the occlusal surface, and it is only an occluding cusp. The contact of the buccal cusp during articula-

tion and/or occlusion with an antagonist tooth is not on its very tip, but rather on the buccal surface of the buccal cusp. Having in mind the prominent crown inclination of the first mandibular premolar and its specific contact area, it is easy to pose the question on their contribution to the mechanism of the distribution of occlusal forces. The durability of teeth depends on occlusal forces and the distribution of those loads.

The mandibular first premolar is the tooth with the highest prevalence of non-carious cervical lesions, as determined in previous studies. (3-6). A specific clinical phenomenon called abfraction is related to the distribution of stress along the tooth. An abfraction lesion is a type of non-carious cervical lesion (NCCL) in the form of the microstructural loss of dental tissue, due to the action of biomechanical occlusal forces in the area of the highest stress concentration - the cervical region. This loss of hard dental tissue in the cervical part of the tooth was termed abfraction by Grippo (7) in 1991, precisely to make a distinct from lesions caused by erosion and abrasion. The incidence and severity of non-carious cervical lesions increase with the age of the patient (8, 3). The presence of non-carious cervical lesions of different morphologies influences the biomechanics of the cervical tooth region. A three-dimensional finite element analysis (FEM) proved to be a good experimental model in research to help understand the complex biomechanics of different tooth regions in other teeth (9). The aim of this paper was to evaluate the influence of different occlusal loads on the mandibular first premolar in the process of the formation of cervical lesions. FEM analysis enables an understanding of the complex process of development and progression of NCCL, considering the specific morphology of mandibular first premolars.

Material and Methods

A mandibular first premolar was scanned by micro computed tomography (μ CT) scanner (SkyScan 1076 Kontich, Belgium). A volumetric 3D CAD tooth model was created using program packages MATLAB (MathWorks, Inc., Natick, USA) and Creo Parametric 1.0 CAD software. On one tooth model a wedge-shaped abfraction lesion, a-V lesion, was modeled. The models were exported to the finite element analysis software ANSYS Workbench (14.0) and a finite element mesh of the models was made by dividing the tooth into a large, but finite, number of smaller structural triangle elements, connected by nodal points. The properties of the tooth material, Young's modulus and Poisson's ratio were used for all tooth tissues. The model was fixed to allow displacement under load by $300\mu\text{m}$, equal to the average thickness of the periodontal ligament. The presence of contact points with adjacent teeth was also simulated. Axial and para-axial loads of 200 N were simulated on the models. To record the complex stress measured in (MPa), von Mises stress (VMS) was used.

A detailed description of the methodology of the study was given in our paper published in *Eur J Dent* 2016; 10: 413-8. Biomechanics of the cervical tooth region and non-carious cervical lesions of different morphologies; a three-dimensional finite element analysis / Published by Wolters Kluwer – Medknow (9).

Results

Stress distribution, as well as the type of deformation, differs in intact first mandibular premolars compared to those with non-carious cervical lesions, and depends on the type of loading (axial or paraxial). A paraxial load of 200 N causes almost five times higher stress in the cervical part of an intact

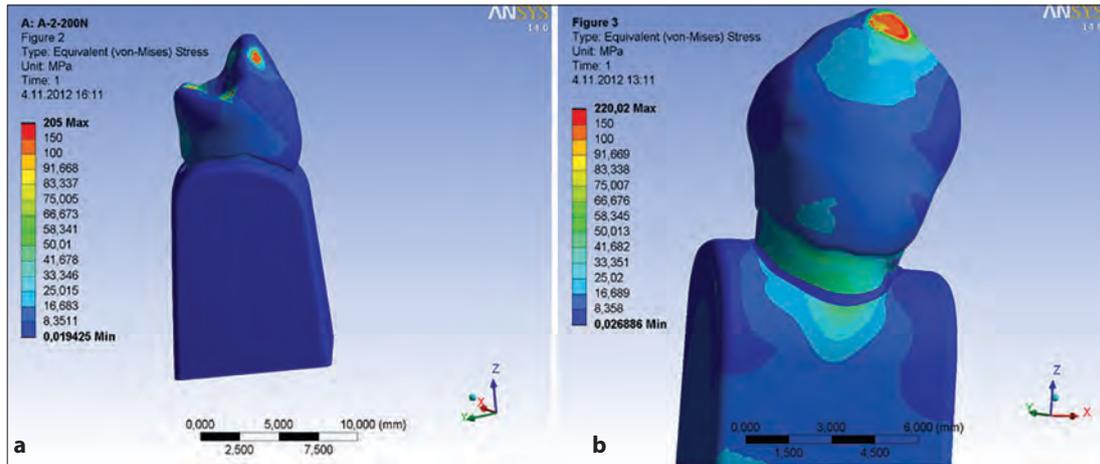


Figure 1. Stress distribution in a mandibular first premolar under axial (a) and paraxial loads (b) of 200 N. The values of von Mises stress measured in the cervical part of the intact tooth under axial load rise up to 12 MPa, while the stress in the same area of the tooth is almost 5 times higher under the action of paraxial forces, and is over 50 MPa.

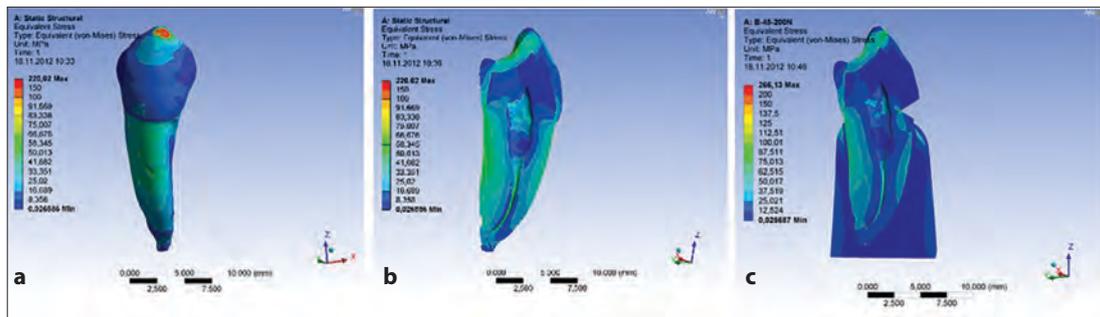


Figure 2. Stress distribution in a mandibular first premolar without lesions (a and b), and with an existing lesion (c) under a 200 N paraxial load. The values of the stress measured inside the tooth model with an abfraction lesion are higher within all dental tissues compared to the intact tooth.

first mandibular premolar compared to an axial load of the same intensity (Figure 1). On a tooth with a cervical lesion, the stress caused by a paraxial load inside all dental tissues becomes even higher (Figure 2). The stress measured on the non-carious cervical lesion is the highest at its bottom (≈ 240 MPa). Although significantly lower stress is presented in an intact tooth, it becomes higher in the zone of the sub-surface cervical enamel, suggesting that the initial fracture of the enamel could occur in these layers (Figure 3).

A paraxial load also causes tensile stress (+) on the buccal side of the intact tooth and compressive stress (-) on the oral side (Figure 4). The values of the deformation of the tooth under para-axial loading were ≈ 10 times higher than the deformation of the tooth under axial load. The greatest deformations were seen in the area of the tooth crown (Figure 5). Different types of loading cause different types of deformation in a tooth with a cervical lesion. When paraxial load occurs on the tooth with a cervical lesion the deformation is greater (0.176 mm)

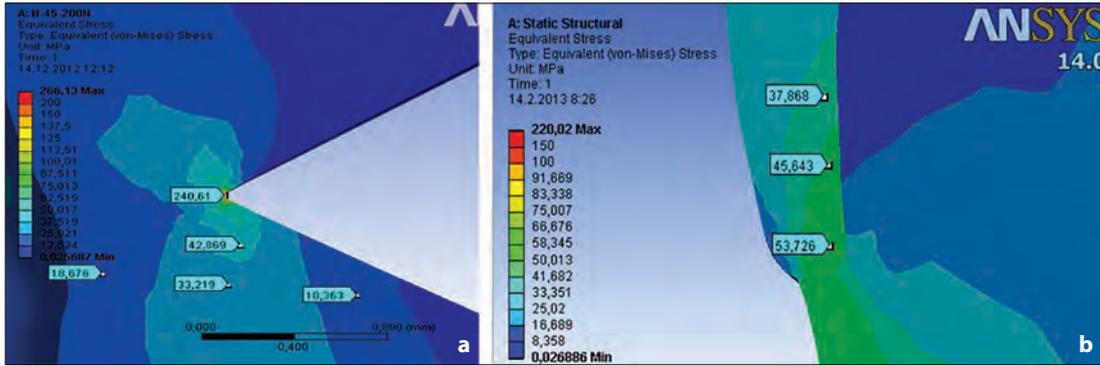


Figure 3. Stress distribution on the sagittal section of a tooth with a lesion (a) and a tooth without a lesion (b) under a paraxial load of 200 N. The values of the stress measured at the bottom of the non-carious lesion are very high (≈ 240 MPa). It was noted that the stress values in the cervical part of the intact tooth are higher in the zone of the sub-surface enamel, suggesting that the initial fracture of the enamel could occur in these layers.

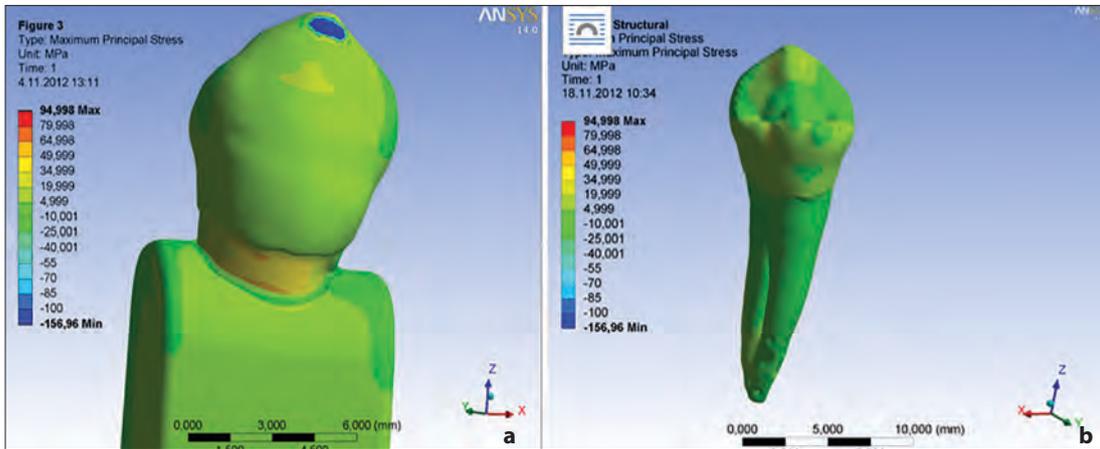


Figure 4. Distribution of principal stresses (Maximum Principal Stress) on the intact tooth. Under paraxial load, tensile stress (+) is present on the buccal side of the tooth (a) and compressive stress (-) on the oral side (b).

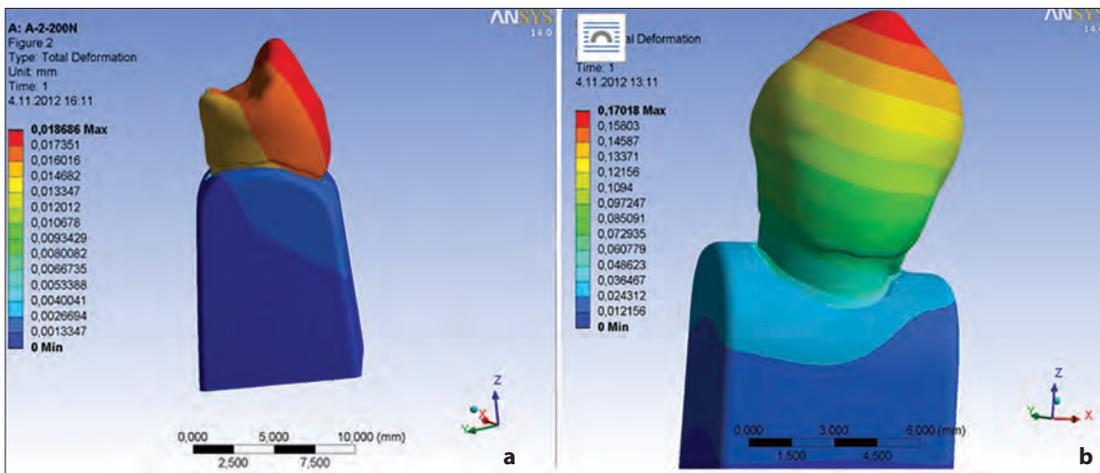


Figure 5. Distribution of deformation under axial (a) and para-axial loads (b) of 200 N.

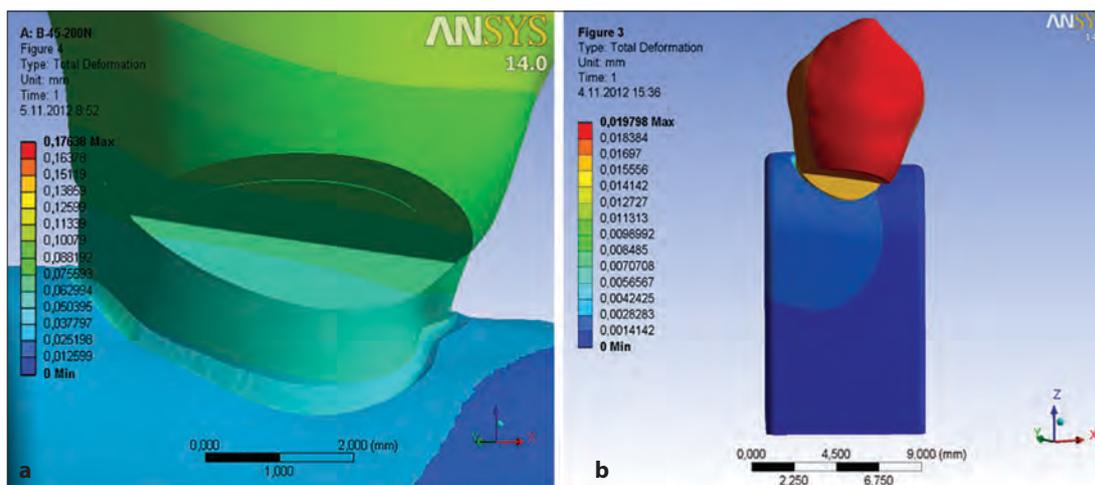


Figure 6. Type of deformation under a paraxial and axial load of 200 N on the tooth with a lesion. The highest values of deformation of the teeth were seen on the model with a cervical lesion, under an axial load at 0.019 mm, paraxial load at 0.176 mm.

compared to cases when an axial load occurs (0.019 mm) (Figure 6).

Discussion

The highest stress on the intact tooth model under both types of load was observed in the occlusal contact regions, under an axial load of 205 MPa, and a paraxial load of 220.02 MPa (Figures 1 and 2a and b). The activity of the occlusal load led to significant stress in the cervical region of the teeth. The von Mises stress measured in the cervical part of the tooth under axial load was up to 12 MPa, while in the same part of the tooth under paraxial load the stress measured was more than 50 MPa. Similar findings were presented by Rees (10), De las Casasa (11), Tanaka (12) and Kuroa (13).

It is known that the dental structures, especially the enamel, have significantly greater compressive strength than tensile, and are much more sensitive to tensile straining than compressive (14). Our findings showed that the buccal surface of the tooth is exposed to the more unfavorable type of stress – tensile stress. In the study by Rees (15), Yaman (16) and Borčić (17) the values

of Maximum Principal Stress on the buccal side of the tooth range from 60-90 MPa, and are similar to our findings, where the Maximum Principal Stress noted on the buccal side of the tooth (tensile stress) was 94.998 MPa (Figure 4).

By analyzing the mechanisms of the formation of abfraction lesions, Rees and Hammadeh (18) developed a theory about the possible undermining of the enamel due to the concentration of force on the enamel-dentin border. Our analysis confirms the observations of these authors that the stress in the cervical part of the teeth is greater in the sub-surface than in the surface zone of the enamel, which is clearly visible on the images of the sagittal section of the tooth (Figure 3b).

If we compare models with a cervical lesion and the intact tooth model, we can see different types of stress distribution. The breakdown of the enamel and dentine continuity on the model with a lesion caused increased stress, with a concentration of stress around the apex/bottom of the lesion. The values of stress were higher in all dental tissues compared to the intact tooth, while the stress values under paraxial loading at the

bottom of the lesion were very high, measuring 266.13 MPa (Figure 3a). The results of this analysis show that the bottom of the cervical lesions concentrates stress under loading, and further exposure of the lesion to stress will lead to the lesion's progression.

The type of deformation of the tooth model depended on the type of load. The deformation values of the tooth under paraxial loading were ≈ 10 times greater than the deformation value of the tooth under axial load (Figures 5 and 6). The maximum values of tooth deformation were seen in the tooth model with a cervical lesion (Figure 6). The most prominent deformations were seen in the area of the tooth crown, especially on the occlusal surface and the tip of the buccal cusp. The deformation values decreased as they approached the apical area (Figure 5b).

Axial load caused the greatest deformation on the buccal surface of the tooth. The deformation decreased moving towards the lingual side (Figure 5a). This finding of tooth deformation, even in the central occlusion, indicates that the morphology, as well as the occlusion, of the mandibular first premolar is specific and often leads to an unfavorable distribution of stress, which could be the reason for the frequent finding of noncarious cervical lesions on these teeth. Various types of FEM models with NCCL of different depth and/or different shape could give more information on progression of NCCL.

Conclusions

The greatest influence on the intensity of stress in dental tissues comes from the type of load on the teeth. The values of the measured stress are greater under the action of a paraxial load. Occlusal loading leads to significant stress in the cervical part of the teeth, although this region is not directly exposed to the effect of mastication forces. The values of stress in an abfraction lesion measured under a paraxial load are extremely

high. Lesions with expressed geometric discontinuity (V lesions) lead to the concentration of high stresses at the bottom of the tooth. Exposing the lesion to further stress will lead to its deepening. The total deformation of the entire tooth under paraxial load was ≈ 10 times higher than the deformation of the tooth under axial load. The pattern of the deformation of the teeth differs depending on the type of load. The greatest deformation under load was measured on the tooth model with an existing abfraction lesion. Although FEM analysis gives realistic simulation and stress measurements, biological variations of tooth morphology, different types of intercuspitation and habitual occlusion are factors that limit this type of analysis. Also, the acting occlusal force in this research is assumed as static, while in reality there is always dynamic force, with a relatively large number of repetitions.

What Is Already Known on this Topic:

Noncarious cervical lesions (NCCL) are more often found on the mandibular first premolars compared to other types of teeth. FEM analysis has proved to be a useful method for experimental research on mechanical forces in human tissues.

What this Study Adds:

Numerous studies by means of FEM analysis have mainly focused on the biomechanics of bone tissue. This study contributes to understanding the connection between the specific morphology of the mandibular first premolar and the action of axial and paraxial forces on the development and progression of NNC lesions.

Authors' Contributions: Conception and design: AAV and SJ; Acquisition, analysis and interpretation of data: AAV, SJ, SZ; Drafting the article: AAV, SJ, SZ; Revising it critically for important intellectual content: AB, AGG and SŠ. Approved final version of the manuscript: AAV, SJ, SZ.

Acknowledgement: Authors would like to thank Prof. Alen Topčić and Prof. Edin Cerjaković from the University of Tuzla, for their help and scientific remarks during the production of the FEM analysis model.

Conflict of Interest: The authors declare that they have no conflict of interest.

References

1. Vuković A, Zukić S, Bajsman A, Selmanagić A. Basics of teeth morphology and dental anthropology [in Bosnian]. 1st ed. Sarajevo: Faculty of Dentistry University of Sarajevo; 2013.
2. Ash MM. Wheeler's Dental anatomy, Physiology and Occlusion. 7th ed. Philadelphia: W.B. Saunders Company; 1993.
3. Jakupović S, Vuković A, Korać S, Tahmišćija I, Bajsman A. The prevalence, distribution and expression of noncarious cervical lesions (NCCL) in permanent dentition. *Mat Soc Med.* 2010;22(4):200-4.
4. Aw C, Lepe X, Johnson GH, Mancl L. Characteristics of noncarious cervical lesions, A clinical investigation. *JADA.* 2002;133(6):725-33.
5. Khan F, Young WG, Shahabi S, Daley TJ. Dental cervical lesions associated with occlusal erosion and attrition. *Australian Dent J.* 1999;44(3):176-86.
6. Borčić J, Anić I, Urek MM, Ferreri S. The prevalence of non-cariou cervical lesions in permanent dentition. *J Oral Rehabil.* 2004;31(2):117-23.
7. Grippo JO. Abfraction: a new classification of hard tissue lesions of teeth. *J Esthet Dent.* 1991 Jan-Feb;3(1):14-9.
8. Palamara J E A, Palamara D, Messer HH, Tyas M J. Tooth morphology and characteristics of noncarious cervical lesions. *J Dent.* 2006;34(3):185-94.
9. Jakupović S, Anić I, Ajanović M, Korać S, Konjhodžić A, Džanković A, et al. Biomechanics of cervical tooth region and noncarious cervical lesions of different morphology; three-dimensional finite element analysis. *Eur J Dent* 2016;10(3):413-8.
10. Rees JS. The effect of variation in occlusal loading on the development of abfraction lesions: a finite element study. *J Oral Rehabil.* 2002;29(2):188-93.
11. De Las Casas EB, Cornacchia TP, Gouvêa PH, Cimini CA Jr. Abfraction and anisotropy--effects of prism orientation on stress distribution. *Comput Methods Biomech Biomed Engin.* 2003 Feb;6(1):65-73.
12. Tanaka M, Naito T, Yokota M, Kohno M. Finite element analysis of the possible mechanism of cervical lesion formation by occlusal force. *J Oral Rehabil.* 2003;30(1):60-7.
13. Kuroe T, Itoh H, Caputo A A, Konuma M. Biomechanics of cervical tooth structure lesions and their restoration. *Quint Int.* 2000;31(4):267-74.
14. Geramy A, Sherafoddin F. Abfraction: 3d analysis by means of the finite element method. *Quint Int.* 2003;34(7):526-33.
15. Rees J S, Hammadeh M, Jagger D C. Abfraction lesion formation in maxillary incisors, canines and premolars: A finite element study. *Eur J Oral Sci.* 2003;111(2):149-54.
16. Yaman S. D, Sahin M, Aydin C. Finite element analysis of strength characteristics of variou resin base restorative materials in Class V cavities. *J Oral Rehabil.* 2003;30(6):630-41.
17. Borčić J, Anić I, Smojver I, Čatić A, Miletić I, Ribarić S.P. 3D finite element model and cervical lesion formation in normal occlusion and in malocclusion. *J Oral Rehabil.* 2005;32(7):504-10.
18. Rees JS, Hammadeh M. Undermining of enamel as a mechanisam of abfraction lesion formation: a finite element study. *Eur J Oral Sci.* 2004;112(4): 347-52.

Qualitative Evaluation of the Bracket-Adhesive-Enamel Junction of Metal Orthodontic Brackets: A Preliminary Report

Fouad Salama¹, Malak Aldosari², Hessa Alrejaye³, Mohammad Aldosari¹

¹Department of Pediatric Dentistry, School of Dentistry, University of Detroit Mercy, USA, Former Professor Department of Pediatric Dentistry and Orthodontics, College of Dentistry, King Saud University, Riyadh, Saudi Arabia, ²Saudi Board Orthodontic Resident, King Saud University, Saudi Arabia, ³Orthodontic Resident, Boston University Henry M. Goldman School of Dental Medicine, Massachusetts, US, ⁴Department of Pediatric Dentistry and Orthodontics, College of Dentistry, King Saud University, Riyadh, Saudi Arabia

Correspondence:

salamafs@udmercy.edu
Tel.: + 313 494 6877
Fax: + 313 494 6781

Received: 29 December 2018; Accepted: 30 July 2019

Abstract

Objectives. The purpose of this *in vitro* investigation was to evaluate qualitatively the surface topography at the bracket-adhesive-enamel junction, bonded to the buccal and lingual surfaces of premolars with composite resin and resin-modified glass-ionomer orthodontic adhesives, using two methods of adhesive removal: a dental explorer and a micro brush. **Methods.** Forty premolar surfaces were allocated to four groups of 10/each, 20/buccal and 20/lingual surfaces. The brackets were bonded to the surface of the enamel and any extra adhesive was removed with a dental explorer or a micro brush. Specimens were evaluated and scored by two calibrated independent raters, at the bracket-adhesive-enamel junction, for adhesive overlap on the bracket, the smoothness of the surface, as well as the presence of projections and depressions, using a digital microscope. The Fisher-exact statistical test was conducted to compare the different groups. **Results.** Regardless of the method used to remove the adhe-

sives, all groups showed partial or complete overlap of the adhesive on the bracket. No statistical difference was found between the groups for adhesive overlap ($P=1.0$). However, resin-modified glass-ionomer was found to be statistically significantly ($P<0.05$) better than composite resin in both smoothness and the lack of projections or depressions, regardless of the instrument of removal. **Conclusion.** Removing excess adhesive with a dental explorer or a micro brush is not an ideal method for adhesive removal, as partial or complete overlap of the adhesive on the bracket existed in all groups. On the other hand, resin-modified glass-ionomer was a superior material to composite resin for better smoothness and surface topography at the bracket-adhesive-enamel junction.

Key Words: Orthodontic Brackets ▪ Surface Topography ▪ Surface Characteristics ▪ Orthodontic Adhesive.

Introduction

Some of the features of ideal orthodontic adhesives are: sufficient working time for the dentist, fluoride release, good bonding, and easy removal without damaging the enamel surface, with minimal polishing needed (1-3). Another ideal feature that has not been tested before is the easy removal of the adhesive from the areas around the enamel and orthodontic bracket, after bonding and before setting, anticipating a smooth surface. Composite resin is the most commonly used adhesive because of its well-established clinical and laboratory performance (4, 5). On the other hand, resin-modified glass-iono-

mer cements have some advantages, which include its ability to form a chemical bond with the enamel and metal, less sensitivity to moisture and saliva contamination, fluoride release, and the ability to serve as a fluoride reservoir (6, 7).

White spot lesions due to decalcification of the enamel surface adjacent to fixed orthodontic appliances are a frequent undesirable consequence of orthodontic treatment (8, 9). Several studies have reported the prevalence of white spot lesions to be as high as 96 percent (10-13). Fixed appliances and bonding materials increase the retention of biofilm and the development of white spot lesions (8, 9). Management of white spot lesions on the enamel surface comprises a variety of approaches to prevent demineralization, and procedures to promote remineralization of any demineralization present (8, 14). A wide variety of methods has been described and implemented for the prevention of such lesions, implemented by the patient and/or the dentist (8, 9, 14). However, not all methods to prevent white spot lesions are successful (15).

The application of adhesives to enamel and orthodontic brackets could be a source of irregular and rough surfaces at the bracket-adhesive-enamel junction after adhesive removal, and could create areas for plaque accumulation, with the resultant demineralization (11, 16, 17). The surface roughness of various metal and esthetic brackets, as well as various orthodontic wires, has been tested. However, to our knowledge no published research has evaluated the surface topography and roughness of the areas around the enamel and the orthodontic bracket after bonding and adhesive removal.

Therefore, the aim of this study was to assess qualitatively the surface topography at the bracket-adhesive-enamel junction using a digital microscope, after bonding to the buccal and lingual surfaces of premolars, using two orthodontic adhesives: composite

resin (Transbond XT, 3M Unitek, Monrovia, California, USA) and resin-modified glass-ionomer (Fuji Ortho LC, GC Corporation, Tokyo, Japan), and two adhesive removal methods, using a dental explorer and a micro brush. The null hypothesis tested in this study was that there is no difference in the surface topography at the bracket-adhesive-enamel junction after removal of the two orthodontic adhesives using a dental explorer or a micro brush.

Materials and Methods

Preparation of Specimens

The study protocol was approved by the Research and Ethical Committee of Human Studies at the College of Dentistry Research Center. Twenty human premolar teeth extracted due to orthodontic treatment, stored in 0.1% thymol solution, were used in this investigation. The teeth included had an intact crown, no attrition, and were free from hypoplastic areas, cracks, gross irregularities, decay and fractures. The enamel surface of each tooth was scaled and polished with a rubber polishing cup and pumice using a low-speed handpiece for 10 seconds, then stored in deionized water at room temperature (27°C) for 48 hours. The apical part of each root was mounted in self-curing acrylic resin (Vertex™ Orthoplast, Vertex-Dental B.V. Asia Pte Ltd, Singapore) to facilitate perpendicular sectioning of each tooth into two sections (buccal and lingual), and then each section was decoronated 4 mm below the CEJ using a diamond saw mounted under a water spray (IsoMet-2000 Precision Saw, Buehler, Lake Bluff, IL, USA). Each section/surface was then placed in a standardized mold and embedded in self-curing acrylic resin, where the buccal and lingual surfaces of each tooth were kept parallel to the floor. The teeth were allocated into four groups, with 10 specimens/group, according to the

adhesive material and removal methods used, with 20 buccal and 20 lingual surfaces (Table 1). Due to the difficulty of collecting teeth and the limited number, the lingual and buccal surfaces of each tooth were used to increase the sample size. The power sample size was 0.81 and the level of significant $\sigma=0.05$, with estimated standard deviation $=0.9$. The sample size should be at least 9 in each group.

Bracket Bonding and Evaluation

Orthodontic premolar brackets with gingival offset (Ortho Classic, Roth 0.022, Ortho Classic Inc., McMinnville, OR, USA) were positioned using firm and even pressure, and bonded to the enamel surface, following the manufacturer's recommendations, using 2 types of orthodontic adhesive: composite resin (3M-Unitek *Transbond™ XT* Light Cure Adhesive, Monrovia, CA, USA) for groups 1 and 2, and resin-modified glass-ionomer (GC Fuji Ortho LC Capsule, GC Corporation, Tokyo, Japan) for groups 3 and 4. The brackets were then bonded onto the mesio-distal and occluso-cervical center of the tooth surfaces. Excess adhesive was removed in 5 applications using a regular size micro applicator brush #2 (Dental Micro Applicator Brush, Shanghai Smedent Medical Instrument Co., Ltd., Shanghai, China) or a dental explorer (Double Ended #5, Hu-Friedy Mfg. Co., LLC, Chicago, USA). One micro brush was used for each specimen and was wiped with gauze after each application. In addition, the explorer was also wiped with gauze after each application. The specimens were light cured using an Ortholux™ Luminous Curing Light (3M Unitek Orthodontic Products, Monrovia, CA, USA) (App. 1600 mW/cm) (LED). One investigator performed all the bonding procedures in a consistent manner and random order. The specimens were stored in distilled water at room temperature for 48 hours. Each speci-

men was then photographed using a digital microscope (Digital Microscope System Model KH 7700, Hirox; USA, Inc., Hackensack, NJ, USA) at fifty times magnification. One photograph, which included the bracket and the surrounding enamel, was taken. Before the evaluation started, the two expert evaluators discussed the evaluation scores and they were calibrated. The two independent examiners did not know the group under evaluation. Each photograph was evaluated and the bracket-adhesive-enamel junction scored at the occlusal edge/side of the bracket. The following parameters were assessed: the adhesive overlap of the bracket, the smoothness of the enamel, and the presence of projections and depressions. The adhesive overlap of the bracket was allocated to one of three classifications: no overlap, where no adhesive was covering any part of the occlusal edge/side of the bracket; partial overlap, where there was adhesive covering any part less than the entire length of the occlusal edge/side of the bracket; and complete overlap, where the adhesive covered the entire length of the occlusal edge/side of the bracket. The smoothness of the enamel was given one of three possible classifications: completely smooth enamel - when no rough area of adhesive was present over the entire length of the occlusal edge/side of the bracket; partially smooth enamel - when some rough areas of adhesive were present but less than the entire length of the occlusal edge/side of the bracket; and no smooth enamel - when a rough area of adhesive was present along the entire length of the occlusal edge/side of the bracket. The presence of projections and depressions on the adhesive was given one of four possible classifications: no projections and depressions, projections present, depressions present, and both projections and depressions present. For all parameters, when disagreement was recorded between the two examiners, the highest score was recorded.

Statistical Analysis

Comparison of different groups and identifying statistically significant differences were performed using the Fisher's exact test. The statistical significance was set at a p -value of <0.05 . Inter-examiner reliability for scoring different parameters at the bracket-adhesive-enamel junction was completed using the Kappa statistic. All procedures were performed using Stata SE15.1 software (StataCorp, College Station, TX, USA).

Results

Inter-examiner reliability for scoring different parameters showed that the Kappa statistic was 0.74, which indicated high agreement. Regardless of the adhesive removal method used, all groups showed partial or complete overlap of the adhesive on the bracket (Table 1).

Groups in which a composite resin was used on the buccal surfaces showed complete overlap of the adhesive in 90% of the

surfaces when the dental explorer was used, and 100% of the surfaces when the micro brush was used (Table 1). Groups in which a resin-modified glass-ionomer was used on the lingual surfaces showed complete overlap of the adhesive on the bracket in 100% of the surfaces when an explorer was used, and 90% of the surfaces when a micro brush was used to remove the excess material (Table 1). The Fisher-exact statistical test showed no significant difference between the groups for complete/partial overlap of the adhesive on the bracket on the buccal or lingual surfaces ($P=1.0$).

A completely rough surface of adhesive on the enamel was found for the composite resin when the dental explorer (10%) or micro brush (30%) were used, while none was found for the resin-modified glass-ionomer (Table 1). A partially rough surface of adhesive on the enamel was found for the composite resin when the dental explorer (90%) or micro brush (70%) were used, while for the resin-modified glass-ionomer 50% of rough surface was recorded when the dental

Table 1. Frequency of the Three Outcomes between the Removal Methods and Adhesive Materials

Outcomes	Groups					
	Dental Explorer (n=20)			Micro brush (n=20)		
	CR (N=10)	RMGI (N=10)	P value	CR (N=10)	RMGI (N=10)	P value
Overlap of the adhesive over the bracket (N=40)						
No overlap	0	0		0	0	
Partial overlap	1	0	1.0	0	1	1.0
Complete overlap	9	10		10	9	
Smoothness of the adhesive on the enamel (N=40)						
Completely smooth	0	5		0	5	
Partially smooth	9	5	0.033*	7	5	0.016*
Completely rough	1	0		3	0	
Presence of projections and depressions on the adhesives (N=40)						
None present	0	9		0	6	
Projections	3	0	<0.001*	1	0	0.001*
Depressions	0	1		0	2	
Both present	7	0		9	2	

CR=Composite Resin; RMGI=Resin-Modified Glass Ionomer; P-value of 2-sided Fisher's exact test; *Significant at $P<0.05$.

explorer or and 40% when micro brush were used (Table 1). Resin-modified glass-ionomer was statistically significantly better for a completely smooth adhesive surface on the enamel compared to resin composite, when using the dental explorer (50%; $P=0.033$) or the micro brush (50%; $P=0.016$).

Composite resin adhesive displayed both projections and depressions in 70% of the specimens when dental explorer was used, and 90% when a micro brush was used to clean the adhesive residues. On the other hand, resin-modified glass-ionomer presented superior topography, where only 10% of specimens had depressions when the explorer was used ($P<0.001$), and 40% ($P=0.001$) had some form of surface topography when using a micro brush (Table 1).

Discussion

The null hypothesis tested in this study was rejected, as there was a difference in the surface topography at the bracket-adhesive-enamel junction after the removal of two orthodontic adhesives, using a dental explorer or a micro brush. In the present study, regardless of the method used to remove the adhesives on the buccal or lingual surfaces, no group prevented overlap of the adhesive on the bracket and all groups showed partial or complete overlap of the adhesive. The measures reported for prevention of white spot lesions have rarely considered the use of orthodontic adhesives and their possible overlap on the brackets as a potential source of formation of irregular and rough surfaces at the bracket-adhesive-enamel junction after adhesive removal (14). The forces of adhesion of cariogenic bacteria to the enamel, the adhesive and the stainless steel bracket were found to be lowest on the enamel and highest on the adhesive (18, 19). Morphological changes in the topography of the enamel, especially roughness, are of considerable clinical importance for the formation

of white spot lesions (20). One study reported that, even with relatively uniform surface roughness, surface free energy was significantly different between resin composite and resin-modified glass-ionomer adhesives, which affects the adhesion of *Streptococcus mutans* (21). Resin-modified glass-ionomers showed significantly higher surface free energy than composite resin (21).

In the present study, there was a significant difference between the groups in the distribution of the smoothness of the adhesive on the enamel surface, and a rough surface was found on the composite resin when a dental explorer or a micro brush was used, while none was found on the resin-modified glass-ionomer. In contrast, more completely smooth adhesive was found using the resin-modified glass-ionomer when a dental explorer or a micro brush was used, and none was found for the composite resin. Again, these results indicate that the application of adhesives for bonding orthodontic brackets to the enamel could be a source of irregular and rough surfaces at the bracket-adhesive-enamel junction after adhesive removal. This may restrict cleansing activity and increase the risk of white spot formation (14). This scenario is supported by a study which reported the lower occurrence of white spot caries lesions in patients who used orthodontic lingual appliances, due to their self-cleansing activity (22).

A rough surface provides opportunities for bacterial adhesion by increasing the surface area and providing suitable niches (23, 24). Differences in surface roughness were reported, with the greater surface roughness of different materials used for brackets than orthodontic adhesives, which was attributed to minor dissimilarities in the surface roughness ($<0.5\mu\text{m}$) of different materials (24). However, another study showed that minor variations in surface roughness had no significant effect on the contact angles for surface free energy, or on the adhe-

sion of bacteria (23, 25). The adherence of *Streptococcus mutans* to a fixed appliance is largely the result of the bracket material, where titanium brackets had the least number of *Streptococcus mutans* and the greatest number of *Candida albicans* (26). The variations in the adhesion of *Streptococcus mutans* between brackets have been attributed to the surface free energy and tension (26). It has been shown that stainless steel had more surface tension, which is demonstrated by the more likely attachment of microorganisms on metallic brackets compared with ceramic brackets (26, 27). Accordingly, substrates/materials with high surface free energy will attract more microorganisms to their surfaces than those with less surface free energy (26). In the present study, there was a significant difference between the groups in terms of the presence of projections and depressions on the adhesive, and both projections and depressions were present in the adhesive in composite resin specimens when a dental explorer or a micro brush was used, while fewer projections and depressions were found in the resin-modified glass-ionomer when a micro brush was used, and no projections and depressions were found when a dental explorer was used. The differences in the distribution of diverse surface irregularities shown in this study may be due to the dissimilar characteristics and composition of each adhesive and orthodontic material surface. This is supported by the studies reporting the influence of surface roughness on the adhesion of bacteria to the surfaces (11, 16, 17). In addition, it has been suggested that the type of filler modifies the surface of orthodontic composite resin (28). However, another study reported that the filler size, volume and composition of different composite resins have no effect on the adhesion of microorganisms (29). It has been reported that glass ionomer and resin composites have a tendency to collect more plaque or microor-

ganisms than different restorative materials *in vivo* and *in vitro* (30). The adhesion of microorganisms to the orthodontic composite resin is attributed to van der Waals forces, as well as hydrophobic and electrostatic factors, and *Streptococcus mutans* adhesion to composite resin is greater than to orthodontic appliances (31). In the present study, excess adhesive was removed from around the brackets during the bonding process to simulate clinical practice. Another study compared the effects on bonding strength of removing excess adhesive from around the bracket base both immediately after placing the bracket on the tooth and after subjecting the adhesive to 5 seconds of light curing to initially secure the bracket in its proper position, and concluded that removing excess adhesive after 5 seconds of light cure significantly decreased the bond strength at 24 hours (19). It has been reported that the adhesive properties influence the consistency of the bond, the ease of debonding and the ease of cleaning the enamel (32).

The design of this study had multiple dimensions, which included the effects of the tooth surface, adhesive type, and the adhesive removal method. Due to the difficulty of collecting teeth, we used the lingual and buccal surfaces of each tooth to increase the sample size. We also used the buccal surfaces for composite resin, and the lingual surfaces for resin-modified glass-ionomer orthodontic adhesives. This is supported by a study, which reported no significant differences in shear bond strength between the buccal and lingual surfaces of premolars, and resin-modified glass-ionomer and composite resin adhesives exhibited sufficient shear bond strength for orthodontic use, with no significant difference between the two adhesives (33).

Limitations of the Study

The present study has some limitations, such as the use of only two orthodontic

adhesives. It would be beneficial to compare more orthodontic adhesives. We also only evaluated the occlusal edge/side of the bracket, which may be easier to clean compared to other edges/sides. In addition, aging of specimens by thermocycling, to imitate the conditions of the oral cavity, was not performed. It would be useful to expose the specimens to thermocycling and saliva to simulate the oral environment. In addition, use of a brush versus a micro brush, and finishing of the adhesives, were not tested in this study. Further research is needed for evaluation of the different methods used to improve the smoothness of the surface at the bracket-adhesive-enamel junction so that it is less attractive to biofilm. In addition, future investigations are necessary to analyze different parameters of the surfaces, such as surface roughness, and the composition of each material on microbial adhesion.

Conclusion

Within the limits of this *in vitro* study, it was concluded that removing excess adhesive with a dental explorer or a micro brush is not an ideal method for adhesive removal, as partial or complete overlap of the adhesive on the bracket existed in all groups. Resin-modified glass-ionomer was a superior material over composite resin for better smoothness and surface topography at the bracket-adhesive-enamel junction. There was a difference in the surface topography at the bracket-adhesive-enamel junction between the methods used in this study. There was a significant difference between the groups in terms of distribution of the smoothness of the adhesives, as well as the presence of projections and depressions on the adhesives.

What Is Already Known on this Topic:

The application of adhesives to enamel and orthodontic brackets could be a source of irregular and rough surfaces at the

bracket-adhesive-enamel junction after adhesive removal, and could create areas for plaque accumulation, with the resultant demineralization. The surface roughness of various metal and esthetic brackets, as well as different orthodontic wires, have been tested. However, to our knowledge no published research has evaluated the surface topography and roughness of the areas around the enamel and the orthodontic bracket after bonding and adhesive removal.

What this Study Adds:

The manuscript provides evidence-based research to support what orthodontists practice every day. As no published research has previously evaluated the surface topography of the areas around the enamel and the orthodontic bracket after bonding, and adhesive removal using different adhesive removal methods, this study aimed to assess qualitatively the surface topography at the bracket-adhesive-enamel junction after bonding using two orthodontic adhesives and the use of two adhesive removal methods.

Acknowledgement: We would like to thank the College of Dentistry Research Center and the Deanship of Scientific Research at King Saud University, Saudi Arabia, for supporting this research. The authors wish to express sincere thanks to Mr. Nassr Al Maflehi for his valuable help in the statistical analysis.

Authors' Contributions: Conception and design: FS; Acquisition, analysis and interpretation of data: FS, MA, and HA; Drafting the article: FS, MA, HA, and MA; Revising it critically for important intellectual content: FS, MA, HA, and MA; Approved final version of the manuscript: FS, MA, HA, and MA.

Conflict of Interest: The authors declare that they have no conflict of interest.

References

1. Pithon MM, Oliveira MV, Ruellas AC, Bolognese AM, Romano FL. Shear bond strength of orthodontic brackets to enamel under different surface treatment conditions. *J Appl Oral Sci.* 2007;15(2):127-30.
2. Shinya M, Shinya A, Lassila LV, Gomi H, Varrel J, Vallittu PK, et al. Treated enamel surface patterns associated with five orthodontic adhesive systems--surface morphology and shear bond strength. *Dent Mater J.* 2008;27(1):1-6.
3. Chicri RO, Sasaki RT, Carvalho AS, Nouer PR, Lima-Arsati YB. Effect of enamel pretreatment on shear bond strength of brackets bonded with resin-modified glass-ionomer cement. *World J Orthod.* 2010;11(1):11-5.

4. Romano FL, Correr AB, Sobrinho LC, Borges de Araújo Magnani MB, Vieira de Siqueira VC. Shear bond strength of metallic brackets bonded with a new orthodontic composite. *Braz J Oral Sci.* 2009;8(2):76-80.
5. Finnema KJ, Ozcan M, Post WJ, Ren Y, Dijkstra PU. In-vitro orthodontic bond strength testing: a systematic review and meta-analysis. *Am J Orthod Dentofacial Orthop.* 2010;137(5):615-22.e3.
6. Coonar AK, Jones SP, Pearson GJ. An ex vivo investigation into the fluoride release and absorption profiles of three orthodontic adhesives. *Eur J Orthod.* 2001;23(4):417-24.
7. Hamed MM, Tawfek ZS, Younis MT. Shear bond strength of resin modified glass ionomer cement using different enamel conditions. *Al-Rafidain Dent J.* 2010;10(1):127-32.
8. Sudjalim TR, Woods MG, Manton DJ. Prevention of white spot lesions in orthodontic practice: a contemporary review. *Aust Dent J.* 2006;51(4):284-9; quiz 347.
9. Heymann GC, Grauer D. A contemporary review of white spot lesions in orthodontics. *J Esthet Restor Dent.* 2013;25(2):85-95.
10. Mizrahi E. Enamel demineralization following orthodontic treatment. *Am J Orthod.* 1982;82(1):62-7.
11. Gorelick L, Geiger AM, Gwinnett AJ. Incidence of white spot formation after bonding and banding. *Am J Orthod.* 1982;81(2):93-8.
12. Ogaard B, Rølla G, Arends J, ten Cate JM. Orthodontic appliances and enamel demineralization. Part 2. Prevention and treatment of lesions. *Am J Orthod Dentofacial Orthop.* 1988;94(2):123-8.
13. Mitchell L. Decalcification during orthodontic treatment with fixed appliances--an overview. *Br J Orthod.* 1992;19(3):199-205.
14. Morrier JJ. White spot lesions and orthodontic treatment. Prevention and treatment [in French]. *Orthod Fr.* 2014;85(3):235-44.
15. Chen H, Liu X, Dai J, Jiang Z, Guo T, Ding Y. Effect of remineralizing agents on white spot lesions after orthodontic treatment: a systematic review. *Am J Orthod Dentofacial Orthop.* 2013;143(3):376-82.e3.
16. Ogaard B. Prevalence of white spot lesions in 19-year-olds: a study on untreated and orthodontically treated persons 5 years after treatment. *Am J Orthod Dentofacial Orthop.* 1989;96(5):423-7.
17. Rosenbloom RG, Tinanoff N. Salivary Streptococcus mutans levels in patients before, during, and after orthodontic treatment. *Am J Orthod Dentofacial Orthop.* 1991;100(1):35-7.
18. Mei L, Busscher HJ, van der Mei HC, Chen Y, de Vries J, Ren Y. Oral bacterial adhesion forces to biomaterial surfaces constituting the bracket-adhesive-enamel junction in orthodontic treatment. *Eur J Oral Sci.* 2009;117(4):419-26.
19. Bishara SE, VonWald L, Olsen ME, Laffoon JF. Comparisons of two approaches for removing excess adhesive during the bonding procedure. *Angle Orthod.* 2000;70(2):149-53.
20. Ferreira FG, Nouer DF, Silva NP, Garbui IU, Correr-Sobrinho L, Nouer PR. Qualitative and quantitative evaluation of human dental enamel after bracket debonding: a noncontact three-dimensional optical profilometry analysis. *Clin Oral Investig.* 2014;18(7):1853-64.
21. Ahn SJ, Lim BS, Lee SJ. Surface characteristics of orthodontic adhesives and effects on streptococcal adhesion. *Am J Orthod Dentofacial Orthop.* 2010;137(4):489-95; discussion 13A.
22. van der Veen MH, Attin R, Schwestka-Polly R, Wiechmann D. Caries outcomes after orthodontic treatment with fixed appliances: do lingual brackets make a difference? *Eur J Oral Sci.* 2010;118(3):298-303.
23. Brusca MI, Chara O, Sterin-Borda L, Rosa AC. Influence of different orthodontic brackets on adherence of microorganisms in vitro. *Angle Orthod.* 2007;77(2):331-6.
24. Lee SP, Lee SJ, Lim BS, Ahn SJ. Surface characteristics of orthodontic materials and their effects on adhesion of mutans streptococci. *Angle Orthod.* 2009;79(2):353-60.
25. Bollen CM, Papaioanno W, Van Eldere J, Schepers E, Quirynen M, van Steenberghe D. The influence of abutment surface roughness on plaque accumulation and peri-implant mucositis. *Clin Oral Implants Res.* 1996;7(3):201-11.
26. Rammohan SN, Juvvadi SR, Gandikota CS, Challa P, Manne R, Mathur A. Adherence of Streptococcus mutans and Candida albicans to different bracket materials. *J Pharm Bioallied Sci.* 2012;4(Suppl 2):S212-6.
27. Eliades T, Eliades G, Brantley WA. Microbial attachment on orthodontic appliances: I. Wettability and early pellicle formation on bracket materials. *Am J Orthod Dentofacial Orthop.* 1995;108(4):351-60.
28. Ahn SJ, Lim BS, Yang HC, Chang YI. Quantitative analysis of the adhesion of cariogenic streptococci to orthodontic metal brackets. *Angle Orthod.* 2005;75(4):666-71.
29. Saku S, Kotake H, Scougall-Vilchis RJ, Ohashi S, Hotta M, Horiuchi S, et al. Antibacterial activity

- of composite resin with glass-ionomer filler particles. *Dent Mater J.* 2010;29(2):193-8.
30. Derks A, Katsaros C, Frencken JE, van't Hof MA, Kuijpers-Jagtman AM. Caries-inhibiting effect of preventive measures during orthodontic treatment with fixed appliances. A systematic review. *Caries Res.* 2004;38(5):413-20.
 31. Velazquez-Enriquez U, Scougall-Vilchis RJ, Contreras-Bulnes R, Flores-Estrada J, Uematsu S, Yamaguchi R. Adhesion of Streptococci to various orthodontic composite resins. *Aust Dent J.* 2013;58(1):101-5.
 32. Clark SA, Gordon PH, McCabe JF. An ex vivo investigation to compare orthodontic bonding using a 4-META-based adhesive or a composite adhesive to acid-etched and sandblasted enamel. *J Orthod.* 2003;30(1):51-8; discussion 23.
 33. Salama F, Aldosari M, Alrejae H, Almosa N. Shear bond strength of orthodontic bracket bonded to buccal versus lingual surfaces. *IOSR J Dent Med Sci (IOSR-JDMS).* 2018;17(1):24-9.

Effects of Treating an Overactive Urinary Bladder in Patients with Multiple Sclerosis

Maida Zonić-Imamović¹, Semir Imamović², Amela Čičkušić¹, Azra Delalić¹,
Renata Hodžić³, Mirza Imamović⁴

¹Clinic for Physical Medicine and Rehabilitation, University Clinical Center Tuzla, Bosnia and Herzegovina, ²Clinic of Anesthesiology and Resuscitation, University Clinical Center Tuzla, Bosnia and Herzegovina, ³Clinic of Neurology, University Clinical Center Tuzla, Bosnia and Herzegovina, ⁴Medical Faculty, University of Tuzla, Bosnia and Herzegovina

Correspondence:
maidazo@yahoo.com
Tel.: + 387 61 728 728
Fax.: + 387 35 303 148

Received: 6 October 2019; Accepted: 27 December 2019

Abstract

Objective. The purpose of this study was to evaluate the efficiency of the anticholinergic therapy with oxybutynin and the effects of daily transcutaneous tibial nerve stimulation (TTNS) on the quality of life of patients with an overactive bladder (OAB) and multiple sclerosis (MS). **Patients and Methods.** The study was designed as a randomized controlled trial. The patients who suffer from MS underwent urodynamic tests which showed that they had an OAB. The tests used to assess symptoms and quality of life were Overactive Bladder Questionnaires (OAB-q) SF. Patients were divided into 2 groups of 30 patients each. The first group received a 5 mg oxybutynin tablet twice a day for 3 months and the second group had TTNS every day for 3 months. **Results.** The anticholinergic therapy showed a statistically significant improvement in all symptoms and quality of life ($P < 0.001$). Side effects such as dry mouth were observed in about 35% of patients. The results of the study TTNS daily therapy showed good performance in the reduction all clin-

ical symptoms of the bladder and improved quality of life, with statistical significance ($P < 0.05$) and with no side effects. It was found that the improved quality of life parameters and the reduced symptoms were more statistically significant in the treatment with oxybutynin tablets than TTNS therapy ($P < 0.001$). **Conclusion.** Our recommendation for the treatment of OAB is oxybutynin in doses of 2x5 mg. If a patient can not tolerate anticholinergic drugs, daily TTNS is recommended to reduce OAB symptoms and improve quality of life, without side effects.

Key Words: Overactive Bladder ■ Oxybutynin ■ TTNS.

Introduction

Difficulties in urination/micturition are frequent in patients with multiple sclerosis (MS), cause health problems and decrease the patients' quality of life (1). Up to 80% of newly diagnosed patients, as well as up to 96% of those who have suffered from MS for more than 10 years, have problems with urination (2). MS is a disease which mostly affects people between 20 and 40 years old at the time of diagnosis. It rarely affects people before the age of 15 and after 60 (3). Women are affected twice as often as men, but men have more severe symptoms. The most common voiding disturbance in patients with multiple sclerosis is a spastic bladder or overactive bladder (OAB) (4). An overactive bladder is defined as the occurrence of

bladder contractions suddenly, without the person having control over it. Overactive bladder syndrome is sometimes called an irritable bladder or detrusor instability (5).

The progression of neurological diseases results in the deterioration of overactive bladder symptoms. A correct diagnosis and treatment can improve the control of the bladder and the patients' quality of life (5). The International Continence Society (ICS) defines the overactive bladder syndrome as an urgency to urinate, with or without urge incontinence and an increased frequency of urination during the day and night (6). Medicines in the class of drugs called antimuscarinics (also called anticholinergics) may alleviate the symptoms of an overactive bladder. They act by blocking certain nerve impulses to the detrusor, which relaxes the detrusor thereby increasing bladder capacity. Different types of anticholinergics, with similar effects on the symptoms of an overactive bladder, are used. The side-effects of these are dependent on the dose given. The medication with certain side effects mentioned in the research was oxybutynin (7, 8). Oxybutynin chloride is a moderate anticholinergic and severe musculotropic drugs. It is one of the first drugs which has been used for more than 30 years in the treatment of OAB patients and, until recently, the only one available in our country. In our study we investigated the effects of oxybutynin chloride (Ditropan) in the 2x5mg doses, which is a half of the maximum daily dose. The most common side-effects are dry mouth, dry eyes, constipation, blurred vision and drowsiness.

In addition to anticholinergics, transcutaneous tibial nerve stimulation (TTNS) is also used in the treatment of OAB, using the TENS apparatus. TENS-Transcutaneous electrical nerve stimulation is a non-invasive exponential current (low-frequency current) method that efficiently suppresses the excessive activity of the urinary bladder. Nervus tibialis is a mixed nerve composed of motor

and sensory nerve fibers that originate from roots L4 to S3 and stimulate the innervation of the bladder, urinary sphincter and pelvic floor by stimulating the nociceptors of spinothalamic tract neurons and reducing or eliminating excessive activity (9).

The purpose of this study was to evaluate the efficiency of the anticholinergic therapy with 2x5mg doses of oxybutynin, and then the effects of daily transcutaneous tibial nerve stimulation (TTNS) on the quality of life of patients with an overactive bladder (OAB) and multiple sclerosis.

Patients and Methods

The study was a randomized controlled trial, that tested the efficacy of oxybutynin anticholinergic therapy and daily transcutaneous tibial nerve stimulation (TTNS) on the quality of life of patients with an overactive bladder (OAB) and multiple sclerosis (MS). Participants were enrolled consecutively as they were visiting the Urodynamics unit of the Physical Medicine and Rehabilitation Clinic, University Medical Center Tuzla for a period of 2 years.

The inclusion criteria were patients with MS who underwent urodynamic testing that showed an OAB with maximum bladder capacity of less than 300 ml. Each patient should have had a normal urine finding before the urodynamic testing. Exclusion criteria were symptoms lasting for less than 6 months, pregnancy, sacral peripheral nerve lesions, urinary tract infections, serious secondary illnesses and detrusor-sphincter dyssynergy-determined by a urodynamic investigation. Patients were divided into 2 groups of 30 patients each. The first group received a 5 mg oxybutynin tablet twice a day for 3 months and the second group had TTNS every day for 3 months.

Medio tens (Iskra Medical) devices were administered to stimulate the nervous tibials posterior and were administered to patients at

home daily. Current intensity, frequency, and pulse duration were set on each apparatus at a frequency of 10 HZ, constant stimulation with intervals of 200 microseconds and duration of stimulation of 30 min. The active self-adhesive electrode (A) was placed behind the internal malleolus and the other 10 cm above the right ankle. Patients were given detailed instructions, how the sensation should be, how to operate the device at home with the above parameters already set. All patients who received daily stimulation were given a device to use at home for a period of 3 months.

OAB-q SF is a specific questionnaire used to assess the frequency of hyperactive bladder symptoms and the quality of life of patients with urinary disorders and consists of 2 subscales. The symptom subscale contains 6 questions rated individually from 1 to 6 and quality of life subscale includes 13 questions rated from 1 to 6.

The symptoms which were monitored and affected the quality of life are: urgency (>than 3 to 24 h), daily voiding (frequency >8 in 24 h), nocturia and urgent incontinence. The OAB-q SF questionnaire for determining symptoms and quality of life was completed before therapy and 3 months after therapy.

Statistical Analysis

Statistical analyses were performed using MedCalc software (ver.12.1.4.0 for Windows; MedCalc, Mariakerke, Belgium). To test the differences between the groups in terms of quantitative variables, the paired t-test and Wilcoxon sum rank tests were done, depending on data distribution. $P < 0.05$ was considered significant.

Results

Sixty patients were examined. There were 33.3% men and 66.6% women. The subjects receiving the anticholinergic drug oxybutynin were on average 45.8 ± 8.13 years old with a disease duration of 8.3 ± 5.1 years,

and the subjects who had electrostimulation n. tibialis with TENS were on average 47.36 ± 7.98 years old with a disease duration of 8.9 ± 4.9 years. ($P > 0.05$).

The stimulation with TENS therapy has shown a statistically significant reduction in all clinical symptoms of the bladder and an improved quality of life. The symptom score before treatment with daily TTNS was 61.2 ± 14.6 and decreased after treatment to 50.8 ± 12.3 ($P = 0.004$). The quality of life score increased from 28.5 ± 12.6 after daily TTNS treatment to 38.3 ± 11.4 ($P = 0.003$) (Figura 1). The anticholinergic therapy with oxybutynin produced a statistically significant improvement in all symptoms and quality of life.

The symptom score before the oxybutynin treatment was 61.9 ± 6 and 32.4 ± 14.8 ($P < 0.001$) after treatment. The quality of life score before the oxybutynin treatment was 27.8 ± 13.7 and 56.1 ± 17.3 ($P < 0.001$) after treatment.

The therapy with oxybutynin tablets and stimulation with TENS therapy have shown a statistically significant reduction in all clinical symptoms of the bladder and an improvement in quality of life. After comparing the two types of treatment, it was concluded that there were no statistically significant improvements in the number of daily mictions in favor of the treatment with oxybutynin tablets ($P = 0.021$), and no statistically significant difference in the number of nocturnal, daytime and nocturnal incontinence groups ($P > 0.05$) (Table 1).

After comparing the quality of life and symptoms measured by the OAB-q SF questionnaire by treatment type, it was found that the improved quality of life parameters and the reduced symptoms were more statistically significant in the treatment with oxybutynin tablets than TTNS therapy ($P < 0.001$). The side effect of a dry mouth after oxybutynin therapy was found in 35% of patients, which did not require discontinu-

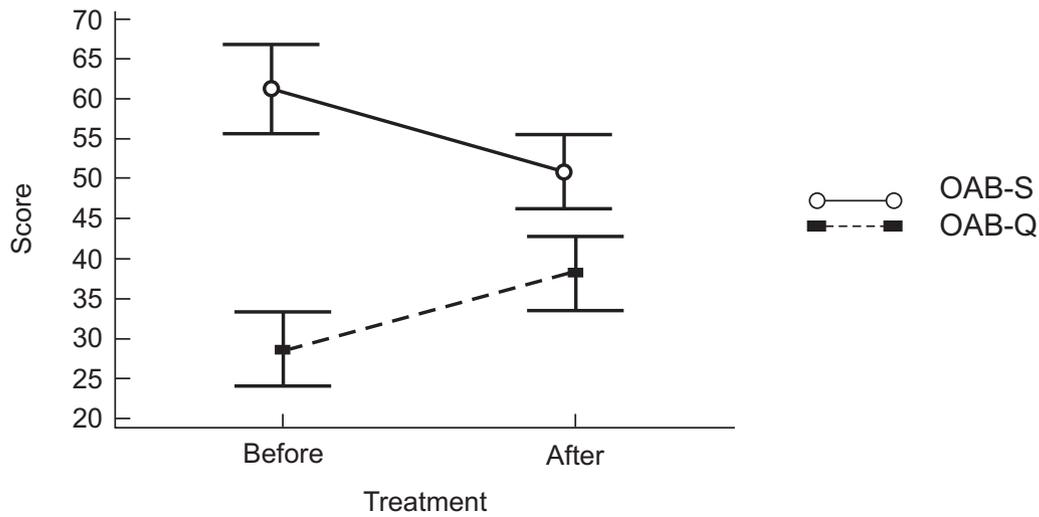


Figure 1. Symptom score and quality of life before and after the treatment with daily transcutaneous tibial nerve stimulation ($P < 0.05$); OAB-S=Overactive bladder symptoms, OAB-Q=Overactive bladder quality of life.

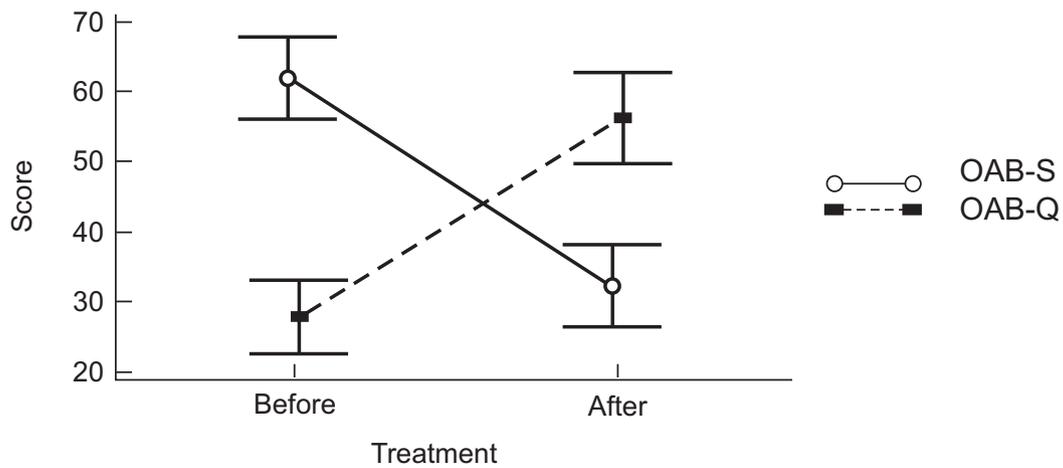


Figure 2. The symptom scores and quality of life before and after treatment with Oxybutynin ($P < 0.0001$); OAB-S=Overactive bladder symptoms, OAB-Q=Overactive bladder quality of life.

Table 1. The Comparison of Clinical Symptoms after the Oxybutynin Treatment and Daily Tibial Nerve Stimulation

Clinical symptoms	Treatment		P [†]
	Oxybutynin ($\bar{x} \pm SD$)	TTNS [*] ($\bar{x} \pm SD$)	
Daily micturition number	7.5±2.8	9.4±3.4	0.021
Night micturition number	2.2±1.6	2.3±1.4	0.729
Daily incontinence number	1.7±1.7	2.4±1.4	0.112
Night incontinence number	0.6±0.8	0.6±0.5	0.719
OAB-Q [‡]	56.1±17.2	38.3±11.4	<0.001
OAB-S [§]	32.4±14.8	50.8±12.3	<0.001

*Transcutaneous tibial nerve stimulation; †Paired t-test; OAB-S=Overactive bladder symptoms, OAB-Q=Overactive bladder quality of life.

ation of therapy. There were no side effects after the TTNS therapy.

Discussion

In our study, oxybutnin at a dose of 10 mg daily, divided into two doses, was shown to be a very effective drug in the treatment of an overactive bladder, where the parameters of the quality of life and the symptoms of overactive bladder were significantly improved. Alhasso et al., (10) searched papers related to the treatment of an overactive bladder with anticholinergics in MS using the Cochrane database. Thirteen surveys were reviewed with 1770 participants and all surveys were designed as parallel groups except one that was a cross-over study. The duration of treatment was 3 to 12 weeks, with one check 24 weeks after starting treatment. It was concluded that the use of anticholinergic drugs in the treatment of OAB produces good results. The results are better when using anticholinergics compared to bladder training, as well as the two modalities compared with each modality individually. There is insufficient data to show the effects of therapy after discontinuation of anticholinergics. Anticholinergics are known to have side effects, such as dry mouth. Side effects such as dry mouth have been reported in about 1/3 of patients using anticholinergic therapy. In our study, we found similar results with regard to the side effects where 35% of patients had a dry mouth but problems were not expressed and therapy was not interrupted.

Although the dose used in this study was half the maximum, it still achieved a significant improvement in all parameters measured by the urodynamic study. Similar results were shown by Rolf et al. (11) who have shown that flexible dosing of anticholinergics in the treatment of OAB is a useful strategy in clinical practice to achieve maximum effects with a maximum level of tolerance. A study was conducted with 1658

patients who used 15 mg trospium chloride (TID) or 2.5 mg oxybutynin 3 times a day, gradually increasing the dose. By the end of the study the dose was 90 mg TID and 15 mg oxybutynin daily. A decrease in incontinence episodes and frequency of urination was observed. Dry mouth was less pronounced in the TID group than the Oxybutynin group at 15 mg daily. The conclusion was that the incidence of incontinence and number of mictions could be significantly reduced by a flexible dose of the drug to prevent side effects such as dry mouth. In this study, TID was shown to be better tolerated than oxybutynin at a dose of 15 mg. Similar results were demonstrated by Yoo et al. (12) who tested the appropriate dose of oxybutynin in clinical practice. The study included 809 patients, of whom 590 received treatment for 12 weeks. They used a different dose of oxybutynin from 5 mg to 30 mg. Most patients received 5 or 10 mg oxybutynin daily. Symptom assessment was performed with POSQ and all symptoms improved. Similarly, drug dosing was done in a study by MacDiarmid et al. (13). The conclusion was that the dose should be flexible with the need to constantly monitor the effectiveness of the treatment and side effects.

Versi et al. (14) examined the occurrence of the side effect of dry mouth with the conventional administration of oxybutnin and slow release oxybutnin. They gradually increased the dose from 5 mg in both groups to a total of 20 mg daily. The incidence of dry mouth increased with increasing dose of oxybutnin in both groups. Thomas et al. (15) investigated the effect of various antimuscarinic (anticholinergic) drugs in OAB treatment by meta-analysis. A study of 69 studies concluded that antimuscarinic drugs used at the recommended doses, presented individually for each drug, had a similar effect, and it was emphasized that oxybutnin at a dose greater than 10 mg per day had more pronounced side effects than other drugs. A

similar study was conducted by Hay-Smith et al., (16) where they reviewed 49 studies in a meta-analysis to find out which anticholinergic drug should be used to treat OAB in adults. It was concluded that it is better to use lower doses as much as possible, which have an effect, to avoid side effects, which was also proven in our study. There was little or no available evidence of the quality of life, cost, or the long-term outcome in these studies.

As antihilonegic drugs have been used for the treatment of OAB for many years, it has become necessary to find new treatments that will improve bladder function with as few side effects as possible. Given the choice of a slightly invasive method (PTNS) or non-invasive one (TTNS), most studies are focused on using this treatment method (17). In our study, we monitored the effect of TTNS therapy in patients who had daily stimulation.

The results of the study with daily stimulation showed good efficacy in reducing all clinical symptoms of the bladder, especially the number of nocturnal incontinence, all of which had a positive effect on the quality of life. TTNS therapy also showed good tolerability. The effectiveness of the therapy was observed as early as the second week of treatment and did not change significantly over the 3 months of treatment duration.

The efficacy as well as tolerance of the therapy provides a great opportunity for patients, especially if they have other additional diseases or symptoms that would prevent them from using anticholinergics. This therapy gives them the ability to be treated without fear of side effects. Voorham et al., (18) demonstrated the acute effect of a single TTNS application in patients with OAB symptoms using urodynamic parameters. Out of the 40 patients, 20 only underwent the urodynamics test, and TTNS stimulation was performed on the other group of 20 patients during the urodynamics test with 1 electrode per n. tibialis and the other on the S2-S4 foramen for 20 min. The results

of the urodynamic parameters for the first group without stimulation were almost unchanged, and in the group after stimulation there was a statistically significant improvement ($P < 0.05$) in bladder capacity, volume of mycation and the first contraction of the detrusor. The study was performed as a diagnostic procedure rather than a treatment.

In France, a multicenter study was conducted in which 70 patients treated with the TTNS technique suffering from MS were monitored (19). Stimulation with TTNS lasted 3 months and the duration of therapy was 20 minutes per day. They used the Qualiveen questionnaire to assess the quality of life. After treatment, 83.3% of patients experienced a statistically significant improvement in clinical parameters and symptoms, as well as the quality of life.

Conclusion

Adequate diagnosis and treatment can improve bladder control for patients with symptoms of OAB. Our recommendation for the treatment of OAB is an anticholinergic (Oxybutynin) in doses of 2x5 mg as it produces good results for all parameters (symptoms) and quality of life. It is unfortunate that electrostimulation therapy which is non-invasive and has no side effects is used so rarely, and produces good results. If patients for any reason can not tolerate anticholinergic drugs, daily TTNS is recommended to reduce OAB symptoms and improve quality of life, without side effects.

What Is Already Known on this Topic:

There are a number of ways to treat OAB, and pharmacological treatment remains the most important in the management of patients with OAB symptoms. Anticholinergics reduce contractility and increase bladder capacity, and the difficulty in prescribing medications for OAB is due to a lack of drug selectivity leading to unwanted side effects. In addition to pharmacological therapy in the treatment of OAB, electrical tibial nerve stimulation is used, which is a non-invasive exponential current (low-frequency) method that suppresses excessive bladder activity.

What this Study Adds:

In this study, we confirmed the effect of pharmacological therapy in the treatment of OAB, but also the positive effects of under-utilized electrostimulation, which are non-invasive and have no side effects. The disadvantage of this study is the short-term follow-up of patients, and there are no studies on the duration of therapy.

Authors' Contributions: Conception and design: MZI, SI and MI; Acquisition, analysis and interpretation of data: MZI, AD, RH and AČ; Drafting the article: MZI, AČ and MI; Revising it critically for important intellectual content: MZI, AD, AČ and SI; Approved final version of the manuscript: MZI, SI, AČ, AD, RH and MI.

Conflict of Interest: The authors declare that they have no conflict of interest.

Reference

- Cianco SJ, Mutchnik SE, Rivera VM, Boone TB. Urodynamic pattern changes in multiplesclerosis. *Urology*. 2001;57(2):239-45.
- Foster H. Bladder symptoms and multiple sclerosis. *Mult Scler Quart Rep*. 2002;21(1):1-34.
- Wingerchuk DM, Lucchinetti CF, Noseworthy JH. Multiple sclerosis: current pathophysiological concept. *Lab Invest*. 2001;81(3):263-81.
- Akkoç Y, Ersöz M, Yüceyar N, Tunç H, Köklü K, Yoldaş TK, et al. Overactive bladder symptoms in patients with multiple sclerosis: Frequency, severity, diagnosis and treatment. Neurogenic Bladder Turkish Research Group. *J Spinal Cord Med*. 2016;39(2):229-33.
- Kalsi V, Fowler C. Therapy Insight: Bladder Dysfunction Associated With Multiple Sclerosis. *Nat Clin Pract Urol*. 2005;(10):492-501.
- Abrams P, Artibani W, Cardozo L, Dmochowski R, van Kerrebroeck P, Sand P. Terminology Report: The Ongoing Debate. *Neurourol Urodyn*. 2006;25:293.
- Zinner N, Tuttle J, Marks L. Efficacy and tolerability of darifenacin, a muscarinic M3 selective receptor antagonist (M3 SRA), compared with oxybutynin in the treatment of patients with overactive bladder. *World J Urol*. 2005;23(4):248-52.
- Chapple CR, Abrams P. Comparison of darifenacin and oxybutynin in patients with overactive bladder: assessment of ambulatory urodynamics and impact on salivary flow. *Eur Urol*. 2005;48(1):102-9.
- Vandoninck V, van Balken MR, Finazzi Agrò E, Petta F, Micali F, Heesakkers JP, et al. Percutaneous tibial nerve stimulation in the treatment of overactive bladder: urodynamic data. *Neurourol Urodyn*. 2003;22(3):227-32.
- Alhasso AA, McKinlay J, Patrick K, Stewart L. Anticholinergic drugs versus non-drug active therapies for overactive bladder syndrome in adults. *Cochrane Database of Systematic Reviews*, 2006;Issue 4. Art. No.: CD003193.
- Rolf-Hasso B, Helmut M, Claudia N, Michael Z. Dose escalation improves therapeutic outcome: post hoc analysis of data from a 12-week, multi-centre, double-blind, parallel-group trial of trospium chloride in patients with urinary urge incontinence. *BMC Urol*. 2010;10:15.
- Yoo D, Han J, Lee K, Choo M. Prescription pattern of oxybutynin ER in patients with overactive bladder in real life practice: a multicentre, open-label, prospective observational study. *Int J Clin Pract*. 2012;66(2):132-8.
- MacDiarmid SA, Anderson RU, Armstrong RB, Dmochowski RR. Efficacy and safety of extended release oxybutynin for the treatment of urge incontinence: an analysis of data from 3 flexible dosing studies. *J Urol*. 2005;174(4 Pt 1):1301-5.
- Versi E, Appell R, Mobley D, Patton W, Saltzstein D. Dry mouth with conventional and controlled-release oxybutynin in urinary incontinence. The Ditropan XL Study Group. *Obstet Gynecol*. 2000;95(5):718-21.
- Kessler TM, Bachmann LM, Minder C, Löhner D, Umbehre M, Schünemann HJ, et al. Adverse event assessment of antimuscarinics for treating overactive bladder: a network meta-analytic approach. *LoS POne*. 2011;23;6(2):e16718.
- Hay-Smith J, Herbison P, Ellis G, Morris A. Which anticholinergic drug for overactive bladder symptoms in adults. *Cochrane Database Syst Rev*. 2005;20;(3):CD005429. Review. Update in: *Cochrane Database Syst Rev*. 2012;1:CD005429.
- Kozma B, Majoros A, Pytel Á, Póka R, Takács P. Efficacy of the percutaneous tibial nerve stimulation in the treatment of lower urinary tract symptoms. *Orv Hetil*. 2018;159(43):1735-40.
- Voorham-van der Zalm P, Elzevier H, Guus AB, Nijeholt L, Pelger R. Simultaneous Sacral and Tibial Transcutaneous Electrical Nerve Stimulation: urodynamic evaluation *Current Urology*. 2007;1(2):77-80.
- De Seze M, Raibaut P, Gallien P, Even-Schneider A, Denys P, Bonniaud V, et al. Transcutaneous posterior tibial nerve stimulation for treatment of the overactive bladder syndrome in multiple sclerosis: results of a multicenter prospective study. *Neurourol Urodyn*. 2011;30(3):306-11.

The Effects of a Workplace Health Promotion Program to Decrease Cadmium Exposure Levels in Nickel-Cadmium Battery Workers

Miroslava Sovičová¹, Hana Tomášková^{2,3}, Lenka Carbolová⁴, Anna Šplíchalová³, Tibor Baška¹, Henrieta Hudečková¹

¹Department of Public Health, Comenius University in Bratislava, Jessenius Faculty of Medicine in Martin, Slovak Republic, ²Department of Epidemiology and Public Health, Faculty of Medicine, University of Ostrava, Czech Republic, ³Public Health Institute, Ostrava, Czech Republic, ⁴General Practitioner Surgery, Raškovice, Czech Republic

Correspondence:

duranova31@uniba.sk
Tel.: + 421 908 506 355
Fax.: + 421 432 633 300

Received: 6 May 2019; Accepted: 14 December 2019

Abstract

Objective. Cadmium exposure is a common problem in the production of nickel-cadmium batteries. However, keeping the respective legislative occupational and safety policies is essential, but there are problems with compliance. We analysed the effect of strategies to increase compliance with precautions during 2013-2015 on 59 workers at a nickel-cadmium battery factory. **Material and Methods.** A health promotion program was implemented in two phases. The first phase included comprehensive education on the importance of appropriate behaviour and changes to the sanitation program. The second phase included renovation of sanitary facilities and modernization of the air exhaust ventilation. **Results.** The initial median cadmium urinary level in workers was 1.9 µg/g creatinine. After the first phase of interventions, levels dropped to 1.0 µg/g creatinine. After the second phase no significant further decrease was observed. **Conclusion.** Comprehensive education and changes in the sanitation pro-

gram were able to halve cadmium levels and can be considered a useful and cost-effective preventive tool.

Key Words: Behaviour ■ Cadmium ■ Compliance ■ Education ■ Workplace.

Introduction

Cadmium is a toxic heavy metal, which occurs in the environment, but it is frequently used in many industrial sectors. For example, in the production of nickel-cadmium batteries, workers are significantly exposed to cadmium dust and fumes via inhalation, but incidental ingestion from contaminated hands, food and cigarettes cannot be neglected (1). Moreover, the metal has a long biological half-life and cannot be metabolized in the human organism. So cadmium exposure, even at low levels, can lead to a wide range of adverse health effects (2). Besides, there are some other factors, i.e. sex, age, dietary intake, iron status, smoking, and length of exposure or place of residence, which can influence the total body burden (3).

To prevent negative effects on workers' health, specific occupational health and safety policies are included in the respective legislation (4). The policies are mandatory for employers and include workplace educa-

tion and training, occupational air monitoring, and provision of adequate personal protective equipment. Despite the obligation to keep these preventive measures, there is sometimes a problem with poor compliance by employees (5). Workplace health promotion programs are quite common strategies for more precise risk reduction, using the most suitable interventions, i.e. improvement in personal hygiene or sanitation, and lead to behavioural changes (6-8).

The aim of this study was to evaluate the effects of a workplace health promotion program on exposure reduction in workers at a nickel-cadmium factory.

Materials and Methods

This study analyses changes in urinary cadmium (U-Cd) levels in professionally exposed workers, during a workplace health promotion program that took place from February 2013 to April 2015 in a nickel-cadmium factory in the Czech Republic. The factory is situated in the centre of a village (1777 inhabitants) and operates in three shifts. Although all the manufacturing processes are fully automated, the workers may be exposed to cadmium oxide via inhalation when handling the components of nickel-cadmium batteries. In the factory, all relevant instruments for occupational safety and health related to cadmium prescribed in the legislation have been implemented, i.e. cadmium air concentrations are below the permissible exposure limit, personal protective equipment is available, and all essential technical preventive measures prescribed by law have been put into practice. Despite this, retrospective analyses of U-Cd levels, conducted by an occupational physician, showed excessive levels and this was the reason for launching this extra preventive action.

The study started in February 2013 when the initial U-Cd exposure levels in workers were analysed during their periodic medi-

cal check-up. Subsequently, in March 2013, the first phase of the workplace health promotion program began. Firstly, the safety engineer, in partnership with the occupational physician, informed workers about the increased U-Cd levels found in February and their possible future health effects. The specific preventive measures in this phase included providing specific information on the importance of personal hygiene and stopping smoking. Wet mopping between the shifts was also added. Although the workers were educated about these preventive measures from the very beginning of their recruitment, most employees neglected them. Later in 2014, the second phase of the workplace health promotion program was introduced. The interventions in this phase consisted of bathroom renovation (more showers added) and a cloakroom divided into "clean" and "dirty" parts, to avoid cross-contamination. Moreover, in 2014-2015 the modernization of the air exhaust ventilation was carried out to eliminate cadmium dust. A detailed description of the preventive measures in the health promotion program is shown in Figure 1.

Further, information on the subjects' health history was obtained solely from medical records (in cooperation with the respective health provider). The health and safety manager from the factory provided detailed information on preventive measures.

The sample included 59 workers tested for cadmium; 36 women and 23 men, with an average age of 39.4 years. Among them, 18 workers were smokers and 12 workers lived in the same village where the factory is situated (Table 1). The workers had on average been working in the nickel-cadmium battery factory for 10 years.

Cadmium concentration is expressed as U-Cd levels. Samples were obtained from the workers at their annual preventive check-ups, in the occupational doctor's clinic. At the beginning of the study all the

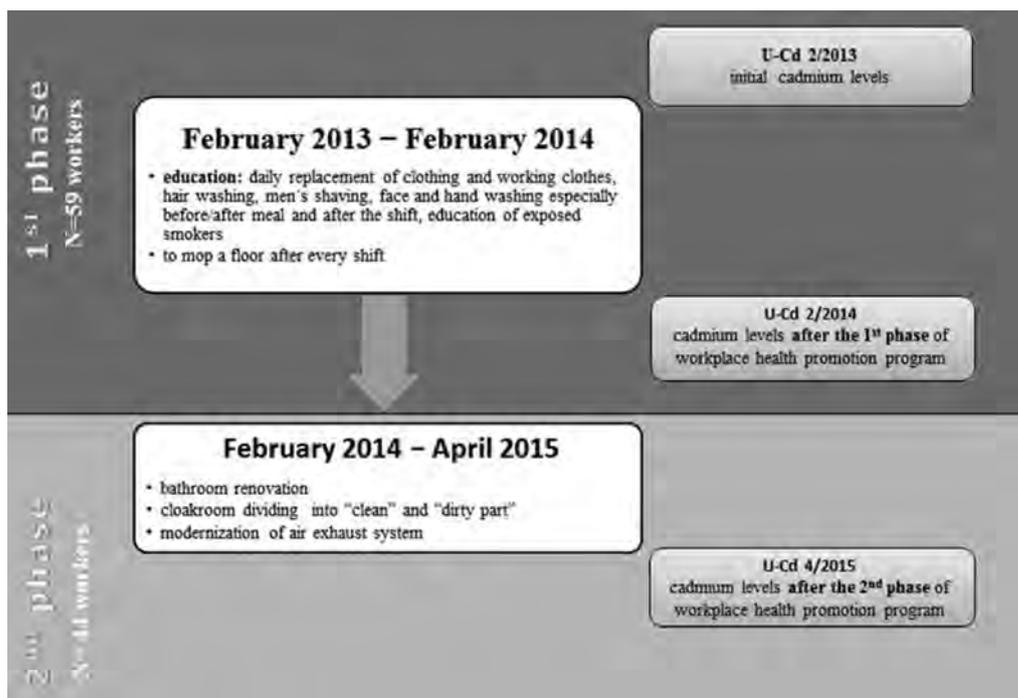


Figure 1. Scheme of Interventions Included in the Workplace Health Promotion Program and Laboratory Analyses Conducted.

Table 1. Characteristics of the Workers in the Nickel-Cadmium Factory

Variable	Females	Males
Sample size (%)	36 (61%)	23 (39%)
Smokers (%)	9(15%)	9(15%)
Residence in the village with the factory	7 (12%)	5 (8%)
Average age in years \pm SD (range)	41.5 \pm 11.1 (22–61)	36.2 \pm 11.7 (21–58)
Exposure duration in years \pm SD (range)	11.0 \pm 8.9 (1–34)	7.9 \pm 4.8 (2–17)

workers signed informed consent to confirm their participation in the study. For the laboratory cadmium testing, we collected morning urine samples. The urine samples were analysed by GT-AAS absorption atomic spectrometry with electro-thermal atomization (coefficient of variation CV: 5%; relative combined uncertainty $U_{c,rel}$: 17%). U-Cd content was adjusted for creatinine in urine, expressed as $\mu\text{g/g}$ creatinine. The chronological sequence of urine tests is as follows:

- U-Cd 2/2013 initial cadmium levels in February 2013, before the preventive interventions,
- U-Cd 2/2014 cadmium levels in February 2014, after the first phase of the workplace health promotion program,
- U-Cd 4/2015 cadmium levels in April 2015, after the second phase of the workplace health promotion program.

Statistical Analysis

The differences in U-Cd levels during the workplace health promotion program were statistically analysed by the non-parametric Wilcoxon signed-rank test, and the difference in factors affecting U-Cd levels in workers were analysed by the Wilcoxon rank-sum test. A P value <0.05 was considered as the level of statistical significance. Descriptive analysis was used to calculate medians, interquartile ranges (IQR), means, standard deviations (SD), minimums and maximums. U-Cd data are demonstrated as medians. The

results are graphically expressed using a box and whisker plot (median, 25th percentile is considered as lower limit, 75th percentile is considered as the upper limit).

Results

The initial median U-Cd level observed in 59 workers was 1.9 µg/g creatinine (IQR 5.1 µg/g creatinine), 19 workers had initial U-Cd levels higher than 5 µg/g creatinine. Although median U-Cd levels in women were higher in comparison to men, the difference was not statistically significant ($P=0.139$). As Table 2 shows, there was no statistical difference in U-Cd levels between smokers and non-smokers ($P=0.863$), or between workers living in the same village as the nickel-cadmium factory and those living outside ($P=0.412$).

1st Phase of the Health Promotion Program

We analysed urine samples from 59 workers. At the beginning of the health promotion program, the initial median U-Cd level in workers was 1.9 µg/g creatinine. After the education and change of the sanitary plan, U-Cd levels dropped by about a half to 1.0 µg/g creatinine, and the difference in concentration was statistically significant ($P<0.001$) (Table 3 and Figure 2).

2nd Phase of the Health Promotion Program

Samples were taken from 44 workers. The median level of U-Cd before the improvement of technical measures was 1.1 µg/g creatinine. Subsequently, after the intervention

Table 2. The Initial U-Cd Concentration and Factors Affecting Cadmium Levels in Workers

Variable	U-Cd [µg/g creatinine]*						
	Median	IQR	Mean	SD	Min.	Max.	P [†]
Workers (N=59)	1.9	5.1	4.9	6.8	0.2	35.6	
Women (N=36)	2.7	6.2	6.0	7.7	0.2	35.6	0.139
Men (N=23)	1.3	2.1	3.0	4.7	0.2	22.6	
Smokers(N=18)	1.3	6.3	5.9	9.0	0.2	35.6	0.863
Non-smokers (N=41)	2.2	4.5	4.6	5.9	0.2	22.6	
Residence (N=12) [‡]	2.5	8.4	6.5	7.8	0.2	20.5	0.412
Residence (N=47) [§]	1.7	4.7	4.7	6.5	0.2	35.6	

*Cadmium urine levels; [†]Wilcoxon rank-sum test; [‡]In the village with the factory; [§]Elsewhere.

Table 3. The Effect of the 1st Phase of the Workplace Health Promotion Program on U-Cd Levels

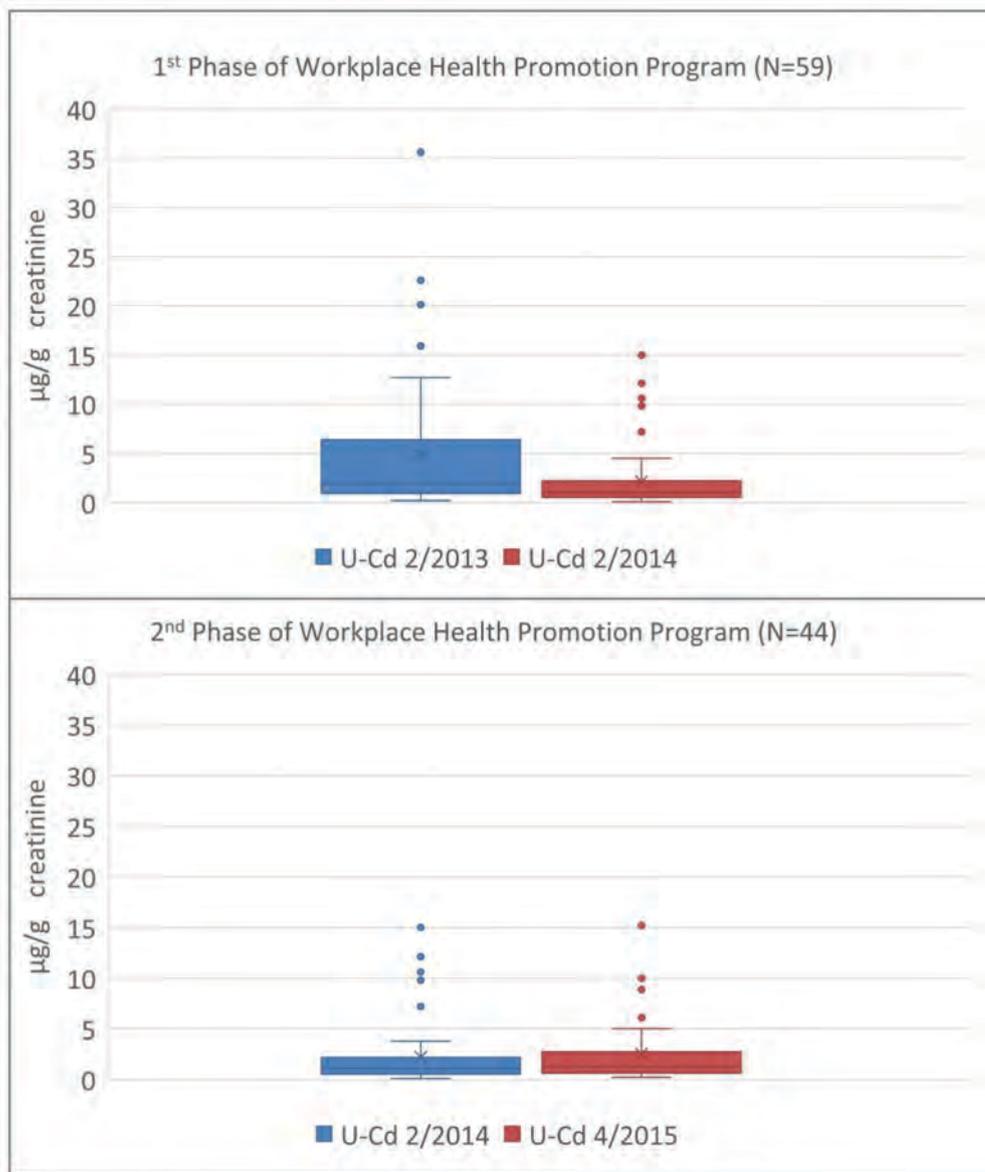
Variable	U-Cd [µg/g creatinine]*						
	Median	IQR	Mean	SD	Min.	Max.	P [†]
N=59							
U-Cd 2/2013	1.9	5.1	4.9	6.8	0.2	35.6	$P<0.001$
U-Cd 2/2014	1.0	1.7	2.1	3.0	0.1	15.0	

*Cadmium urine levels; [†]Wilcoxon signed-rank test.

Table 4. The Effect of the 2nd Phase of the Workplace Health Promotion Program on U-Cd Levels

Variable	U-Cd [µg/g creatinine]*						
	Median	IQR	Mean	SD	Min.	Max.	P value [†]
N=44							
U-Cd 2/2014	1.1	0.5	2.3	3.4	0.1	15.0	$P=0.728$
U-Cd 4/2015	1.2	2.0	2.5	3.3	0.2	15.2	

*Cadmium urine levels; [†]Wilcoxon signed-rank test.



U-Cd=Urine cadmium level.

Figure 2. The urinary cadmium levels (U-Cd) after the 1st and 2nd phase of health promotion program.

(technical preventive measures), the median level of U-Cd did not change significantly ($P=0.728$) (Table 4, Figure 2).

Discussion

Generally, women, smokers and the population living near factories have significantly higher cadmium levels in their blood or

urine (3, 9-11). Although these studies described a strong association of these factors, our results did not confirm any significant relationship. The women in our sample had a similar job description to the men. Full automation of the manufacturing processes has led to reduction of cadmium exposure in workers, and some positions have become more favourable for women. Simi-

larly, the exposure duration for workers was relatively long, so the variations in exposure factors may be reflected in U-Cd levels (12). The insignificant impact of smoking on cadmium levels can be explained by the strict smoking ban in the factory (13). However, there was no influence of place of residence on U-Cd levels in workers, which indicates that the measures carried out in the factory to protect the surrounding environment are effective.

The initial median cadmium level in workers was below the Czech occupational exposure limit (14), but still higher in comparison with the environmentally exposed population (15). Nevertheless, although the factory declared cadmium air concentrations below the permissible exposure limit and the presence of all statutory preventive measures, U-Cd levels in 19 workers exceeded the occupational exposure limit. So according to the previous studies, we assumed that insufficient compliance with the basic preventive measures by these workers, such as poor hygiene, could be closely associated with excessive oral exposure to chemicals (16). Therefore, apart from cadmium airborne monitoring, behavioural changes contributing to improvement in workers' personal hygiene are essential (5, 8, 17). Practicing good personal hygiene showed a significant positive effect on U-Cd levels in our sample, indeed, within a relatively short time period. Although behavioural change seems to be a rather unsophisticated preventive measure, the effect on workers' exposure can be very significant (7). Moreover, supervision by the safety engineer significantly contributes to a notable behavioural change (18).

We supposed that the second phase of the health promotion programme could bring a further decrease in U-Cd levels. However, there was surprisingly no significant decrease in U-Cd levels. This indicates that if the compliance with the basic preventive measures is insufficient, the renovation

of sanitary facilities and modernization of air exhaust ventilation would be pointless.

There were some limitations to our study. Firstly, the sample of workers exposed to cadmium was relatively small and was not divided proportionally by sex, smoking status or residence. Moreover, due to the small sample size, no statistically significant differences were found in the analysis of the influence of these factors. On the other hand, the gender distribution, proportion of smokers, and the number of exposed employees in the workplace represents a typical situation in this type of industry. Thanks to modern technologies, mechanical overload has been eliminated, and this generally makes these jobs more preferable for women. Moreover, in the employment process non-smokers are preferred and strict non-smoking policies are adhered to in the workplace. Similarly, we only used cadmium urine levels for our analysis, which are considered to be a long-term exposure biomarker. Although some authors prefer blood samples to demonstrate short-term changes better (12, 19, 20), in our case urine testing was a standard part of the check-up and therefore no additional invasive procedures were needed. Finally, there was no control group from the same village where the factory is located, who would only be exposed environmentally. We assume that the limitations mentioned above did not substantially alter the measured levels and did not undermine the main contribution of the article, that is, to demonstrate clearly the effect of comprehensive employee education in a workplace with increased risk of cadmium exposure.

Conclusion

The study clearly indicates that, although health and safety measures are prescribed by law, there is a problem with compliance by workers in practice. The significant decrease in U-Cd levels demonstrates that education is a con-

vincingly useful and cost-effective way to reduce occupational chemical exposure, increase workers' compliance and save employers from the future possible compensation costs.

What Is Already Known on this Topic:

Cadmium is a toxic heavy metal, exposure to which even at low levels can lead to serious adverse health effects. Legislatively based preventive measures are prescribed for workplaces, but their effectiveness can be limited by workers' poor compliance.

What this Study Adds:

We evaluated the effect of preventive measures on cadmium levels in workers under the real conditions of a nickel-cadmium factory. After the education of workers and changes in the sanitation plan, the initial median cadmium level 1.9 µg/g creatinine dropped by about a half. Subsequently, technical preventive measures did not show any decrease in cadmium levels. The results demonstrate the importance of further education to promote workers' compliance with legislatively based preventive measures, to minimize the potential harmful effects of cadmium exposure.

Authors' Contributions: Conception and design: MS and TB; Acquisition, analysis and interpretation of data: HT, LC, AŠ and MS; Drafting the article: MS and TB; Revising it critically for important intellectual content: TB and HH; Approved final version of the manuscript: MS, HT, LC, AŠ, TB and HH.

Conflict of Interest: The authors declare that they have no conflict of interest.

References

- Agency for Toxic Substances and Disease Registry (ATSDR). Cadmium and Cadmium Compounds. Atlanta, Georgia: US Department of Health and Human Services; 2012.
- Järup L, Alfvén T. Low level cadmium exposure, renal and bone effects - the OSCAR study. *Bio-Metals*. 2004;17(5):505-9.
- Olsson IM, Bensryd I, Lundh T, Ottosson H, Skerfving S, Oskarsson A. Cadmium in Blood and Urine-Impact of Sex, Age, Dietary Intake, Iron Status, and Former Smoking-Association of Renal Effects. *Environ Health Perspect*. 2002;110(12):1185-90.
- European Commission. Council Directive 98/24/EC of 7 April 1998 on the protection of the health and safety of workers from the risks related to chemical agents at work (fourteenth individual Directive within the meaning of Article 16 (1) of Directive 89/391/EEC). Brussels:European Commission;1998.
- Decharat S. Heavy Metals Exposure and Hygienic Behaviors of Workers in Sanitary Landfill Areas in Southern Thailand. *Scientifica (Cairo)*. 2016;2016:9269210.
- Cancelliere C, Cassidy JD, Ammendolia C, Côté P. Are workplace health promotion programs effective at improving presenteeism in workers? A systematic review and best evidence synthesis of the literature. *BMC Public Health*. 2011;11:395.
- MacMillan F, Karamacoska D, El Masri A, McBride KA, Steiner GZ, Cook A, et al. A systematic review of health promotion intervention studies in the police force: study characteristics, intervention design and impacts on health. *Occup Environ Med*. 2017;74(12):913-23.
- Rumchev K, Brown H, Wheeler A, Pereira G, Spickett J. Behavioral interventions to reduce nickel exposure in a nickel processing plant. *J Occup Environ Hyg*. 2017;14(10):823-30.
- Bernhard D, Rossmann A, Wick G. Metals in cigarette smoke. *IUBMB life*. 2005;57(12):805-9.
- Järup, L, Berglund M, Elinder CG, Nordberg G, Vanter M. Health effects of cadmium exposure—a review of the literature and a risk estimate. *Scan J Work Environ Health*. 1998;24(Suppl 1):1-51.
- Hellström L, Persson B, Brudin L, Grawé KP, Öborn I, Järup L. Cadmium exposure pathways in a population living near a battery plant. *Sci Total Environ*. 2007;373(2-3):447-55.
- Vacchi-Suzzi, C, Kruse D, Harrington J, Levine K, Meliker JR. Is Urinary Cadmium a Biomarker of Long-term Exposure in Humans? A Review. *Curr Environ Health Rep*. 2016;3(4):493-4.
- Howard J. Smoking is an occupational hazard. *Am J Ind Med*. 2004;46(2):161-9.
- Decree No.432/2003 of the Ministry of Health of the Czech Republic defining the classification of occupations, fixing the limit indicators of biological exposure tests and requirements for notification of work with asbestos and biological agents [in Czech] Available from: <http://www.zakonyprolidi.cz/cs/2003-432>.
- National Institute of Public Health. Environmental Health Monitoring System in the Czech Republic: Summary Report 2015. [in Czech]. Prague: National Institute of Public Health; 2016.
- Far HS, Pin NT, Kong CY, Fong KS, Kian CW, Yan CK. An evaluation of the significance of mouth and hand contamination for lead absorption in lead-acid battery workers. *Int Arch Occup Environ Health*. 1993;64(6):439-43.

17. Chuang H, Lee MT, Chao K, Wang J, Hu H. Relationship of blood lead levels to personal hygiene habits in lead battery workers: Taiwan, 1991–1997. *Am J Ind Med.* 1999;35(6):595-603.
18. Haas EJ. The Role of Supervisory Support on Workers' Health and Safety Performance. *Health Commun.* 2019:1-11.
19. Bulat ZD, Đukić-Ćosić D, Đokić M, Bulat P, Matović V. Blood and urine cadmium and bioelements profile in nickel-cadmium battery workers in Serbia. *Toxicol Ind Health.* 2009;25(2):129-35.
20. Guo ZJ, Wang JY, Gong LL, Gan S, Gu CM, Wang SS. Association between cadmium exposure and urolithiasis risk. *Medicine (Baltimore).* 2018;97(1):e9460.

Neuroenhancing Substances Use, Exam Anxiety and Academic Performance in Bosnian-Herzegovinian First-Year University Students

Jasna Kusturica¹, Ajša Hajdarević², Haris Nikšić³, Amira Skopljak⁴, Zana Tafi⁵, Aida Kulo¹

¹Department of Pharmacology, Clinical pharmacology and Toxicology, Faculty of Medicine, University of Sarajevo, Sarajevo, Bosnia and Herzegovina, ²Medical student, Faculty of Medicine, University of Sarajevo, Sarajevo, Bosnia and Herzegovina, ³Department of Pharmacognosy, Faculty of Pharmacy, University of Sarajevo, Sarajevo, Bosnia and Herzegovina, ⁴Department for Family Medicine, Faculty of Medicine, University of Sarajevo, Sarajevo, Bosnia and Herzegovina, ⁵Institute of Occupational Medicine, Health Care Centre of Canton Sarajevo, Sarajevo, Bosnia and Herzegovina

Correspondence:

jasna.kusturica@mf.unsa.ba
Tel.: + 387 61 916 177
Fax.: + 387 33 217 540

Received: 18 March 2019; Accepted: 14 November 2019

Abstract

Objective. The aim of this study was to assess the relationship between the use of neuroenhancing substances, exam anxiety and academic performance among first-year Bosnian-Herzegovinian (BH) university students. **Methods.** In a cross-sectional study, an *ad hoc* questionnaire was delivered to a sample of BH first-year university students. The following data were collected: socio-demographic features, consumption of neuroenhancing substances, the West-side Test Anxiety Scale (WTAS) and academic performance. **Results.** A total of 214 students were included. Consumption of lifestyle substances, coffee, energy drinks, nicotine, alcohol, and marijuana, for the purpose of neuroenhancement increased during the week before the exams. OTC cognitive enhancer use was

reported by 31.0%, and of benzodiazepines by 1.5% of students. No psychostimulants were used. A high to extremely high exam WTAS score was reported in 38.3% students. The exam WTAS score was positively correlated with consumption of coffee ($\rho=0.31$; $P<0.001$), energy drinks ($\rho=0.18$; $P=0.009$), and nicotine ($\rho=0.22$; $P=0.001$), and negatively correlated with last exam grade ($\rho=-0.33$; $P<0.001$). The exam WTAS score was a significant independent predictor (OR=0.55; 95% CI 0.31 to 0.97, $P=0.039$) for self-assessed academic performance. Self-assessed academic performance was positively correlated with last exam grade ($\rho=0.15$; $P=0.043$). **Conclusions.** Although first-year BH university students do not seem to use either prescription or illicit psychostimulants, the consumption of nicotine, alcohol, and marijuana is worrying. However, the consumption of these neuroenhancing substances seems not to be related to better self-assessed academic performance. Finally, exam anxiety seems to be a significant problem among BH first-year university students.

Key Words: Performance-Enhancing Substances
■ Lifestyle Drugs ■ Psychostimulants ■ Anxiety ■ Academic Performance.

Introduction

The topic of neuroenhancement, defined as the use of the substances by healthy subjects in order to enhance their mood or cognitive function, has become increasingly popular (1, 2). These substances are frequently used among students in their academic en-

vironment to improve their academic performance (1, 3). The most commonly used neuroenhancing substances are known as soft enhancers [i.e. lifestyle substances, such as caffeine, nicotine, alcohol, and over-the-counter pharmacy products (OTC)] (4). Unlike the use of soft enhancers, the use of psychostimulants, both prescription (e.g. methylphenidate, dexamethylphenidate, and modafinil) and illicit (e.g. amphetamines) presents a more serious threat for public health due to their potential for misuse (5-7). The reported prevalence of psychostimulant use for neuroenhancement among students varies between studies, probably at least partially due to the different definitions of neuroenhancement, and the ways the prevalence was reported (e.g. lifetime prevalence versus past year prevalence). Prevalence of psychostimulants use varies from 2.5% to 55.0% in the United States (US) and Canada (7), and is at about 9.5% among UK and Irish students (8), but only 0.6% among Italian medical students (9). Regarding the use of both prescription and illicit psychostimulants, prevalences of 5.5% and 0.12% among Australian students (10), 5.8% and 3.5% among German students (11, 12), 4.1% and 0.6% among Swiss students (4), and 2.5% and 0.6% among Dutch students (13), have been reported respectively.

Evidence of the neuroenhancement efficacy of substances used for this purpose in healthy humans, including data from randomized clinical trials, is still very limited (5, 14, 15). Available data suggest some effects of caffeine and nicotine on attention and memory function (16-18). Regarding OTC cognitive enhancers, despite the insufficient evidence for their efficacy (19, 20), their popularity and international sales are rapidly growing, and exceed \$1bn a year (21). The cognitive effects of psychostimulants (processing speed, decision-making, planning, and cognitive perseveration) have been shown to be more evident in subjects

with lower baseline cognitive performance (7, 22).

Studies have shown that university students use neuroenhancing substances not only for cognitive enhancement, but also to cope with psychosocial stressors (6, 23), including exam anxiety which is reported to be a widespread but underestimated and neglected problem (24). In a survey conducted in Germany, more than 50.0% of first and second year, and 70.0% of third, fourth and fifth-year medical students stated that obvious exam anxiety had not been considered by lecturers (25). Also, a study in Iran on first-year students documented moderate exam anxiety in 40.3%, and severe exam anxiety in 11.9% of students (26).

To our knowledge, no previous study has investigated this topic on Bosnian-Herzegovinian (BH) university students, and, having reviewed the literature on the topic, we hypothesized that their level of exam anxiety is high, as well as their use of cognitive enhancers. The aim of this study was to assess the relationship between use of neuroenhancing substances, exam anxiety and academic performance among BH first-year university students.

Subjects and Methods

Study Design and Study Population

This cross-sectional study included first-year students at the Medical Faculty and the Faculty of Economics of the University of Sarajevo, in the 2015/2016 academic year. Ethical approval was obtained from the Medical Faculty of the University of Sarajevo.

Data Collection

The students participated in an anonymous questionnaire. A written information sheet explained the purpose of the study, including the warning that only substance use

for the purpose of cognitive enhancement was to be considered, and students had the opportunity to accept or decline any further participation with no repercussions. The questionnaire related to (1) age, gender, socioeconomic status (i.e. low, medium, high), place of residence; (2) questions related to the week before the exams, including: (2a) the exam Westside Test Anxiety Scale (WTAS); (2b) assessment of any increase in physical activity compared to an ordinary week; (2c) assessment of any increase in the consumption of coffee, energy drinks, cigarettes, alcohol and marijuana compared to an ordinary week; (2d) assessment of OTC and prescription drug use and the reasons for their use; (3) academic performance (i.e. last exam grade, self-assessment of academic performance).

As a measure of academic accomplishment, academic performance was also self-assessed based on the statement: "My academic performance is higher than other students' performance", using a 5-point scale as follows: 1=not at all/ never true; 2=slightly/seldom true; 3=moderately/sometimes true; 4=highly/usually true; 5=extremely/always true. Increased consumption of lifestyle substances and marijuana was rated on the same 5-point scale.

Statistical Analysis

Data were coded and analysed using the SPSS statistical package (SPSS Inc., Chicago, IL, USA) version 17. Continuous numerical variables with normal distribution were expressed as mean±standard deviation, and those that were not normally distributed as median and 25th and 75th percentiles. Numerical variables were compared using either parametric or nonparametric tests, when appropriate. Correlation between the variables was tested using the Pearson R test or the Spearman Test. Stepwise binary logistic regression was used to assess how

well the predictor variables (i.e. place of residence, physical activity, last exam grade, exam WTAS score, consumption of coffee, energy drinks, nicotine, alcohol, marijuana, and OTC use) predicted self-assessed academic performance. Self-assessed academic performance was converted from the 5-point scale into 2 categories: No (never true to seldom true) or Yes (moderately to always true). The multivariate logistic model included covariates that had reached a p-value less than 0.25 level of statistical significance in the univariate analysis. In the multivariate regression analysis, P-value less than 0.05 was set to identify association between covariables.

Results

Of the 218 first-year students available, 214 (98.2%) responded, and 210 students answered all the questions. Their median age was 20 (20-21) years. The students were mainly women 74.0% (158/214). Regarding socioeconomic status, 88.5% (186/210) students reported middle, 10.9% (23/210) low, and 0.5% (1/210) high status. The majority of students reported that they were living with their parents (59.6%), 21.1% in a rented apartment, 10.8% in their own apartment, and 8.5% in a dormitory.

Regarding changes in physical activity in the week before exams, 14% of the students reported increased physical activity to be usually or always true, 27.6% reported it to be seldom or sometimes true, and the majority (58.4%) reported no change in physical activity.

Consumption of lifestyle substances for the purpose of neuroenhancement increased during the week before the exams (Table 1). Consumption of coffee increased in 72.9% (156/214), of energy drinks in 58.4% (125/214), of nicotine in 37.8% (81/214), of alcohol in 24.7% (53/214), and of marijuana in 19.0% (40/211) students.

Table 1. The Proportion of Students with Increased Consumption of Lifestyle Substances Coffee, Energy Drinks, Nicotine, Alcohol and Marijuana the Week before Exams, Compared to an Ordinary Week

Student's rating	Proportion of students with increased consumption				
	Coffee (N=214)	Energy drinks (N=214)	Nicotine (N=214)	Alcohol (N=21)	Marijuana (N=211)
Never true (%)	27.1	41.6	62.1	75.2	81.0
Seldom true (%)	11.2	11.2	3.7	7.9	3.3
Sometimes true (%)	9.8	13.1	7.0	5.6	3.8
Usually true (%)	17.3	14.0	7.0	4.7	6.6
Always true (%)	34.6	20.1	20.1	6.5	5.2

Table 2. Pre-Exam Anxiety Score Measured by the Westside Test Anxiety Scale

Pre-exam anxiety score	N (%) of students
1.0–1.9 (comfortably low test anxiety)	18 (8.29)
2.0–2.5 (normal or average test anxiety)	24 (11.0)
2.5–2.9 (high normal test anxiety)	35 (16.1)
3.0–3.4 (moderately high)	57 (26.3)
3.5–3.9 (high test anxiety)	51 (23.5)
4.0–5.0 (extremely high anxiety)	32 (14.7)

OTC cognitive enhancer use was reported by 31.0% of the students. The main reasons for their use were to calm down (herbal sedatives) and to improve concentration (ginkgo biloba, royal jelly, vitamins, green tea). Of prescription drugs, only benzodiazepines were used, by 1.5% of students. No prescription or illicit psychostimulant use was reported.

The average WTAS score was 3.17±0.78, and it was significantly higher in women compared to men (3.24±0.76 vs. 2.99±0.82; P=0.037), and among economics students compared to medical students (3.45±0.84 vs. 2.96±0.63; P<0.001). A high (3.5–3.9) to extremely high (4.0–4.5) exam WTAS score was found in 38.3% of the students (Table 2).

Positive correlations were found between the exam WTAS score and the consumption of most lifestyle substances, i.e. coffee (rho=0.31; P<0.001), energy drinks (rho=0.18; P=0.009), and nicotine (rho=0.25; P=0.001), while the WTAS score had no correlation with the consumption of alcohol

(rho=0.12; P=0.074), marijuana (rho=0.07; P=0.288) or OTC drugs (rho=0.13; P=0.059).

Regarding academic performance, the average last exam grade was 8.16±1.48, and it was higher among medical students compared to economic students [9(8;10) vs. 7(6;8); p<0.001]. Regarding self-assessed academic performance, the majority of students (53.7%) reported that it is sometimes true that their academic performance is higher compared to other students' performance. This was never true in 3.0%, seldom true in 9.0%, usually true in 26.9%, and always true in 7.5% students.

A positive correlation was noted between the last exam grade and self-assessed academic performance (rho=0.15; P=0.043), while the exam WTAS score was negatively correlated with the last exam grade (rho=-0.33; P<0.001).

Also, binary logistic regression analysis identified two independent predictors of self-assessed academic performance: the exam WTAS score as a negatively associated pre-

Table 3. The Logistic Regression Model Assessing Independent Predictors of Self-Assessed Academic Performance

Variables	B	SE	Wald	P	Exp(B)	95% CI for EXP(B)	
						Lower	Upper
Living with parents	1.462	0.732	3.991	0.046	4.315	1.028	18.109
Living in a dormitory	0.789	0.758	1.084	0.298	2.201	0.498	9.717
Living in a rented apartment	1.006	0.885	1.293	0.256	2.735	0.483	15.488
Living in own apartment	-	-	5.016	0.171	-	-	-
Physical activity	0.241	0.170	2.015	0.156	1.272	0.912	1.775
Last exam grade	0.261	0.153	2.893	0.089	1.298	0.961	1.754
WTAS score	-0.598	0.289	4.270	0.039	0.550	0.312	0.970
Coffee consumption	0.0025	0.133	0.035	0.852	1.025	0.790	1.330
Energy drinks consumption	0.185	0.138	1.801	0.180	1.203	0.918	1.577
Nicotine consumption	-0.038	0.132	0.083	0.773	0.963	0.744	1.246
Alcohol consumption	-0.125	0.261	0.228	0.633	0.883	0.530	1.472
Marijuana consumption	-0.458	0.301	2.320	0.128	0.633	0.351	1.140
OTC use	-0.038	0.192	0.039	0.844	0.963	0.660	1.404
Constant	-3.442	2.142	2.583	-108	0.032	-	-

WTAS=Westside Test Anxiety Scale; OTC=Over the Counter; B=Coefficient; SE=Standard error of the coefficient; Exp(B)=Odds ratio; CI=Confidence interval; Model justification: Omnibus Tests of Model Coefficients $\chi^2(4)=243.69$, $p<0.0005$; Hosmer and Lemeshow Test $\chi^2=0.000$, $P=1.000$; Cox & Snell $R^2=0.160$; Nagelkerke $R^2=0.221$.

dicator [B (SE)=-0.60 (0.29), Wald(1)=4.27, OR=0.55; 95% CI 0.31 to 0.97, P=0.039], and living with parents as a positively associated predictor [B (SE)=0.46 (0.73), Wald(1)=3.99, OR=4.32; 95% CI 1.03 to 18.11, P=0.046]. Other variables tested (i.e. living in a rented apartment, living in own apartment, living in a dormitory, physical activity, last exam grade, coffee, energy drinks, nicotine, alcohol and marijuana consumption, OTC use) were shown not to predict self-assessed academic performance (Table 3).

Discussion

Fortunately, no students from our sample of BH first-year university students used psychostimulants, either prescription or illicit, for neuroenhancement purpose. The students, however, used prescription benzodiazepines, some OTC drugs and, more frequently, lifestyle substances.

Although caffeine is also the first choice for neuroenhancement in other countries,

the prevalence of its use in our country seems to be higher. The traditional widespread consumption of coffee in our country may explain this finding.

The average pre-exam anxiety level in our study was moderately high (WTAS score of 3.17 ± 0.78). However, high (23.5%) to extremely high (14.7%) levels were found with "alarming frequency". Similarly, in a study by Pighi et al. (2018) almost a third of the Italian medical students found studying stressful (9). The gender implications found in our study have also been seen in several previous studies (27-30), and the authors explained that this was due to the differences in the social roles assigned to men and women, as well as due to the increased emotional vulnerability of women (23, 29). Furthermore, in our study, economic students, compared to medical students, had a lower last exam grade and a significantly higher WTAS score.

In our study, anxiety was positively correlated with the consumption of caffeine and

nicotine. In line with this, Italian medical students who worried about academic performance were more prone to use cognitive enhancers (9). However, more research is needed to explore whether anxiety makes students take more of these substances for relaxation and sedation, or whether anxiety is a side effect of their consumption. Increased exam anxiety was also associated with a lower last exam grade and, in addition, with lower self-assessed academic performance. On the other hand, living with parents was shown to be an independent predictor, significantly positively associated with self-assessed academic performance.

Although alcohol and marijuana are rarely used for the purpose of neuroenhancement (4) [e.g. 5.1% and 1.8% prevalence rates among Swiss students (4), and 3.8% and 1.0% among Australian students (10), respectively], in our study a high increase in alcohol (24.8%) and marijuana (19.0%) consumption during the week before an exam was found. Neither alcohol nor marijuana consumption was correlated with exam anxiety, which was also found in a study of German medical students (25). The high increase in alcohol and marijuana consumption in our study may be explained by the fact that we evaluated first-year university students, who may still tend to experiment with substance use, or have limited knowledge of the side effects of alcohol and marijuana, or have a low level of responsibility towards education.

In our study, OTC cognitive enhancers, specifically ginkgo biloba, royal jelly, magnesium, green tea, vitamin tablets, herbal sedatives, or analgesics, were used in 31.0% of students, similarly to 28.1% of Swiss university students (ginkgo biloba, zinc, vitamin tablets, herbal sedatives), but more than 9.5% of Dutch university students, where the specific OTC drugs used were not reported (4, 13). Of prescription drugs, only benzodiazepines were used in 1.3% stu-

dents, similar to the 1.1% past-year prevalence among Australian students, and lower than the 2.1% prevalence reported among Swiss students (4, 13).

None of our students reported the use of prescription or illicit psychostimulants compared to the prevalence in other countries mentioned earlier (4, 8, 10-13, 31). Although these comparisons should be considered with caution because our study included only first-year students, the study of medical students in the US also showed psychostimulant non-users to be more likely to be first year students or to grow up outside of the US (32). Also, the reason for the unpopularity of prescription psychostimulants among BH first year university students may be their unavailability, as those drugs are not approved in BH. In the US and Canada, student psychostimulant users reported obtaining those drugs from a peer with a prescription (31), while in the UK and Ireland, two-thirds of student non-users stated that the lack of access was the only reason why they had not tried such drugs (8).

Although better academic success is assumed to be the main reason for the use of neuroenhancing substances, the literature data have reported no long-term academic benefits from them (2). This is in line with our results, where the consumption of nicotine, alcohol, marijuana and OTC cognitive enhancers seemed not to be related to better self-assessed academic performance.

Limitations of the Study

This study had several limitations: the cross-sectional study design largely based on an *ad hoc* questionnaire; self-reported data and the lack of objective parameters of cognitive enhancers' benefits for academic results. Also, the study population included only first-year students from only two faculties of one city, and consequently the results cannot represent the whole population of first-

year university students in BH. In addition, the regression analysis performed, dichotomizing the outcome variable, may have reduced the information originally contained in the questionnaire. However, despite the small sample size, our results indicated a significantly high level of exam anxiety among first-year medicine and economics students, suggesting the need for larger studies to confirm those findings and to inform interventional strategies, both for promotion of healthy ways of coping with stress, and for reducing consumption of neuroenhancing substances with addiction potential, i.e. nicotine, alcohol, marijuana, benzodiazepines.

Conclusion

Although the BH first-year university students seemed not to use either prescription or illicit psychostimulants, the consumption of nicotine, alcohol, and marijuana is worrying. However, the consumption of these neuroenhancing substances seems not to be related to better self-assessed academic performance. Finally, exam anxiety seems to be a significant problem among BH first-year university students, with a higher level of exam anxiety most frequently seen among students with a greater increase in coffee, energy drink, and nicotine consumption, as well as among students with lower last exam grades and lower self-assessed academic performance.

What Is Already Known on this Topic:

Neuroenhancing substances are frequently used among students in the academic environment. In general, the neuroenhancing use of prescription drugs and illicit substances is considered more problematic than the use of lifestyle substances and over-the-counter drugs. Evidence of long-term academic benefits from neuroenhancing substances use is lacking, while exam anxiety is considered one of the most important factors that affect academic achievement.

What this Study Adds:

Lifestyle substances are the most common choice for neuroenhancement prior to exams among BH first-year university students. Compared to other countries, we highlight the par-

ticularly frequent increase in nicotine, alcohol and marijuana consumption, while the use of prescription and illicit psychostimulants was not reported. While a high percentage of students struggle with exam anxiety, which was shown to be an independent predictor of lower academic performance, none of the substances used was shown to contribute to better academic performance.

Authors' Contributions: Conception and design: JK, AK and AH; Acquisition, analysis and interpretation of data: JK, AK and AH; Drafting the article: JK and AK; Revising it critically for important intellectual content: HN, AS and ZT; Approved final version of the manuscript: JK, AK and AS.

Conflict of Interest: The authors declare that they have no conflict of interest.

References

- Schuijver JW, de Jong IM, Kupper F, van Atteveldt NM. Transcranial electrical stimulation to enhance cognitive performance of healthy minors: A complex governance challenge. *Front Hum Neurosci.* 2017;11:142.
- Fond G, Micoulaud-Franchi JA, Macgregor A, Richieri R, Miot S, Lopez R, et al. Neuroenhancement in healthy adults, part I: Pharmaceutical cognitive enhancement: A systematic review. *J Clin Res Bioeth.* 2015;6:213.
- Maier LJ, Schaub MP. The use of prescription drugs and drugs of abuse for neuroenhancement in Europe. *Eur Psychol.* 2015;20:155-66.
- Maier LJ, Liechti ME, Herzig F, Schaub MP. To dope or not to dope: neuroenhancement with prescription drugs and drugs of abuse among Swiss university students. *PLoS One.* 2013; 8(11):e77967.
- Weyandt LL, Oster DR, Marraccini ME, Gudmundsdottir BG, Munro BA, Rathkey ES, et al. Prescription stimulant medication misuse: Where are we and where do we go from here? *Exp Clin Psychopharmacol.* 2016;24(5):400-14.
- Jensen C, Forlini C, Partridge R, Hall W. Australian university students' coping strategies and use of pharmaceutical stimulants as cognitive enhancers. *Front Psychol.* 2016;7:277.
- Marraccini ME, Weyandt LL, Rossi JS, Gudmundsdottir BG. Neurocognitive enhancement or impairment? A systematic meta-analysis of prescription stimulant effects on processing speed, decision-making, planning, and cognitive perseveration. *Exp Clin Psychopharmacol.* 2016;24(4):269-84.

8. Singh I, Bard I, Jackson J. Robust resilience and substantial interest: a survey of pharmacological cognitive enhancement among university students in the UK and Ireland. *PLoS One*. 2014;9:e105969.
9. Pighi M, Pontoni G, Sinisi A, Ferreri S, Mattei G, Pingani L, et al. Use and Propensity to Use Substances as Cognitive Enhancers in Italian Medical Students. *Brain Sci*. 2018;8(11):pii:E197.
10. Riddell C, Jensen C, Carter O. Cognitive enhancement and coping in an Australian university student sample. *J Cogn Enhanc*. 2018;2:63-9.
11. Wolff W, Brand R, Baumgarten F, Lösel J, Ziegler M. Modeling students' instrumental (mis-) use of substances to enhance cognitive performance: Neuroenhancement in the light of job demands-resources theory. *Biopsychosoc Med*. 2014;8:12.
12. Franke AG, Christmann M, Bonertz C, Fellgiebel A, Huss M, Lieb K. Use of coffee, caffeinated drinks and caffeine tablets for cognitive enhancement in pupils and students in Germany. *Pharmacopsychiatry*. 2011;44(7):331-8.
13. Schelle KJ, Olthof BM, Reintjes W, Bundt C, Gusman-Vermeer J, van Mil AC. A survey of substance use for cognitive enhancement by university students in the Netherlands. *Front Syst Neurosci*. 2015;9:10.
14. Hawkes N. Modafinil does enhance cognition, review finds. *BMJ*. 2015;351:h4573.
15. Kennedy DO, Jackson PA, Haskell CF, Scholey AB. Modulation of cognitive performance following single doses of 120 mg Ginkgo biloba extract administered to healthy young volunteers. *Hum Psychopharmacol*. 2007;22(8):559-66.
16. Mednick SC, Cai DJ, Kanady J, Drummond SP. Comparing the benefits of caffeine, naps and placebo on verbal, motor and perceptual memory. *Behav Brain Res*. 2008; 3;193(1):79-86.
17. Adan A, Serra-Grabulosa JM. Effects of caffeine and glucose, alone and combined, on cognitive performance. *Hum Psychopharmacol*. 2010;25(4):310-7.
18. Heishman SJ, Kleykamp BA, Singleton EG. Meta-analysis of the acute effects of nicotine and smoking on human performance. *Psychopharmacology (Berl)*. 2010;210(4):453-69.
19. Canter PH, Ernst E. Ginkgo biloba is not a smart drug: an updated systematic review of randomised clinical trials testing the nootropic effects of G. biloba extracts in healthy people. *Hum Psychopharmacol*. 2007;22(5):265-78.
20. Morita H, Ikeda T, Kajita K, Fujioka K, Mori I, Okada H, et al. Effect of royal jelly ingestion for six months on healthy volunteers. *Nutr J*. 2012;11:77.
21. Chinthapalli K. The billion dollar business of being smart. *BMJ* 2015;351:h4829.
22. Kraus LJ. Increasing Awareness of Nootropic Use. Report of the council on science and public health 9-A-16. [cited 2019 February 5]. Available from: <https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/about-ama/councils/Council%20Reports/council-on-science-public-health/a16-csaph9.pdf>.
23. Pohl S, Boelsen H, Hildt E. Moral attitudes toward pharmacological cognitive enhancement (PCE): Differences and similarities among Germans with and without PCE experience. *Front Pharmacol*. 2018;9:1451.
24. Neudert S, Jabs B, Schmidtke A. Strategies for reducing test anxiety and optimizing exam preparation in German university students: A prevention-oriented pilot project of the University of Würzburg. *J Neural Transm*. 2009;116(6):785-90.
25. Tektaş OY, Paulsen F, Sel S. Test anxiety among German medical students and its impact on lifestyle and substance abuse. *Med Teach*. 2013;35(11):969.
26. Miri HR, Piroozan A, Hesam AA, Naderi N, Rezaei P. Determining the level of test anxiety and some of its contributing factors among the freshmen students. *Life Sci J*. 2013;10(9s):149-55.
27. Latas M, Pantic M, Obradovic D. Analysis of test anxiety in medical students. *Med Pregl*. 2010;63(11-12):863-6.
28. Nourse R, Adamshick P, Stoltzfus J. College binge drinking and its association with depression and anxiety: A prospective observational study. *East Asian Arch Psychiatry*. 2017;27(1):18-25.
29. Javadi M, Jourabchi Z, Shafikhani AA, Tajik E. Prevalence of depression and anxiety and their association with body mass index among high school students in Qazvin, Iran, 2013-2014. *Electron Physician*. 2017;9(6):4655-60.
30. Afzal H, Afzal S, Siddique SA, Naqvi SA. Measures used by medical students to reduce test anxiety. *J Pak Med Assoc*. 2012;62(9):982-6.
31. Smith ME, Farah MJ. Are prescription stimulants "smart pills"? The epidemiology and cognitive neuroscience of prescription stimulant use by normal healthy individuals. *Psychol Bull*. 2011;137(5):717-41.
32. Emanuel RM, Frelsen S, KashimaK, Sanguino S, Sierles FS, Lazarus CJ. Cognitive Enhancement Among Medical Students Cognitive-Enhancement Drug Use Among Future Physicians: Findings From A Multi Institutional Census of Medical Students. *J Gen Intern Med*. 2013;28(8):1028-34.

Maternal Dental Health Knowledge and Its Relation to the Dental Caries Experience of Their Children in Mamyzawa Camp of Refugees in Erbil, Iraq

Bushra Rashid Noaman¹, Rebwar Fadil Khalid², Lezan Dawood Fattah³

¹Paedodontic Department, Tishk International University, Erbil, Iraq, ²Tishk International University, Erbil, Iraq, ³Tishk International University, Dentistry Faculty, Conservative Department, Erbil, Iraq

Correspondence:

bushra.rashid@tiu.edu.iq
Tel.: + 9 647 510 207 481

Received: 10 March 2019; Accepted: 27 November 2019

Abstract

Objectives. This study aimed to evaluate the mothers' dental health knowledge and its relation to their children's oral health behavior and practice in a camp of refugees. **Method.** This descriptive cross-sectional observational study was conducted in Mamyzawa refugee camp in Erbil City, Iraq, in November 2017. Seventy-nine preschoolers (43 aged 4 years and 36 aged 5 years) and their mothers (79) were chosen for this study. The study was accomplished in two days. The first day the mothers' oral health knowledge, children's behavior towards oral hygiene, eating behaviors of their children and their use of dental services were assessed by a questionnaire. The day after, examinations of the dental health status of the children were performed. SPSS statistics software was used to analyze the collected data. **Results.** Mothers' knowledge of oral health was low, and 63% of the children had dental caries. Five-year old children had more dental caries (77.8%) than the four-year old (51.20 %). Frequency of sweet consumption, brushing assistance, and irregular use of dental services were the main factors that had relation to the high dental caries in those children. **Conclusion.** The mothers living in Mamyzawa refugee camp do not have enough knowledge of oral health,

which was led to high caries prevalence among their children, indicating that an intensive education program is required for the mothers and oral health care for their children.

Key Words: Dental Health Survey ▪ Dental Caries
▪ Oral Health Knowledge ▪ Refugees ▪ Oral Health Behaviors.

Introduction

Conflicts in Iraq have forced some people to migrate to the safe parts of the country such as Kurdistan. Since the June 2014 attack by ISIS in Mosul and different parts of the center of Iraq, thousands of people have migrated to the north of Iraq (Kurdistan region). This migration changed the lives of those people, including their home, economics, and health. The priority for the migrant people was survival, which led to forgetting other basic health requirements. From these requirements were the oral health of the adults and their children. Forgetting these requirements led to a decline in their health over time. Refugees are a vulnerable population and have fewer opportunities for access to dental care because they have no voice to ask for what they need. This can lead to increased risk for problems in oral and general health (1).

Health care providers need to understand the refugees' perspectives about their prob-

lems to be able to find solutions. Community-Based Participatory Research (CBPR) was recommended to recognize the factors that affect the oral health status of children (1). Since mothers have a major role in preserving the oral health of their children, mothers should work in collaboration with the researchers to take constructive action, and not only for increasing the researchers' knowledge about those populations. Therefore, it is necessary to include the mothers in all research involving an oral health promotion program for children since they have an important potential in motivating their children for oral health (2, 3).

There is an indication that refugees and migrant people and their children experience significantly inferior oral health than the non-migrant population, and an understanding of the reasons for this is needed (4). It is obvious that low socio-economic status has a negative impact on oral health. Dental caries prevalence is higher among socially disadvantaged populations, including those living in rural areas, indigenous and culturally diverse families, and those living in poverty (5, 6). Refugees are economically and socially deprived. In addition to their poverty, refugees complain about obstacles which prevent them from obtaining dental care. A pilot study conducted in Canada with a group of refugees concluded that the parents mentioned obstacles to maintaining early childhood oral health (ECOH) including the mood of the child, sugar intake control, and economic reasons (7). U.S. Surgeon General's Report stated that the impact of poor oral health on Quality of Life can affect vital functions such as eating and speaking which may restrict daily activities in school and family relations (8).

Strategies to meet the requirements of essential general and dental health of children in the refugees' culture must include health education plans for the entire family, and implementation of healthier mouth care and

appropriate use of dental services. Behavioral and lifestyle factors and oral health care are important factors in reducing the prevalence and severity of dental caries (9). In a study performed in a refugee camp it was found that a common daily practice among all the refugee children was high sweet consumption, with a strong association between caries and frequent sugary diet consumption (10). While other research suggested that parents' oral health knowledge may alter the oral health habits of their children (11).

Thus, this study aimed to evaluate the dental caries experience and dental care practices among preschool children living in Mamyzawa camp, Erbil, Iraq and to study its relationship with mother's oral health knowledge and oral health behavior.

Materials and Method

This descriptive cross-sectional observational study was conducted in the Mamyzawa refugee camp in Mamyzawa province, Erbil City, northern Iraq, in November 2017.

Materials

Disposable mirrors and probes, Professional PenLite (white halogen light, Welch Allyn, (USA) were used in this study. World Health Organization Oral Health Assessment Form for Children, 2013 (Annex 2) (12) was used for the recording the severity of dental caries. Questionnaire papers, according to Annex 8, WHO (12) was used to collect information about children behaviors and maternal knowledge.

Method

Selection and Description of Participants

There were 470 children living in the camp with their families. From these children all the preschool children were chosen, since

these refugees have no kindergarten and live in the camp since 2014. The children in this age group are entirely reliant on their homes for health care and eating habits. There were eighty-nine children aged 4-5 years, and after applying the inclusion and exclusion criteria, the total number who met the inclusion criteria was 79 children aged 4 years (N=43) and 5 years (N=36). The mothers of these children were included in answering the questionnaire. Totally cooperative children who gave good time without any movement during the examination, free of any disease systemically and mentally, and whose parents agreed to participate with their children in this study were included. The children who didn't meet these criteria were excluded from the study.

Standardization and Calibration

Four examiners shared the work of conducting the survey. To ensure uniform interpretation, understanding and training, and the index used in the survey, an interval of seven days passed between preparation and calibration, so the examiners had time to assimilate their knowledge of the index and practice conducting the survey (13). Intra-examiner reproducibility was assessed to eliminate variations within each examiner. The Kappa test was used to evaluate intra-examiner reproducibility. Each examiner examined 10 children and after 30 minutes he re-examined the same children to check the reproducibility. Almost perfect agreement was obtained for each examiner. The kappa test scores for dental caries assessment provided nearly perfect intra-examiner reliability (0.92, 0.90, 0.90, 0.93).

Oral Health Knowledge Questionnaire

The mothers of the 79 children answered the questionnaire. To obtain reliable information about the health status of their chil-

dren and risks to health, in the first step, the questionnaire was pretested for clarity with 10 mothers. The questionnaire was conducted by means of an interview between the researchers and the mothers, the day before the dental examination. The language of the interview was according to the mothers' native languages (Kurdish or Arabic). The questionnaire was intended to evaluate the mothers' oral health knowledge and their children's oral health behavior and practice. The mothers' oral health knowledge included reasons for brushing, the exact amount of toothpaste needed for a child, the importance of visiting a dentist, the reason for visiting a dentist (pain or no pain), and the significance of fluoride. The mothers' knowledge about tooth brushing included the age when the child's tooth brushing should begin, frequency of brushing and if the child should be assisted during brushing or not. Frequency of sweet consumption and the time of sweets intake were included in the questionnaire. The use of dental facilities was assessed by previous dental visits and the type of treatment the child received on that visit (10, 12).

Dental Examinations

The children were examined for dental caries using disposable mirrors and disposable probes. Infection control measures were undertaken by using masks and gloves by the examiners and disposable trays, and all of those were changed for each child. The place of the examination was in the hall of the school in the camp, in sequence without crowding. The research assistants taught the children how to brush and monitored them during brushing before the examination. The time was early in the morning, so the examiners were not fatigued. The duration of the examinations was 3 hours for each examiner, in order to gain reliable results, which included time for rest. The examina-

tions were performed on an ordinary chair using artificial light. The World Health Organization Oral Health Assessment Form for children, 2013, was used (12). The examination involved registration of the dentition status, which included decayed, missing due to caries and filled teeth (dmft). Caries is documented as extant when a lesion present on a smooth surface or in pits and fissures has an obvious cavity, in addition, undermined enamel, or obviously detected with softened floor. A tooth which is restored but carious and a tooth with temporary filling were included as decayed. The retained root of a tooth destroyed by caries was also considered as decayed (12).

Ethics Statement

The research started after agreement of the camp authority. Then the researchers gained the consents of parents. The consent included the fact that their children would undergo a dental examination and their mothers would answer a questionnaire related to oral health knowledge, attitudes and practice. This research started after approval had been granted by the research committee of Tishk International University, Erbil, Iraq (Document No.IU.RC.FR.001E). The research adhered to the World Medical Association Declaration of Helsinki.

Statistical Analysis

Data gained from the questionnaires and dental examinations were evaluated by statistical analysis software (IBM SPSS Statistics 22). The qualitative and quantitative variables were summarized using descriptive tables. The dependent variable is the percentage of caries prevalence (and mean dmft) of the individual child was used as a reference for descriptive statistics. The independent variables used in this study included age, gender, dental health knowledge,

oral hygiene habits, sweet consumption and dental visits. They were evaluated for association with dmft using the Chi-square and ANOVA tests, the level of significance was set at $P < 0.05$.

Results

Seventy-nine preschool children were living in the camp (42 males and 37 females). The children aged 5-years-old were more affected by dental caries (77.8%, $dmft = 3.55 \pm 3.79$) than the 4-year-olds, but the difference in dmft was not statistically significant ($P = 0.068$). Both males and females were nearly equally affected (64.4%, 62.2% respectively). In total, 63% of the children had dental caries (Table 1).

Table 2 shows the mothers' knowledge about oral health care in relation to the mean dmft. Eighty-six percent of the mothers answered that tooth brushing is for preventing dental caries, and their children's dmft was 2.72 ± 3.55 . The questionnaire revealed that they believe the amount of toothpaste used for tooth brushing is mostly filling the toothbrush (51.9%, $dmft = 3.01 \pm 3.77$) followed by half a brush (30.4%, $dmft = 1.33 \pm 2.24$), while only 14 mothers knew that the amount of toothpaste should be pea size ($dmft = 2.07 \pm 2.23$), with a statistically significant difference. Only two of the mothers knew the role of fluoride ($dmft = 1.5 \pm 2.12$), and 77 mothers did not know ($dmft = 2.94 \pm 3.60$), with no significant difference. Only 26.6% of the mothers knew the importance of the dental visit by asking the mother when the child should visit the dentist.

The children's toothbrushing and dental caries experience are shown in Table 3. Ninety one percent of children started brushing after three years of age ($dmft = 2.75 \pm 3.57$). There was significant difference between the children whose frequency of brushing was more than 2 times a day compared with

Table 1. Descriptive Statistics: Caries Prevalence and Severity, by Age and Gender

Variables		N	Children affected (N)	Caries (%)	Mean dmft±SD	P*
Age	4 years	43	22	51.2	2.37±3.33	0.068
	5 years	36	28	77.8	3.55±3.79	
Gender	Male	42	27	64.3	2.80±3.16	0.336
	Female	37	23	62.2	3.03±4.04	

*One-Way ANOVA test: Significant difference at $P < 0.05$.

Table 2. The Relationship between Mother's Oral Health Care Knowledge and Children's dmft Index

Variables		N (%)	Mean dmft±SD	P*
Reason for brushing	Prevent caries	68 (86.1)	2.72±3.55	0.062
	More cleanliness	11 (13.9)	4.09±3.67	
Amount of toothpaste	Full	41 (51.9)	3.01±3.77	0.001
	Half	24 (30.4)	1.33±2.24	
	Pea size	14 (17.7)	2.07±2.23	
Importance of dental visit	Check-up	21 (26.6)	1.71±2.23	0.076
	For pain	58 (73.4)	3.34±3.87	
Fluoride role	Prevent caries	2 (2.5)	1.50±2.12	0.992
	I don't know	77 (97.5)	2.94±3.60	

*One-Way ANOVA Test; Significant difference at $P < 0.05$.

Table 3. Children's Toothbrushing and Dental Caries Experience

Variable		(N=79; %)*	Mean dmft±SD	P†
Age of starting brushing	2 years	7 (8.9)	4.50±3.41	0.061
	≥3	72 (91.1)	2.75±3.57	
Frequency of brushing/day	0	2 (2.56)	1	0.030†
	1	49 (62.0)	5.38±5.51	
	≥2	28 (35.4)	2.44±2.89	
Brushing assistance	No	48 (60.8)	3.41±4.039	0.043
	Yes	31 (39.2)	2.58±3.247	

*Distribution of children in the sample; †Chi square was used: Significant difference at $P < 0.05$; †Relates to comparing those who brushed one/day with those who brushed twice or more a day.

children who brushed their teeth 1 time a day ($P=0.030$). Sixty one percent of mothers did not assist their children in brushing while 39.2% do, and there was significant difference at $P < 0.05$ between the dmft index score for both children (3.41 ± 4.03 and 2.58 ± 3.24 respectively).

Table 4 illustrates the children's snacking behavior and dental caries experience. Ac-

ording to the mothers, who were asked about the frequency of sweet intake in a day and its recommended time, two of the children never consumed sweets ($dmft=1.5 \pm 0.77$), 48 children consumed sweets 1-2 times daily ($dmft=2.48 \pm 3.88$) and twenty-nine ≥3 times daily ($dmft=4.28 \pm 2.99$), with a statistically significant difference.

Table 4. Children's Snacking Behavior and Dental Caries Experience

Variables		N	With caries (%)	Mean dmft±SD	P*
Frequency of snacks	Never	2	100	1.50±0.77	0.031 [†]
	1-2	48	54.1	2.48±3.88	
	≥3	29	79.0	4.28±2.99	
Time of snacks	After meal	50	56.0	2.92±3.91	0.538 [‡]
	Between meals	27	34.2	2.81±3.05	
	Before bedtime	2	100	4.00±1.41	

Chi square was used: Significant difference at P<0.05; [†]Relates to comparing those who had 1-2 and ≥3 frequency of snacks; [‡]Refers to the comparison between the means of dmft for the three types of time of snacks.

Table 5. Children's Dental Visits and Dental Caries Experience

Variables		N	% and No of children	With caries %	Mean dmft	P*
Has the child visited a dentist?	No	33	42/79	84.7	4.41±3.90	0.006
	Yes	46	58/79	33.3	0.82±1.42	
When was the last dental visit?	>6 months	32	70/46	87.5	5.214±4.40	0.003
	<6 months	14	30/46	78.5	3.939±3.69	
Type of treatment	Examination	28	60/46	76.9	5.33±4.13	0.006
	Extraction	12	27/46	100	4.58±3.058	
	Filling	6	13/46	100	3.923±4.26	

Chi square test: Significant difference at P<0.05.

Table 5 shows the use of dental services. The mothers were asked if the child had already visited a dentist. Forty-six of the children had visited a dentist before, and 33.3% of those children had caries (dmft=0.82±1.42), while 33 of the children had not visited a dentist and 84.7% of them had caries (dmft=4.41±3.90) with a statistically significant difference (p<0.05). The answers about the last visit to the dentist revealed that most of the children had visited a dentist more than 6 months earlier (32/46), and only fourteen children had visited a dentist less than six months earlier (78.5% caries) with dmft 5.214±4.405 and 3.939±3.690 respectively, with a statistically significant difference at p<0.05. The questions showed that 28 of the children had their teeth examined and 76.9% of them had caries (dmft=5.33±4.13), 12 had teeth extracted (dmft= 4.58±3.058) and only six had fillings

(dmft=3.92 ±4.26) with a statistically significant difference at p<0.05.

Discussion

The aim of this study was to understand maternal dental health knowledge and its relation to the prevalence of dental caries in their children in Mamyzawa camp. There was no information available about the oral health, dental care practices and opinions of parents in the Mamyzawa refugees camp in Erbil especially those refugees who were living in the camp nearly for four years.

Mothers of preschool children were chosen to evaluate their knowledge about oral health. The dental status of this group of children would give information about the mothers' ability to take care of their oral health. In addition, this age is of importance in relation to caries in the primary

teeth (12). The results show that 63% of the children living in the camp had dental caries. Five-year-old children were affected by dental caries more than the 4-year-olds (but this was not statistically significant), which agrees with other studies (9, 10). This indicates the continuation of increasing dental problems with increasing age (14). This also indicates that, those children will probably have more oral problems in the future.

The mothers have poor knowledge about the reasons for tooth brushing and their children had a high level of dental caries, even with mothers who know that the reason is for more cleanliness. This result agrees with Dgheim (10) as the sample was from refugees' camp. In this case, it is obvious that there is a gap between maternal knowledge and oral hygiene practices in their children. The mothers need to be motivated to understand the consequence of this neglect which may result from their difficult life away from their home.

Most of the children in this camp were brushing their teeth using dental brush and toothpaste. The recommended amount of toothpaste needed was not known by most of the mothers. This indicates the necessity for an education program about the effect of large amounts of toothpaste, since the child may swallow it increasing the risk for dental fluorosis (15). In general, the mothers do not know that they should visit the dentist regularly for a check-up. This also agrees with other researchers' findings (9, 10). Only two of the 79 mothers knew the role of fluoride (2.5%), making the education essential to increase the caregivers' knowledge in the camp.

More than 91% of the children started brushing after 3 years of age and the frequency of brushing was once daily in more than half the children. In addition, 60% of the mothers did not know that they should assist their children in brushing their teeth, which agrees with a Saudi Arabia study

which showed the importance of assisting the child during brushing (16).

Children's snacking behavior revealed that they had poor dietary habits, which is likely to have a negative effect on their dental health. Most of the children consume snacks ≥ 3 times daily and had $dmf = 4.28$, which agrees with other studies (10, 17). Other factors such as mother's caries and early cariogenic feeding habits may be the reason why some children with low sweet consumption still have dental caries (11).

In general, most of the families in this camp only seek dental services when the child is in pain. Forty-two percent of the children had not visited a dentist ($dmft = 4.41 \pm 3.90$) and their caries experience was statistically significantly greater than that of those children who had visited a dentist. The other possible reason for the higher caries is the irregular visits to the dentist. Moreover, the most frequent service provided was examinations only, where 76.9% of them had caries, this agrees with the research conducted in a Palestinian refugee camp in Lebanon (10).

Refugees are vulnerable populations who have less chance of access to dental care because they lack a voice to speak up about what they need, and this can lead to increased risk of problems in their general health as well as oral health (1). Refugees have low economic status (7). In research about refugees' life, it was suggested that when refugees socialize with the citizens of the country in which they live, they have better access to dental services (18). Therefore, living in a camp can affect the lifestyle of the refugees (19). Refugee parents require applicable and valuable oral health education that recognizes their particular social health beliefs (4). In Iraq, dental services are very cheap in government health centers and can be accessed by poor people, in contrast to industrialized countries, such as Canada (20). Private dental universities also

provide dental services at affordable prices; however, transportation is expensive which can be considered as an obstacle against utilizing the dental services by those refugees who live in the rural area of Erbil City. The results of this study show that the refugees in the current study need motivation and education in oral health care. In addition, the researchers suggest that there is a need for representatives, experts, scholars, and other sponsors to work to improve the oral well-being of refugees (21). Primary care physicians can have an important role in improving new refugee oral health by educating them about individual oral hygiene practices, the benefit of fluoride, and necessity of using preventive oral health services. In addition, the supervision by those physicians can often enable recommendations of dental services for the start of oral health care (22). In a review about maternal and child oral health in the Middle East, the authors concluded that implementing theory-driven oral health promotion programs, authorizing healthcare staff with oral health promotion tools will permit for timely access to preventive oral health treatment among mothers and children (23).

Limitations of the Study

Limitations of the study including lack of generalizability to other situations, limited to the age group studied, no inter-examiner reliability in the collection of data and, due to the cross-sectional study design, one cannot infer cause and effect.

Conclusions

This survey revealed that the mothers living in Mamyzawa camp have little knowledge of oral health and how to care for the dental health of their children. The main factors associated with the high prevalence and severity of caries as measured by the number

of decayed, missed and filled primary teeth (dmf) are the frequency of brushing, frequency of sweet consumption, brushing assistance, and irregular dental service usage. The researchers in this study suggest that these refugees need intensive oral health care, which should include scheduled oral examinations, treatment, oral health education and monitoring to influence health plans and programs in this camp. In addition, the mothers require an educational program on oral and dental health.

What Is Already Known on this Topic:

Refugees are a vulnerable population, lacking a voice to express what they need. The refugees in the Mamyzawa camp have lived for four years in this camp and they need intensive health care.

What this Study Adds:

The oral health status of the children in the camp was assessed by this study, in addition to the oral health knowledge of their mothers. This study revealed that the dental health of the preschoolers in this camp is poor, and there is a low level of dental knowledge.

Acknowledgments: The researchers would like to acknowledge the research assistants; Saya Hadi Rauf, Jwan Aras, Jwana Majid and Zhakaw Amang for their help in collecting data during the study. We acknowledge Tishk International University for the financial support for this study. Thanks to THD-Italy for their help in recruiting and directing the refugees during the study.

Authors' Contributions: Conception and design: RFK and BRN; Acquisition, analysis and interpretation of data: BRN, RFK and LDF; Drafting the article: BRN and LDF; Revising it critically for important intellectual content: BRN and RFK; Approved final version of the manuscript: BRN, RFK and LDF.

Conflict of Interest: The authors declare that they have no conflict of interest.

References

1. Olshansky E. The use of Community-Based Participatory Research to understand and work with Vulnerable Population. In: de Chesnay M, Anderson B, editors. *Caring for the Vulnerable*. 4th edition. Burlington, MA: Jones and Bartlett Publishers, LLC; 2016. p. 269-75.

2. Moallemi S, Virtanen Z, Ghofranipour JI, Murto-maa H. Influence of mothers' oral health knowledge and attitudes on their children's dental health. *Eur Arch Paediatr Dent*. 2008;9(2):79-83.
3. Sarnat H, Kagan A, Raviv A. The relation between mothers' attitude toward dentistry and the oral status of their children. *The AAPD*. 1984;6(3):128-31.
4. Riggs E, Gibbs L, Kilpatrick N, Gussy M, van Gemert C, Ali S, et al. Breaking down the barriers: a qualitative study to understand child oral health in refugee and migrant communities in Australia. *Ethn Health*. 2014;20(3):37-41.
5. Oliveira LB, Sheiham A, Bonecker M. Exploring the association of dental caries with social factors and nutritional status in Brazilian preschool children. *Eur J Oral Sci*. 2008;116(1):37-43.
6. Kilpatrick N, Neumann A, Lucas N, Chapman J, Nicholson J. Oral Health Inequalities in a National Sample of Australian Children Aged 2-3 and 6-7 Years. *Aust Dent J*. 2012;57(1):38-44.
7. Prowse S, Schroth RJ, Wilson A, Edwards J, Sarson J, Levi, JA, et.al. Diversity Considerations for Promoting Early Childhood Oral Health: A Pilot Study. *Int J Dent*. 2014;175084.
8. Evans CA, Kleinman DV. The Surgeon General's report on America's oral health: opportunities for the dental profession. *J Am Dent Assoc*. 2000;131(12):1721-8.
9. Israel BA, Schulz AJ, Parker EA, Becker AB. Review of community-based research: Assessing partnership approaches to improve public health. *Annu Rev. Public Health*. 1998;(19):173-202.
10. Dgheim T, Badr S, Ragab H. Relationship between caries experience and mothers' dental care knowledge and attitude among Palestinian refugees in Lebanon. *IAJD*. 2016;6(3):119-25.
11. de Silva-Sanigorski A, Ashbolt R, Green J, Calache H, Keith B, Riggs E, et. al. Parental self-efficacy and oral health-related knowledge are associated with parent and child oral health behaviors and self-reported oral health status. *Community Dent Oral Epidemiol*. 2012;41(4):1-8.
12. World Health Organization. Oral Health Surveys. Basic Methods. Design of an oral health survey, index ages and age groups. 5th ed. Geneva: WHO; 2013. [cited Dec 2019]. Available from: https://apps.who.int/iris/bitstream/handle/10665/97035/9789241548649_eng.pdf;jsessionid=CFC23471D0113CC209735222FD9CA547?sequence=1.
13. Eklund SA, Moller IJ, LeClercq MH, World Health Organization, The Oral Health Programme. Calibration of examiners for oral epidemiologic surveys. Geneva: WHO; 1993.
14. Mahejabeen R, Sudha P, Kulkarni SS, Anegundi R. Dental caries prevalence among preschool children of Hubli: Dharwad city. *J Indian Soc Pedod Prev Dent*. 2006;1;24(1):19-22.
15. Kanduti D, Sterbenk P, Artnik, B. Fluoride: a review of use and effects on health. *Mater Socio-Medica*. 2016;28(2):133-7.
16. Al-Malik M, Holt R, Bedi R. Prevalence and patterns of caries, rampant caries, and oral health in two- to five-year-old children in Saudi Arabia. *J Dent Child*. 2003;70(3):235-42.
17. Hashim R, Williams SM, Thomson WM. Diet and caries experience among preschool children in Ajman, United Arab Emirates. *Eur J Oral Sci*. 2009;117(6):734-40.
18. Maserejian N, Trachtenberg F, Hayes C, Tavares M. Oral Health Disparities in Children of Immigrants: Dental Caries Experience at Enrollment and during Follow-Up in the New England Children's Amalgam Trial. *Am J Public Health*. 2008;68(1):14-20.
19. Bhalla A, Lapeyre F. Social Exclusion: Towards an Analytical and Operational Framework. *Dev Change*. 1997;28(3):413-33.
20. Ghiabi E, Matthews DC, Brilliant MS. The oral health status of recent immigrants and refugees in Nova Scotia, Canada. *J Immigr Minor Health*. 2014;16(1):95-101.
21. Keboa MT, Hiles N, Macdonald ME. The oral health of refugees and asylum seekers: a scoping review. *Global Health*. 2016;12(1):59.
22. Cote S, Geltman P, Nunn M, Lituri K, Henshaw M, Garcia RI. Dental caries of refugee children compared with US children. *Pediatrics*. 2004;114(6):e733-40.
23. Abuhaloob L, MacGillivray S, Mossey P, Freeman R. Maternal and child oral health interventions in Middle East and North Africa regions: a rapid review. *International Dental Journal*. 2019;69:409-18.

Degloving Injury of the Lower Extremity: Report of Two Cases

Alexandros Kyriakidis¹, Ioannis Katsaros¹, Evangelos Vafias¹, Loukas Agorgianitis¹,
Vladimiro Kyriakidis¹, Athanasios Zacharopoulos²

¹Department of General Surgery, General Hospital of Amfissa, Amfissa, Greece, ²Department of Orthopedic Surgery, General Hospital of Amfissa, Amfissa, Greece

Correspondence:

gikats13@gmail.com
Tel.: + 30 6970 801 235
Fax.: + 30 2265 022 086

Received: 18 February 2019; Accepted: 18 September 2019

Abstract

Objective. The aim of our article is to highlight the importance of the immediate treatment of lower extremity degloving injuries, in order to prevent complications. **Cases Presentation.** Here we present two cases of degloving injury of the lower extremity, both resulting from motorway accidents. The first one concerned a 65-year-old man suffering from multiple limb fractures and a degloving injury of the right thigh, which was immediately treated with extensive debridement and primary full-thickness skin graft re-approximation. The second case involved a 63-year-old woman who presented with cervical vertebrae fractures and a degloving injury of the left posterior leg, which, due to the severity of her condition, was treated with a delayed approach resulting in skin necrosis, which required surgical debridement, alginate dressing and foam cover. **Conclusions.** The optimal approach to treatment of degloving injuries is challenging and they warrant immediate surgical attention. An early diagnosis and the evaluation of tissue viability are important in order to prevent limb-threatening situations.

Key Words: Degloving Trauma ■ Tissue Injury ■ Skin ■ Reconstructive Surgery.

Introduction

Degloving injuries are when skin or underlying tissues are stripped from the respective bone structures. They are usually a result of traumatic road accidents, wringer or industrial roller injuries. The lower and upper extremities are the most common sites (1, 2).

The skin often remains intact and the limb assimilates a “fluid-containing bag”, due to the presence of an extensive hematoma between the skin and the underlying fascia (compartment syndrome) (3). In the case of skin damage, a full-thickness skin graft is observed (4). In both cases the large regional vessels may be injured, resulting in capillary bed impairment (5). Edema formation also plays a very important role, as it increases the tissues’ oxygen demands in order to diffuse the functioning capillaries (6, 7). These incidents warrant proper surgical management in order to prevent massive sloughing.

The objective of our article is to point out the necessity of a prompt approach to these injuries in order to secure the viability of the lower limb and prevent complications.

Cases Presentation

Presentation of both cases was conducted according to the CARE Guidelines (Consensus-based Clinical Case Reporting Guideline Development) and the patients’ informed consent was obtained (8).

Case 1

A 65 year-old male patient was admitted to our hospital following a high-speed road accident on his motorbike. He was suffering from an open (grade I) fracture of his right distal radius and ulna, a right femoral diaphyseal fracture, as well as a large degloving injury of his right thigh (Figure 1). The injured lower limb presented in external rotation and was shorter than the other one. The degloving injury covered a triangular region extending from the perineum (medially) to the greater trochanter (laterally) and the middle of the anterior surface of the femur (inferiorly). It was accompanied by edema and erythema, but there was no active bleeding.

The patient was immediately transferred to the operating theater. Under general anesthesia extensive debridement of the injured lower limb took place, by removing the subcutaneous fat from the damaged skin and applying it as a free graft. The femoral fracture was stabilized using external fixation. Furthermore, the right forearm fracture was also stabilized utilizing an external fixation. During a 2-month follow-up period, the pa-



Figure 1. Degloving injury of the right thigh.

tient showed no signs of infection, no skin necrosis at the degloving injury site, and the patient was able to move using a cane.

Case 2

A 63-year-old female patient was transferred to our emergency department after a car accident. She suffered from multiple fractures of the C6 and C7 vertebral bodies and spinous processes, and an extensive degloving injury of the left posterior leg extending from the popliteal fossa to the middle of the gastrocnemius muscles (Figure 2a). Additionally, hematomas of the left scapular region and the left temporal region were recorded.

The patient was initially evaluated and treated for her cervical and cranial injuries. Following that (after five hours), the lower limb wound was approximated using simple sutures. After three days, full-depth dermal necrosis at the site of the degloving injury was noted and thorough surgical debridement followed. The patient was treated after-



Figure 2a. Degloving Injury of the Posterior Left Leg.



Figure 2b. Degloving Injury of the Posterior Left Leg – 3 months following treatment.

wards using an alginate dressing and foam cover. After a three-month follow-up period the degloving injury was almost completely healed (Figure 2b).

Discussion

Skin is the most extensive organ of the human organism and plays a multifunctional role (excretory, protective, sensory and temperature regulation). It can be damaged in multiple ways, including direct trauma, stretching, degloving and undermining during an operation (9). In the case of a firm and violent pull, skin may be peeled back over the underlying tissues, resulting in degloving injuries (9).

Depending on the extent of the damage, a wide variety of reconstructive surgical techniques are available for tissue repair. Yan et al. propose three patterns of degloving injury (a. purely degloving injury, b. degloving injury with involvement of deep soft tissues, c. degloving injury with deep bone fractures) and adjust their treatment approach accordingly (10). An immediate full-thickness skin graft after an extensive debridement is considered a feasible treatment approach even in elderly patients, in the case of non-extensive injuries (10, 11). If the skin is intact, it can be de-fatted and re-applied immediately as a full thickness graft (12). In the case of skin damage, split skin grafts can be retrieved and used immediately if the wound site is suitable. These grafts can also be stored for a secondary procedure 1 to 2 weeks following the injury. Securing or even restoring the extremity's sensibility is a challenge for the operating team. Suturing injured nerves can be tricky, and even when careful primary nerve anastomosis is achieved, the results are often unsatisfactory, probably as a result of the mechanism of the nerve injury (13).

As far as soft tissue elements are concerned, an initial evaluation of their viability is crucial. This will guide the debridement and determine whether primary closure or immediate reconstruction are feasible. Direct observation is always a useful tool in this direction. Skin with rapid capillary refill, bleeding edges and good colour is most likely to be viable. It is therefore recommended that thorough debridement of all non-perfused, non-viable tissues be performed immediately, in order to avoid the development of sepsis. Any damaged muscles should be resected to prevent the sequelae of severe myonecrosis or acute tubular necrosis. Denuded areas should be temporarily covered with either moistened dressings, xenografts or both. Reconstructive procedures, if needed, should be guided by the condition of local tissues. The treatment goal should be wound coverage with a pliable, sensitive, and cosmetically similar tissue that will allow early mobilization. In the case of an open injury, all the appropriate protective measures must be taken in order to prevent serious life-threatening infections, such as tetanus and gas gangrene (4).

Conclusions

Degloving injuries are very serious and potentially limb-threatening soft tissue lesions. They are usually the result of high-energy accidents. They may impair the skin and underlying soft tissues, rendering the human organism defenseless and vulnerable to soft-tissue necrosis. The treatment approach depends on the time of diagnosis and the extent of tissue injury. In the early stages and with good soft-tissue condition, immediate re-application of a full thickness graft is the treatment of choice. In later stages, a more reconstructive approach should be followed in order to counter contamination and inflammation of the surrounding tissue.

What Is Already Known on this Topic:

Degloving injuries involve skin and underlying tissues being stripped from their respective bone structures. Various techniques have been described for their treatment extending from initial debridement and full thickness graft re-appliance to extensive reconstructive operations.

What this Case Adds:

An immediate surgical approach is vital in order to secure the optimal functional and aesthetic result to the affected area. A delayed approach can lead to limb-threatening complications.

Authors' Contributions: Conception and design: AK and AZ; Acquisition, analysis and interpretation of data: IK, EV and LA; Drafting the article: IK, EV and LA; Revising it critically for important intellectual content: AK, IK and AZ; Approved final version of the manuscript: AK, IK, EV, LA, VK and AZ.

Conflict of Interest: The authors declare that they have no conflict of interest.

References

1. Khan AT, Tahmeedullah, Obaidullah. Degloving injuries of the lower limb. *J Coll Physicians Surg Pak.* 2004;14(7):416-8.
2. Lim SM, Lee ST. The pattern and management of traumatic soft tissue injuries of the lower limb. *Ann Acad Med Singapore.* 1982;11(2):145-53.
3. Waikakul S. Revascularization of degloving injuries of the limbs. *Injury.* 1997;28(4):271-4.
4. Yuan K, Zhao B, Cooper T, Jin Z, Zhou X, Chen X, et al. The management of degloving injuries of the limb with full thickness skin grafting using vacuum sealing drainage or traditional compression dressing: A comparative cohort study. *J Orthop Sci.* 2019.
5. Graf P, Biemer E. Degloving injuries of the soft tissues of the heel. An indication for microvascular revascularization! [in German]. *Chirurg.* 1994;65(7):642-5.
6. Huemer GM, Schoeller T, Dunst KM, Rainer C. Management of a traumatically avulsed skin-flap on the dorsum of the foot. *Arch Orthop Trauma Surg.* 2004;124(8):559-62.
7. Yang SC, Su JY, Yu SW, Tu YK. Retrograde tibial nail for femoral shaft fracture with severe degloving injury. *Chang Gung Med J.* 2004;27(6):454-8.
8. Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D, et al. The CARE guidelines: consensus-based clinical case reporting guideline development. *BMJ Case Rep.* 2013;2013.
9. Weinand C, Prommersberger KJ, Hahn P, Giunta RE, Krimmer H. Strategy for defect coverage in extensive degloving and crush injuries of 4 fingers [in German]. *Handchir Mikrochir Plast Chir.* 2000;32(6):424-9.
10. Yan H, Gao W, Li Z, Wang C, Liu S, Zhang F, et al. The management of degloving injury of lower extremities: technical refinement and classification. *J Trauma Acute Care Surg.* 2013;74(2):604-10.
11. Jeng SF, Hsieh CH, Kuo YR, Wei FC. Technical refinement in the management of circumferentially avulsed skin of the leg. *Plast Reconstr Surg.* 2004;114(5):1225-7.
12. Lin GT. Bone resorption of the proximal phalanx after tendon pulley reconstruction. *J Hand Surg Am.* 1999;24(6):1323-6.
13. Muneuchi G, Suzuki S, Ito O, Saso Y. One-stage reconstruction of both the biceps brachii and triceps brachii tendons using a free anterolateral thigh flap with a fascial flap. *J Reconstr Microsurg.* 2004;20(2):139-42.

An Unusual Bilateral Duplication of the Suprascapular Vein and Its Relation to the Superior Transverse Scapular Ligament Revealed by *Anatomage Table*

Eleni Panagouli, Alexandra Tsirigoti, Georgia Kotsira, Theano Demesticha, Panagiotis Skandalakis, Theodore Troupis, Dimitrios Filippou

Department of Anatomy and Surgical Anatomy,
Medical School, National and Kapodistrian
University of Athens

Correspondence:

eleni72000@yahoo.gr

Tel.: + 30 210 746 2394

Fax.: + 30 210 746 2398

Received: 21 July 2019; Accepted: 28 December 2019

Abstract

Objective. The aim of our paper is to present a rare variation of the suprascapular vein, its incidence and clinical significance. **Case Report.** A rare case of a double suprascapular vein was observed in a digitalized human cadaver on *Anatomage Table 5.0*. The vein divided into two branches, one passing over the transverse scapular ligament, while the other one coursed underneath the ligament, inside the notch. **Conclusion.** This variation has major clinical importance as it is associated with the appearance of Suprascapular nerve entrapment syndrome.

Key Words: Suprascapular Artery ■ Scapular Notch ■ Suprascapular Nerve ■ Transverse Scapular Ligament ■ 3D Anatomy.

Introduction

In most cases, the Suprascapular vein (SV) passes through the base of the posterior triangle of the neck, and drains into the

external jugular, which is a branch of the subclavian vein (1). In the middle half of the superior border of the scapula, the SV is usually accompanied by the suprascapular artery (SA). Most commonly, both the artery and the vein pass above the superior transverse scapular ligament (STSL), while the suprascapular nerve (SN) passes through the foramen formed by the STSL (1, 2). The suprascapular nerve derives from the superior trunk of the brachial plexus, passes through the suprascapular notch, under the STSL and ends at the infraspinatus fossa (3). According to the literature, the location of the SA, SN and SV seems to be highly variable, presenting different patterns (3), with multiple veins being reported in 21.3% of cases (4).

The aim of our paper is to present an interesting clinically significant variation of the SV which to our knowledge has only been presented in one study in the available literature (3). Additionally, the novelty of the case is that it was revealed in a digitalized human cadaver on *Anatomage Table 5.0*.

Case Report

An electronic anatomical review was performed on digital cadavers included in *Anatomage Table 5.0*. *Anatomage Table 5.0* is an advanced 3D anatomy visualization

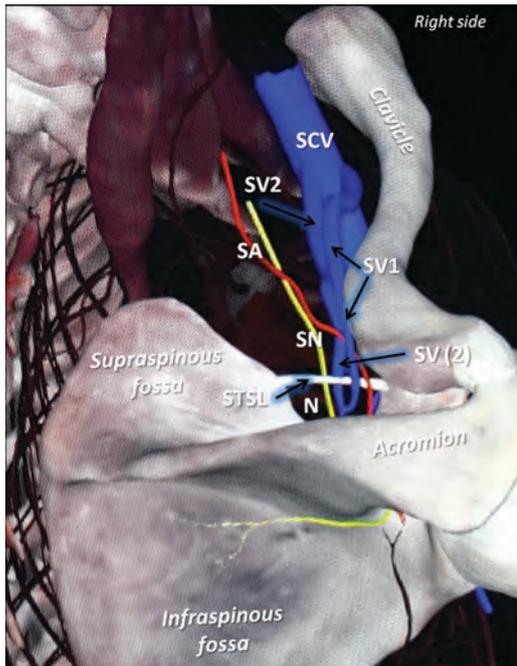


Figure 1. Right side: The suprascapular vein (SV) divided into two branches, one (SV1) passing over the superior transverse scapular ligament (STSL) with the suprascapular artery (SA), and the other (SV2) below the ligament, inside the notch (N), together with the suprascapular nerve (SN). Both of them drain into the subclavian vein (SCV). Figures are published with the permission of Anatomage Inc.

system developed for educational purposes, which has been adopted by many of the world's leading medical schools and institutions. According to the description of the product and its creators, *Anatomage Table 5.0* is the only fully segmented real human 3D anatomy system. Users are able to visualize anatomy exactly as they would on a fresh cadaver. Individual structures are reconstructed in accurate 3D, resulting in an unprecedented level of real accurate anatomy, dissectible in 3D. Anatomy is presented as a fully interactive, life-sized touch screen experience. The *Anatomage Table 5.0* contains three digitalized cadavers, specifically a Korean female who died of pneumonia (gastric cancer), a Caucasian male sentenced to death and diagnosed with a brain tumor, and a Korean male who died from respiratory complications, while being treated for acute leukemia.

In the present case, we discovered a bilateral case of a double SV in the Korean female cadaver, who contracted her disease at the age of 26. The SV was divided in two branches on both sides, one passing over the

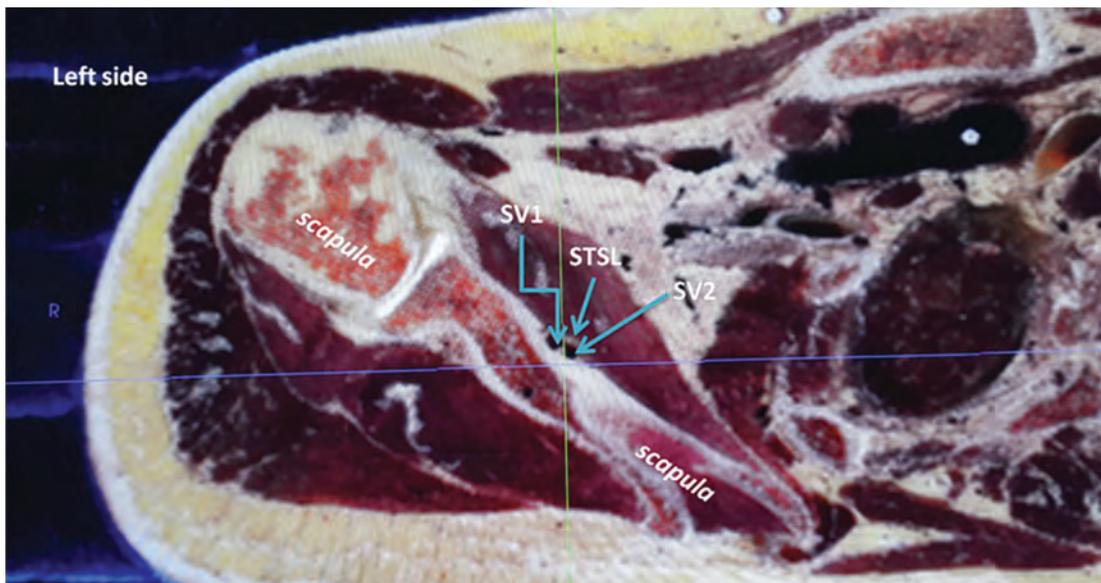


Figure 2. Left side: Cross section - Double suprascapular vein (SV), the one (SV1) passing over the superior transverse scapular ligament (STSL) and the other one (SV2) inside the notch. Figures are published with the permission of Anatomage Inc.

STSL, together with the suprascapular artery, while the other one coursed underneath the ligament, inside the notch, accompanying the SN (Figure 1, 2). The two branches drained independently into the subclavian vein, one at the anterior and the other at the posterior aspect of the vein (Figure 1). The SA and nerve followed the typical course on both sides. We did not observe other artery or vein variations in the shoulder region.

Discussion

The SV presents major deviations in its course and number, according to the available literature. The vein may be duplicated in some cases (2.4% - 19.8%) and triplicated in others (1.98%) and it might pass above or below the STSL (variable incidence) (3, 4). Two major studies have been conducted on the SV's pattern (3, 4). Yang et al. in their study performed an anatomical examination of 103 cadaveric shoulders from 55 Korean cadavers (53 right shoulders, 50 left shoulders including 28 males and 27 females; mean age, 70.4 years; range, 36–94 years) (3). In all cases, a single artery and nerve were mentioned, whereas the number of the SVs

varied, 19.4% of them being double and 1.9% triple (3). Apart from two rare cases in which the ligament or the ossified bridge was absent (thus a total of 101 STSLs were studied), in all the other cases the SN passed under the STSL (101/103, 95.4% of the shoulders). The arrangement of the vessels in the suprascapular notch varied (Table 1).

Yang et al. classified the location of the suprascapular vessel into three types: Type I (59.4% of the cases) where all suprascapular vessels pass above the STSL, Type II where the vessels cross over and under the STSL (29.7%) and Type III (10.9%) where the suprascapular vessels pass below the suprascapular ligament or bony bridge (3). In Type II four subtypes were mentioned. Our case corresponds to subtype IIa (10/101 shoulders, estimated according to Yang et al. up to 9.9%) where the SA runs above the STSL and the SV is divided, with the two branches crossing simultaneously above and below the ligament.

Polguy et al. presented a new classification of the suprascapular vessels at the suprascapular notch region, after examining 106 formalin-fixed cadaveric shoulders (55 right, 51 left) (4). In all the shoulders (100%,

Table 1. Classification of the Course of Suprascapular Vessels

Topography of suprascapular vessels around STSL	*Cadavers=101; (%; N)	†Cadavers=106; (%; N)
All vessels above STSL	54.4 (55)	(I) 17 (18)
All vessels below STSL	9.9 (10)	(II) 12.3 (13)
Artery above and vein below STSL	2.9 (3)	(III) 61.3 (65)
Artery below and vein above STSL	10.9 (11)	–
Artery above and double vein adversarially STSL	9.9 (10)	–
Artery below and double vein adversarially STSL	3.9 (4)	–
Artery below and double vein below STSL	0.99 (1)	–
Artery and double vein above STSL	4.95 (5)	(IV) 0.94 (1)
Artery and two branches of triple vein above STSL and one branch below STSL	1.98 (2)	–
Other variations‡	–	(IV) 8.5 (9)

*Yang et al. (3); †Polguy et al. (4); STSL=Superior transverse scapular ligament; ‡Other variations refer to accessory veins cases in which the vessels passed under the anterior coracoscapular ligament.

106 out of 106 shoulders) the SN passed below the STSL. Polguy et al. classified the topography of the suprascapular vessels with reference to STSL in four types (Table 1) (4). Type IV included only two extremities (2.4%) with double SV. On the first, both branches of the double SV ran above the STSL and on the second beneath the anterior coracoscapular ligament. None of these types corresponded to our case.

The course and location of the suprascapular vessels are of major clinical significance. Suprascapular nerve entrapment syndrome (SNES) is a neuropathy caused by the compression of the SN during its course through the suprascapular notch. SNES was first described by André Thomas in 1936 and is responsible for pain and dysfunction of the shoulder girdle at a rate of 1-2% (5). This syndrome affects the infraspiratus and supraspiratus muscles, which are innervated from the SN, causing their atrophy.

According to Labertowicz et al. the occurrence of an accessory vein (double or triple vein), in cases in which the SA crosses under the STSL together with the SN, resulted in nerve damage due to blood pressure and high incidence of SNES (6). Other causes of nerve damage include traumatic injuries in the areas of the clavicle or scapula and its joints, iatrogenic injuries in the process of a surgical operation, excessive overload in athletes or physical laborers, tuberculous alterations of this area, or even systemic diseases.

Conclusion

The presence of a double SV is mentioned in only two articles (19.8% -20/101 cases in the article of Yang et al., 2.4%, 2/106 cases in the article of Polguy et al.) according to the international available bibliography. Specifically, a double SV passing adversarial to the STSL, as presented in our case, was reported only in the research by Yang et al. (Type IIa

- 10/101, 9.9%). This variation has major clinical importance as the arrangement and number of the vessels crossing through the foramen is associated with the appearance of SNES. Additionally, knowledge of the Suprascapular triad's analytic topography may prevent surgical injuries during procedures.

What Is Already Known on this Topic:

The Suprascapular vein (SV), in most cases, passes above the superior transverse scapular ligament (STSL) accompanied by the suprascapular artery (SA), while the SN passes through the foramen, formed by the STSL. Variations of the course of the SV are not rare and present important clinical significance, especially for Suprascapular nerve entrapment syndrome (SNES).

What this Case Adds:

We present a bilateral double SV, one passing over the STSL together with the suprascapular artery, while the other one courses underneath the ligament with the SN. Such an arrangement is rare, found in about 9.9% of cases. This variation has major clinical importance as the arrangement and number of vessels crossing through the foramen is associated with the appearance of SNES. Moreover, the novelty of our paper is that this variation was observed in a digitalized cadaver on Anatomage Table 5.0, the only fully segmented real human 3D anatomy system.

Authors' Contributions: Conception and design: EP and DF; Acquisition, analysis and interpretation of data: AT, GK and TD; Drafting the article EP, AT and GK; Revising it critically for important intellectual content: TT, DF and SP; Approved final version of the manuscript: EP, AT, GK, TD, TT, PS and DF.

Conflict of Interest: The authors declare that they have no conflict of interest.

References

1. Standring S, Borley NR, Collins P, Crossman AR, Gatzoulis MA, Healy JC, et al. (editors.). Gray's anatomy. The anatomical basis of clinical practice. 40th ed. Edinburgh: Elsevier; 2008.
2. Pyrgakis P, Panagouli E, Venieratos D. Anomalous Origin and Course of the Suprascapular Artery Combined with Absence of the Suprascapular Vein: Case Study and Clinical Implications. N Am J Med Sci. 2013; 5(2):129-33.
3. Yang HJ, Gil YC, Jin JD, Ahn SV, Lee HY. Topographical anatomy of the suprascapular nerve and vessels at the suprascapular notch. Clin Anat. 2012;25(3):359-65.

4. Polgaj M, Rozniecki J, Sibiński M, Grzegorzewski A, Majos A, Topol M. The variable morphology of suprascapular nerve and *vessels* at suprascapular notch: a proposal for classification and its potential clinical implications. *Knee Surg Sports Traumatol Arthrosc.* 2015;23(5):1542-8.
5. Pećina M. Who really first described and explained the suprascapular nerve entrapment syndrome? *J Bone Joint Surg Am.* 2001;83(8):1273-4.
6. Labętowicz P, Synder M, Wojciechowski M, Orzyk K, Jeziński H, Topol M, et al. Protective and Predisposing Morphological Factors in Suprascapular Nerve Entrapment Syndrome: A Fundamental Review Based on Recent Observations. *Biomed Res Int.* 2017;2017:4659761.

Eccentric Macular Hole Formation Following Successful Macular Hole Surgery

Jasmin Zvorničanin, Edita Zvorničanin, Damir Husić

University Clinical Center Tuzla, Department of Ophthalmology, Tuzla, Bosnia and Herzegovina

Correspondence:

zvornicanin_jasmin@hotmail.com

Tel.: + 387 61 134 874

Fax.: + 387 35 303 250

Received: 4 October 2019; Accepted: 28 December 2019

Abstract

Objective. Postoperative eccentric macular hole formation is a rare complication after vitrectomy with internal limiting membrane peeling for a macular hole. We report a rare case of late eccentric macular hole formation following successful macular hole surgery. **Case Report.** A 73-year old woman was referred with a long standing full thickness macular hole in both eyes. The patient underwent sequential cataract surgery, 23 gauge sutureless pars plana vitrectomy with internal limiting membrane peeling and inverted flap in both eyes. Control examination six months after the surgery revealed best corrected visual acuity of 20/40 in both eyes, complete closure of the macular hole, with retinal atrophy in both eyes. Control examination eighteen months after the surgery revealed a stable finding in the right eye and an eccentric temporal macular hole in the left eye. The patient was closely observed for one year with no signs of visual acuity reduction or macular hole changes. **Conclusion.** Postoperative eccentric macular holes may occur after a long follow up period. Most cases remain stable for a long period of time and do not require further surgical intervention. This case highlights the need for close monitoring of patients after macular hole surgery with internal limiting membrane peeling.

Key Words: OCT ■ Vitrectomy ■ Complication.

Introduction

Macular holes (MH) are defined as a retinal break in the fovea involving the partial to complete dehiscence of the neural retinal layers. Surgical treatment options for MH include: pars plana vitrectomy and intravitreal ocriplasmin application (1). Vitrectomy, with internal limiting membrane (ILM) peeling and gas tamponade has become a routine technique for MH surgery, with a postoperative closure rate of 90% (1, 2). However, macular ILM peeling has been associated with complications, including trauma to the retina, macular phototoxicity, focal retinal hemorrhages, macular edema, postoperative swelling of the arcuate retinal nerve fiber layer (SANFL) followed by dissociated optic nerve fiber layer (DONFL), foveal displacement and, in extremely rare cases, iatrogenic eccentric full-thickness retinal breaks (2).

We report a rare case of late eccentric macular hole formation following successful macular hole surgery.

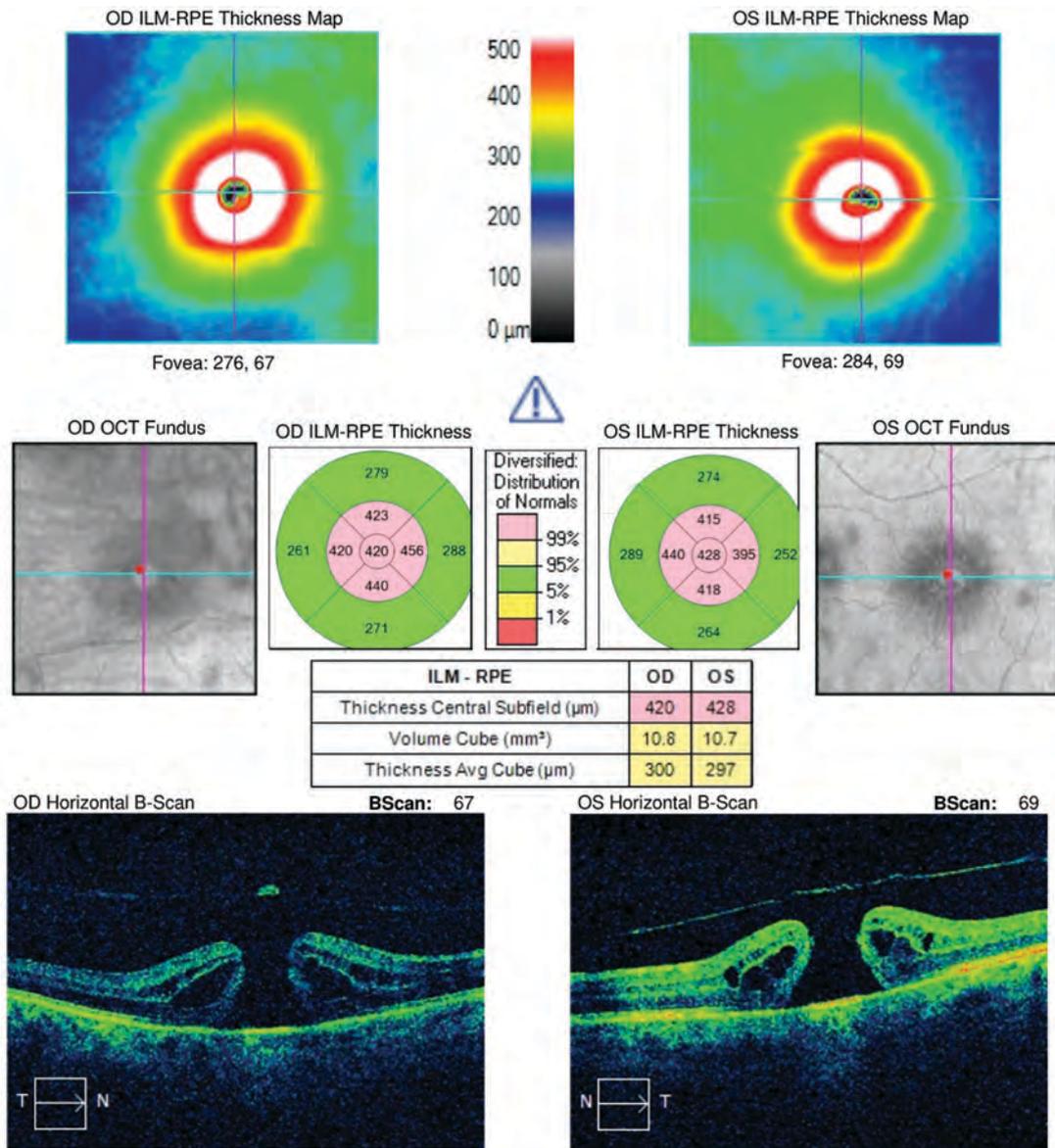
Case Report

A 73-year old woman was referred with low vision in both eyes, noted 1 year previously. Clinical examination revealed a best corrected distance visual acuity (BCDVA) of 20/400 in the right eye and 20/200 in the left one. Anterior segment examination of both

eyes showed moderate cataracts. The intra-ocular pressure measured was 15 mmHg bilaterally. Fundus examination of both eyes revealed the presence of full thickness macular holes (FTMH). Optical coherence tomography (OCT) confirmed the presence of FTMH in both eyes, with a basal hole diameter of 278 μ m in the right eye and 334 μ m in the left (Panel A). OCT images were acquired with the Cirrus HD-OCT (Carl Zeiss

Meditec, Dublin CA) using the Smart HD Cross Scan Pattern, which captures and averages 100 B-scan images with automatic centering at the fovea or region of interest. The patient was scheduled for surgical treatment of both eyes.

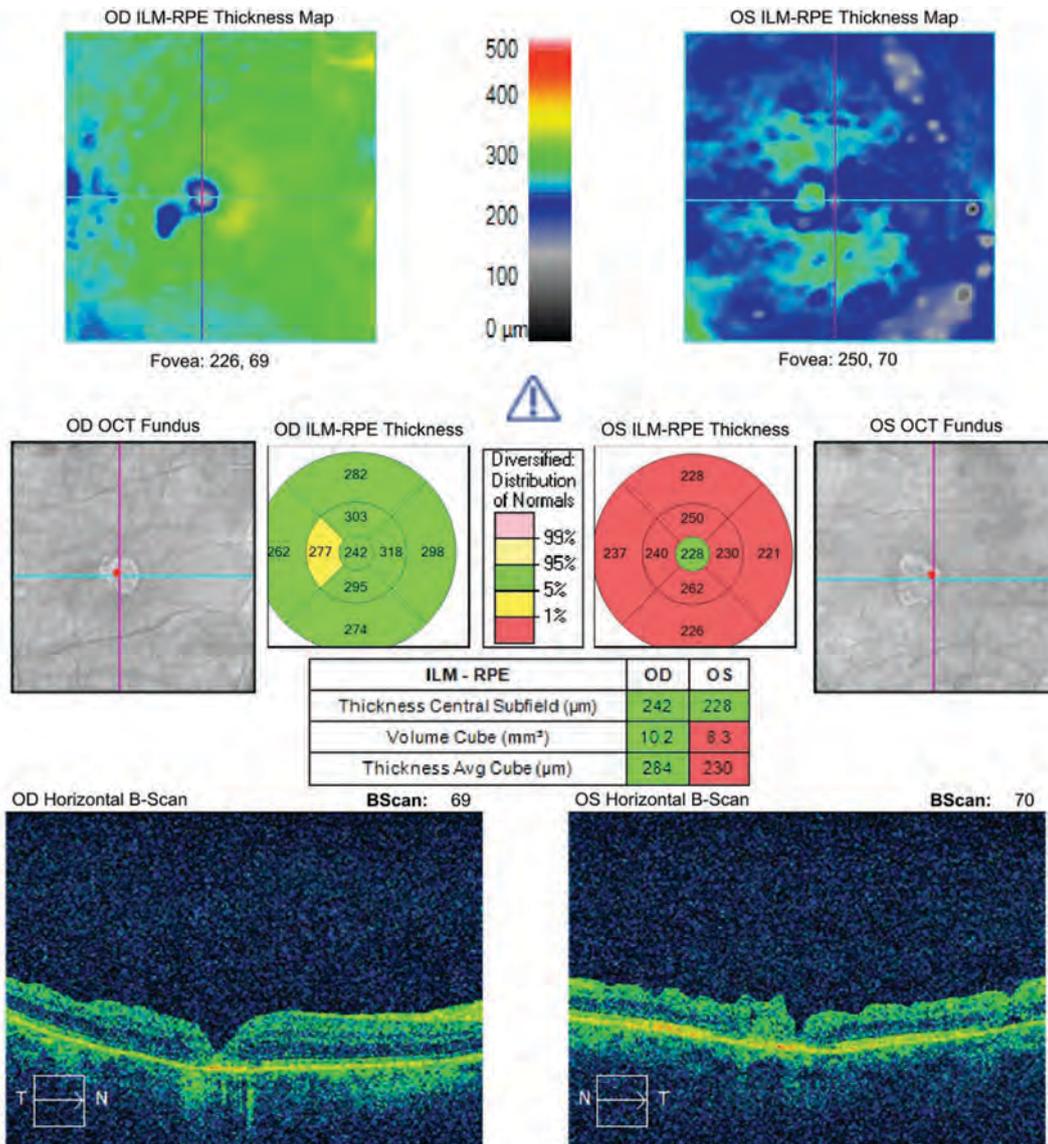
Two months after the initial examination, the patient underwent sequential cataract surgery with 23 gauge sutureless pars plana vitrectomy of both eyes in general an-



Panel A. Pre-operative OCT showing bilateral FTMH, with a basal hole diameter of 278 μ m in the right eye and 334 μ m in the left eye.

esthesia. The ILM peeling was assisted with Brilliant Peel® (Fluoron, Geuder AG Heidelberg, Germany) and performed with ILM forceps (Grieshaber, Alcon Laboratories, Inc., Fort Worth, TX). The ILM was grasped with ILM forceps and peeled off in a circular fashion for approximately 2 disc diameters around the macular hole. The ILM was not removed completely from the retina but was left attached to the edges of the MH. Periph-

eral parts of the ILM were trimmed with the vitrector, and the central part was used as a multilayer ILM flap to cover the MH. Having in mind the duration and the size of the MH, we subsequently enlarged the ILM peeling area 360° around the macula up to the vascular arcades. We used a gas tamponade with 18% Sulfur Hexafluoride (SF6), and advised postoperative face-down positioning for a minimum of 3 days. Both sur-

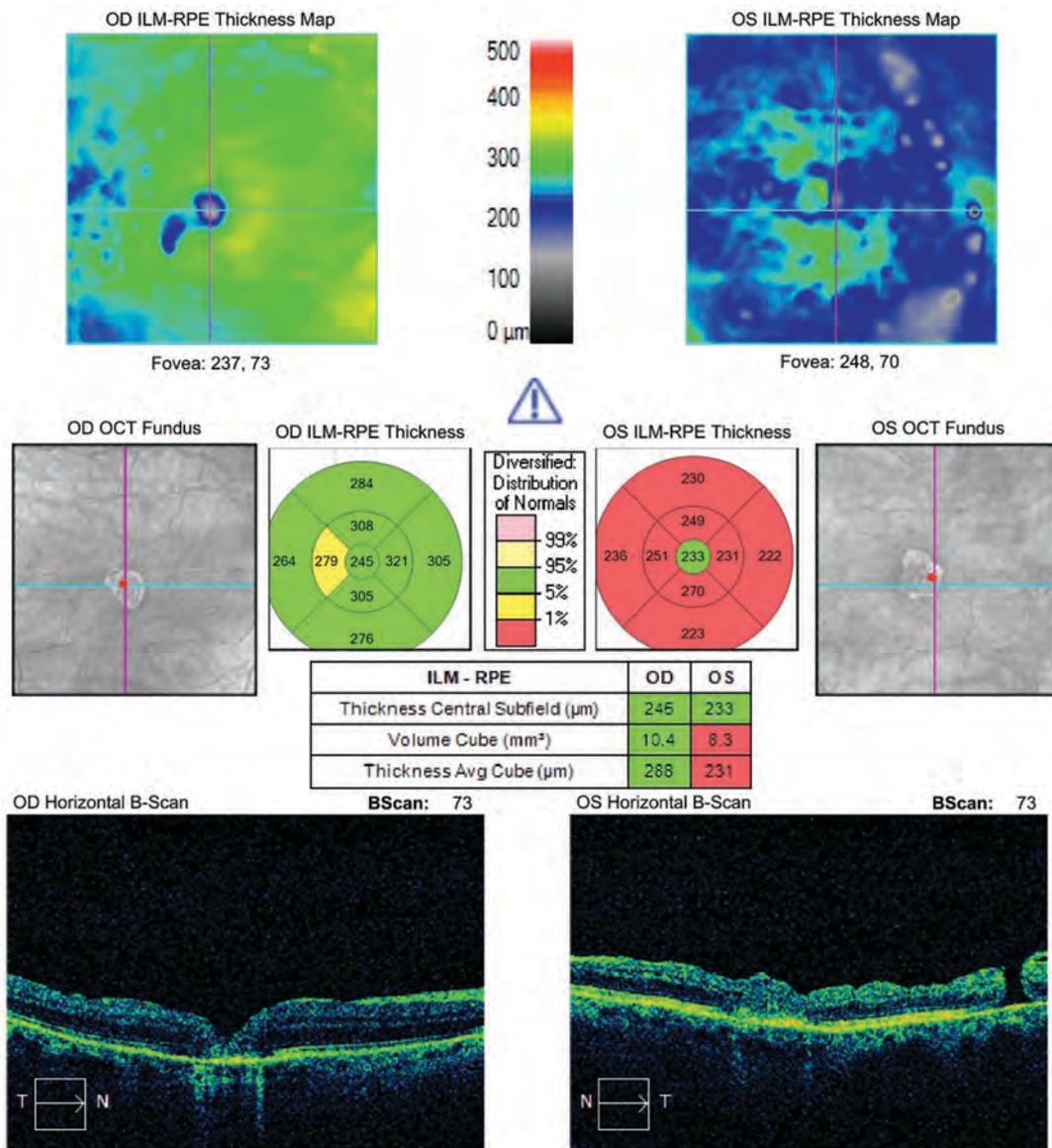


Panel B. Postoperative OCT 6 months after the surgery showing the closure of the FTMH in both eyes, with retinal gliosis in the fovea, resulting in an almost completely absent IZ with discontinuous junction of the IS/OS line and inner retina nerve fiber layer dimpling, more pronounced in the left eye.

geries were performed by the same surgeon under the same operative conditions, with the same postoperative regimen.

Gradual postoperative visual improvement was noted, and a follow-up examination six months after the surgery revealed BCDVA of 20/40 in both eyes, and best corrected near visual acuity of Jaeger 4 in both eyes. Fundus examination showed complete resolution of FTMH in both eyes, with as-

sociated macular atrophy. Control OCT examination showed complete closure of the FTMH in both eyes, with retinal gliosis in the fovea, resulting in an almost completely absent interdigitation zone (IZ) and a discontinuous junction between the photoreceptor inner and outer segment (IS/OS) line, more pronounced in the left eye. Furthermore, inner retina nerve fiber layer dimpling was present in both eyes, more pronounced



Panel C. Control OCT 18 months after the surgery showing a stable finding in the macula of the right eye, and the eccentric MH temporal to the fovea in the left eye.

in the left eye, indicating possible surgical trauma (Panel B). A follow-up examination 18 months after the surgery revealed the same BCDVA in both eyes, a stable finding in the macula of the right eye, while an eccentric temporal MH was found in the left eye (Panel C). No additional surgery was suggested at that time. Follow-up examinations, three, six and twelve months following the occurrence of the eccentric MH, showed preserved BCDVA and stable OCT findings.

Discussion

The presence of an eccentric MH is a rare finding in patients after ILM peeling, reported in less than 0.6% of cases (2, 3). Several theories have been proposed concerning the pathogenesis implicated, including induced surgical trauma, the use of intraocular dyes during the peeling, removal of the ILM layer itself inducing a weakening of retinal glial structures, and the contraction of the residual ILM (3, 4). Tangential ILM edge contracture may explain the delayed occurrence of the eccentric MH and its location at the edge of the ILM peeling area. However, we found no signs of any epimacular membrane proliferation, which could be the cause of eccentric MH formation (3, 4). Nevertheless, in our case OCT images presented significant retinal atrophy with inner retina nerve fiber layer dimpling, which suggest that mechanical surgical trauma probably played the most important role in the pathogenesis of this eccentric MH (4).

A postoperative MH may either be lamellar or full-thickness and located centrally, paracentrally, or eccentrically (4). Eccentric MHs close to the fovea are linked to poor visual prognosis as compared to more distant eccentric MHs (3, 4). Regarding further intervention, it is necessary to consider the BCDVA, the location of the MH, and its evolution in terms of size (3). In rare cases, an eccentric MH may enlarge and lead to central MH re-

opening (2, 4). In our case, no further intervention was recommended since the BCDVA and fundus findings remained stable.

Conclusion

It is important to make a detailed postoperative examination in all patients after vitrectomy with ILM peeling, regardless of the BCDVA and stable central macular finding.

What Is Already Known on this Topic:

Internal limiting membrane peeling is the standard of treatment for macular holes. Postoperative eccentric macular hole formation is a rare complication after vitrectomy with internal limiting membrane peeling for a macular hole.

What this Case Adds:

Eccentric macular holes may occur long after the internal limiting membrane peeling. Our case demonstrates how bilateral macular hole surgery in one patient can result in different postoperative findings in both eyes. Eccentric macular hole cases can be successfully managed conservatively by observation.

Authors' Contributions: Conception and design: JZ and EZ; Acquisition, analysis and interpretation of data: JZ, EZ and DH; Drafting the article: JZ and EZ; Revising it critically for important intellectual content: JZ and EZ; Approved final version of the manuscript: JZ, EZ and DH.

Conflict of Interest: The authors declare that they have no conflict of interest.

References

1. Bikbova G, Oshitari T, Baba T, Yamamoto S, Mori K. Pathogenesis and Management of Macular Hole: Review of Current Advances. *J Ophthalmol.* 2019;2019:3467381.
2. Asencio-Duran M, Manzano-Muñoz B, Vallejo-García JL, García-Martínez J. Complications of Macular Peeling. *J Ophthalmol.* 2015;2015:467814.
3. Sandali O, El Sanharawi M, Basli E, Lecuen N, Bonnel S, Borderie V, et al. Paracentral retinal holes occurring after macular surgery: incidence, clinical features, and evolution. *Graefes Arch Clin Exp Ophthalmol.* 2012;250:1137-42.
4. Brouzas D, Dettoraki M, Lavaris A, Kourvetaris D, Nomikarios N, Moschos MM. Postoperative eccentric macular holes after vitrectomy and internal limiting membrane peeling. *Int Ophthalmol.* 2017;37:643-8.

Teodora Krajewska, Official Female Doctor of Tuzla and Sarajevo: Medical Practitioner, Woman of Science, Polish Patriot and Feminist

Brigitte Fuchs¹, Husref Tahirović²

¹Department of Cultural and Social Anthropology at the University of Vienna, Vienna, Austria,

²Department of Medical Sciences of the Academy of Sciences and Arts of Bosnia and Herzegovina, Sarajevo, Bosnia and Herzegovina

Correspondence:

fuchsb196@gmail.com

Tel.: + 43 650 640 5150

Fax.: + 43 1 4277 495 33

Received: 30 November 2019; Accepted: 30 December 2019

Abstract

A biographical note on Teodora Krajewska (1854-1935) reveals the details of her life and professional activities as an Austro-Hungarian and Yugoslav health officer (*Amtsärztin*) in Tuzla (1893-1899) and in Sarajevo (1899-1923). Teodora Krajewska, née Kosmowska was the third of nine official female doctors employed by the Austro-Hungarian administration in occupied Bosnia and Herzegovina (BH: 1878-1918) and charged with the special task of popularising public health and hygiene, particularly among Muslim women. A Polish intellectual and fervent patriot from Warsaw, Krajewska had left Congress Poland as a young widow in 1883 to study medicine in Geneva, Switzerland. In 1890, she became the first woman in Europe to be employed as an assistant professor at the medical faculty of the University of Geneva but was forced to resign in 1892. In the same year, she was both awarded her doctorate and appointed to the position of an Austro-Hungarian female health officer in Tuzla. After being nationalised in Austria, she reported for duty in Tuzla in March 1893. In 1899, she accepted her transfer to a newly created position in Sarajevo where

she was active as an official physician until 1922/23. She contributed to contemporary medical science through her research on leprosy and osteomalacia in Bosnia. She returned to Warsaw in 1928 and devoted herself to the translation of Serbo-Croatian literature and writing her memoirs on her life and activities in BH.

Key Words: Teodora Krajewska ■ Female Health Officer ■ Bosnia and Herzegovina 1878–1918 ■ Tuzla ■ Sarajevo.

Introduction

After Austro-Hungarian (AH) troops occupied the Ottoman province of Bosnia and Herzegovina (BH), the local populations immediately became the target of an Austro-Hungarian civilising mission, which primarily involved the implementation of a general system of public health and hygiene and a structure of general education. In 1890, an Austro-Hungarian medical commission charged with surveying the health of BH's population recommended the government commit female health officers to the occupied territory. Their goal would be to combat epidemic and endemic diseases, particularly (endemic) syphilis, among the female Muslim population without antagonising the Muslim elite of the country. Though female physicians were not accredited in Austria, BH's governor, the Minister of Finance Benjamin de Kállay, approved of this suggestion and concerned himself personally with the

creation of positions for female health officers in the districts of Tuzla (1891) and Mostar (1892). The Austro-Hungarian administration, however, only hesitantly effectuated the plan of employing female health officers in all districts, creating further positions in Sarajevo and Banjaluka in 1899, in Travnik in 1902, and in Bihać as late as 1908.

The choice of Tuzla as the first residence of an official female doctor seems to have been related to the head of the district, Antun Vuković von Vučijidol, exhibiting a thoroughly positive attitude towards female physicians (1). The first Austro-Hungarian official female doctor in Tuzla, Anna Bayerová, however, had complained upon her arrival in 1891 that she had been equipped with neither an office, clinic or residence, nor with the (free) medication she was expected to distribute among her patients. She abandoned her office in Tuzla after three months of conflict with the local administration and resigned her service after an authorised transfer to Sarajevo where she was not permitted to practice her function.¹

In 1892, the position of female doctor in Tuzla was again advertised by the administration and, in 1892/1893, filled by Teodora Krajewska whose life, professional work in Tuzla and Sarajevo, and research activities constitute the primary concern of this paper.

Teodora Krajewska's Biography

Teodora (Theodora) Kosmowskich Krajewska is among the best-known female physicians of her time. Contemporarily, many features and portraits in newspapers and journals that concerned both her person and professional work were published in German (2-8), French (9) and Polish (10). In Poland, she is known as a Polish intellectual and female pioneer of medicine (11-13).

¹ See Dr. Anna Bayerová: The First Official Female Doctor in Bosnia and Herzegovina. *AMA*. 2019;48(1): 121-6.

Her authoritative biography, written by her nephew, Zbigniew Danielák, is included in the *Polski Słownik Biograficzny* (Polish Biographical Dictionary) (14), and she is also mentioned as a female pioneer of medicine in Laura Lynn Windsor's international *Encyclopedia* (15). She is also included in numerous collective biographies of Polish female intellectuals and physicians (16-17), and in Ctibor Nečas' monograph on the Austro-Hungarian female health officers in BH (18). She is mentioned frequently in writings on both the health-care system in BH at the time of the Austro-Hungarian occupation (19-26) and on the local Polish communities (27). She has also been featured by several writers (28, 29) and chroniclers (30) in BH.

Krajewska left an autobiographical "Diary" (*Pamiętnik*) which, in fact, she had written during her retirement in Warsaw. It predominantly contains memoirs of her medical practice in Bosnia and impressions of her childhood and youth in Warsaw under Russian rule (1). *Pamiętnik* was first edited in 1989 by the Polish historian and archivist Bogusława Czajeczka (1938-2003) who prefaced Krajewska's memoirs with a biography (12). Krajewska's memoirs reveal the deep imprint that the suppression of the Polish language in Congress Poland had left on her intellectual formation as a pupil and young woman. She remained deeply dedicated to the national cause of Poland throughout her life and sought to actively support and promote Polish compatriots and communities whenever she could and wherever she went.

Teodora Krajewska (Picture 1) was born as one of eight daughters to Ignacy Kosmowski and his wife Seweryna Głowczyński in Warsaw in 1854². She attended the II. girls' gymnasium in Warsaw, passing her school-leaving exam in 1872 'with honours' (14).

² Nečas (1992: 71) gives September 5, 1854 as the exact date of her birth; this date is quite probably confusing the dates of birth (unknown) and death (September 5, 1935).

Her father, a civil servant of the communal educational administration in Warsaw, was a supporter of the idea of women's education and of their participation in nation building. Feminism, however, was debated controversially among the Western-oriented Polish intellectuals who, as with Krajewska's family, largely shared a social background derived from the Polish *Szlachta* nobility. In 1874, Teodora qualified as a mathematics teacher and began to conduct lessons in her former school. In 1876, she married Antonín Krajewski, a philology teacher in a Warsaw boys' gymnasium, who had participated in the anti-Russian January Uprising in 1863/64 (14). The couple formed the centre of a patriotic intellectual circle until the premature death of her husband in 1880. As a young widow, Krajewska started again to work as a teacher in a private school operated by her aunts Leokadia and Bronisława Kosmowski. Her personal interests had shifted to the study of literature and she was able to publish her first literary efforts in a Warsaw newspaper in 1882 (14).

At that point, however, she had made up her plan to take up academic studies in Switzerland, though her family expected her to remarry (13). She reports that she had first considered studying philology, but her parents had convinced her to choose medicine (31). In 1883, she headed for Geneva without obtaining the financial resources which would have enabled her to survive permanently without gainful activities. At first, she enrolled at the Natural Sciences Faculty of Geneva University, becoming also one of the most active members and later the president of the Geneva based 'Société des étudiants polonais' (32).

She was awarded a Bachelor of the Natural Sciences degree in 1885, immediately thereafter enrolling at the university's medical faculty. Troubled by financial circumstances, she accepted her Polish friends' help in procuring her a grant to continue her



Picture 1. Dr. Teodora Krajewska, née Kosmowska (1893). Source: Mackiewicz, Joanna. Pierwsze kobiety z dyplomem lekarza na terenie zaborów rosyjskiego i austriackiego. *Medycyna Nowożytna. Studia nad Kulturą Medyczną*. 1999;6(2):82. Original caption: Fot. 2. Dr Teodora z Kosmovskich Krajewska. Fot. w pracowni M. Schultheisa w Tulli ok. 1893 r. (ze zbiorów rodzinnych).

medical studies. While still studying, Moritz Schiff³, professor of physiology at Geneva University, appointed Krajewska as his assistant in 1890 and, later, as head of his laboratory (14). Krajewska was therefore the first woman to ever be appointed an 'assistant professor' and soon became confronted by the animosity of male colleagues who were not ready to accept women in academic positions. Due to the pressure they exerted, she reluctantly resigned in 1892. In the same year, she was awarded her medical doctor's de-

³ Moritz Schiff (1823-1896) is a physiologist who contributed substantially to the study of the circulatory system and the action of the vagus nerve. Contemporarily, he was notorious rather than famous, as he relied on vivisection.

gree; her thesis 'Recherches physiologiques sur la reaction de dégénérescence' being awarded a first prize by Geneva University (14). In need of an income, Krajewska could not consider practising in Warsaw, because the administration of Congress Poland did not recognise foreign diplomas (1). As she reports, a Polish friend informed her of the Austro-Hungarian call for applications from fluent 'Slavic-' and German-speakers for two positions for female health officers in occupied BH. Her application proved a success due to the interventions of Polish friends on her behalf (1), and she was appointed as a female health officer of Tuzla on November 28, 1892. Before she could report for duty in Tuzla, she had to travel to Vienna where she learned that her nationalisation and the recognition of her Swiss diploma⁴ would take 'a couple of months' (1). She therefore passed her time in Vienna taking lessons in Bosnian and attending lectures as a guest at the Medical Faculty of Vienna University.

As a new Austrian and female physician, she immediately offered her support to the Austrian 'Association of Women's Advanced Education' (*Verein für erweiterte Frauenbildung*) and advocated Austrian women's right to academic studies in the Cracow daily newspaper *Nowa Reforma*. In 1894, she was a member of a delegation of Austrian women to the Minister for Cultus and Education (14). Against this background, Krajewska became the most frequently featured Bosnian female physician in the Austrian and German women's press. In Tuzla, the governor's wife, Vilma de Kalláy, née Bethlén visited her and published a report on her work among Muslim women in 1899 (6).

⁴ Danielák (1970: 102) remarks correctly that she was the first Austrian female physician because her Swiss diploma was recognized in Austria, while the Austrian authorities continued to refuse the 'nostrification' of the Swiss diplomas of both Czech domestic official physicians in BH, Anna Bayerová and Bohuslava Kecková.

Krajewska arrived in Tuzla on March 20, 1893 and was sworn into office nine days later. In the context of the creation of new positions for female health officers in 1899, she was invited to continue her work in Sarajevo. She accepted the transfer due to the chance to join the local Polish community, remarking in her memoirs repeatedly how much she had missed the company of Polish compatriots in Tuzla. Though her workload in Sarajevo was substantial, she immediately began her tireless activity for the Polish Club⁵; she gave Polish lessons to the children of the members of Sarajevo's Polish community, organised events and lectures, and collected donations at the outset of the Polish Revolution of 1905 (14).

Her social activities, however, were at no point restricted to Poland; she gave lessons in reading and writing to a young Muslim woman in Tuzla until said woman ran off to marry (1); she organised a collection of donations for the inhabitants of Travnik after the city had burnt down in 1903 (1), and she struggled for equal pay for the Austro-Hungarian female health officers, who were discriminated against considerably vis-à-vis their male colleagues (18).

She always remained in close contact with her numerous relatives and used her annual six-week leave to visit her sisters and friends in Poland. She also took repeated leaves to participate in medical and feminist conferences such as a gynaecologists' conference in Geneva in 1896, an international women's conference in Berlin, and an international medical congress in Budapest in 1909 in which she presented her research on endemic osteomalacia in Bosnia. After World War I, she hoped to return to Poland but the lack of an adequate employment op-

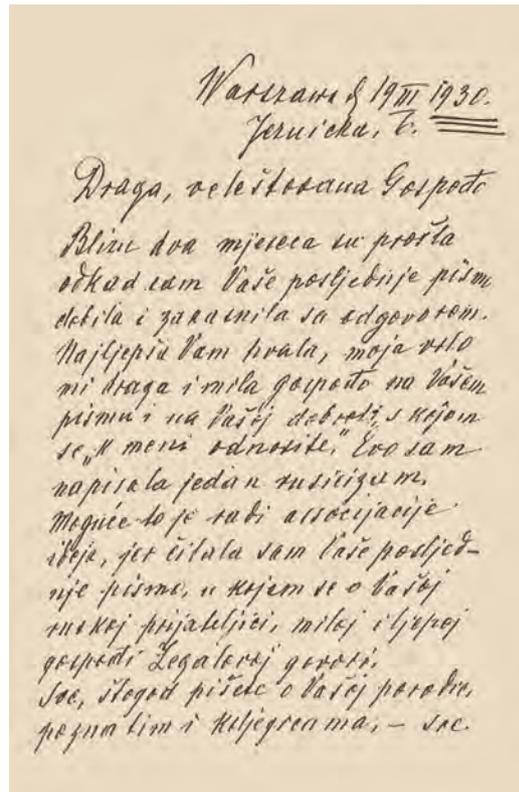
⁵ For the historical background of Polish exiles who had left partitioned Poland and founded so-called 'colonies' elsewhere, e.g. in Bosnia, see Tomasz Jacek Lis, *Polskie osadnictwo i duchowieństwo w Bośni i Hercegowinie od 1894 do 1920 roku*, Toruń 2014.



Picture 2. Dr. Teodora z Kosmovskich Krajewska's oath of allegiance to King Peter I that she will abide by the constitution and exercise her duty according to the laws and regulation of the Yugoslavian authorities.

portunity in Warsaw prompted her to stay in BH. She took the oath of office to the Kingdom of Yugoslavia on March 5, 1919 (Picture 2).

At that point, however, her sight had already deteriorated to a point that she decided to have a cataract operation in Prague. When the operation failed, she was forced to retire in 1922. Since her pension did not suffice and she had no savings she continued working as a physician in a tuberculosis clinic in Sarajevo until 1925 (12). In 1928, she finally returned to her beloved hometown, Warsaw, in the Second Polish Republic she had longed for. She, however, did not 'feel at home anymore' and her family had left for Southern Poland during the time she had been active in BH (13). She missed



Picture 3. First page of a letter by Teodora Krajewska addressed to Mrs. Milica Popovic in Sarajevo dated March 19, 1930.

Bosnia and the friends she had had to leave back there greatly and expressed her nostalgia for Bosnia in a letter to Milica Popović in Sarajevo in the spring of 1930, remarking, 'I have become deeply committed to Bosnia, country and people' (Picture 3).⁶ She started to translate Serbo-Croatian literature and published Verka Škurla-Ilijić's (1891-1971) novel *Hanumica* (1928) in the Polish weekly women's newspaper 'Bluszcz' as a special supplement.⁷ She dedicated her last years to writing her unfinished memoirs and died on September 5, 1935 in her home in Warsaw.

⁶ Letter by Teodora Krajewska addressed to Mrs. Milica Popovic in Sarajevo dated 19 March 1930 (Archives of Husref Tahirović).

⁷ The novel also became published as a book, see Werka Szkurla Ilijic; *Hanumica*, przeł. T. Krajewska, Warszawa: Towarzystwo Wyanwnicze 'Bluszcz', ca. 1928.

Krajewska's Professional Activities in Tuzla, 1893-1899

In March 1893, Krajewska finally arrived in Tuzla and introduced herself immediately to her superiors who informed her about the country and people. She was sworn into office on March 29, 1893, her status becoming permanent on September 11, 1895 (33). As compared to her Czech predecessor Anna Bayerová who had pursued the aim of being a 'female doctors for all women', Krajewska adhered to the Austro-Hungarian guidelines in caring predominantly for Muslim women and children. In 1893, when she started to practice, she treated 553 patients, 36.5% of whom were Muslims. However, the share of Muslim patients in relation to other patients was to steadily rise from that point. In 1898 she treated 607 patients, the Muslim share equalling 69% (34). Her statistics account for the treatment of 4,739 patients from March 1893 to July 31, 1899, most of whom were women and children. Nevertheless, she also treated 193 men (4%), her statistics comparatively exhibiting the highest share of adult males who had themselves treated by a female doctor (34).

From Krajewska's memoirs, it can be concluded that there was no urgent need to persuade (Muslim) women in Tuzla of the benefits of utilising public health. However, even the patients who at first were predominantly Christians consulted her in her surgery or sent for her, revealing that the policy of being treated free of charge by a female doctor introduced in 1891 had been widely accepted by 1893. She was also tasked with creating a maternity ward in the community hospital (*Gemeindespital*) established by the Austro-Hungarian military administration in 1879. Rehoused in 1886, the hospital with 30 beds and an external clinic was declared a civil public hospital in 1894 (34). Nevertheless, despite these extra responsibilities, Krajewska still continued to dutifully visit Mus-

lim families in their homes to teach Muslim women hygiene and to collect data on their living conditions. She fought against unhygienic habits such as all household members, guests and passing foreigners sharing the water pitcher (*ibrik*), towels or cutlery, and the widespread avoidance of ventilating living rooms or taking baths (35). In order to explain to people that they and their children might catch infectious diseases such as '*frenjak*' (endemic syphilis, '*frenga*'), she was also ordered to other localities of the Tuzla district (35). In 1894, the authorities assigned her to participate in combating a cholera epidemic that had spread along the railway line from Hungary via Croatia to BH.

In the annual reports on her professional activities, she criticised, in unison with Kecková in Mostar, the common diet in BH, consisting predominantly of cornmeal, 'fat meat' and 'fat milk', the excessive consumption of coffee and tobacco and the inadequate diet administered to infants and toddlers (35). However, in contrast to her Czech colleague, Krajewska did not exhibit a significant amount of sympathy for her clientele. As many Austro-Hungarians did, she disliked the existence of Slavic Muslims, and depicts poor rural Muslims repeatedly as 'beyond description' in her memoirs (1). Her dislike is particularly expressed in the way she was disgusted by the local population dressing in 'oriental' attire which she judged to be 'unhealthy' and 'ugly' (1). Moreover, she complained vehemently about the inability and/or unwillingness of her mostly poor, illiterate clients to follow her advice, considering them a class of people lacking 'intelligence' (36). On the other hand, she remarked that she much preferred to talk to members of the Muslim elite, because they were 'progressive' and 'rational'.

At an 1896 international feminist congress in Berlin, Krajewska expressed her conviction that the Austro-Hungarian Empire (AHE) had to 'import civilisation and

progress' to BH, and Bosnian women must be educated regarding hygiene 'from above' (37). While her memoirs demonstrate that she never lost her distinct class consciousness and Orientalist attitudes, they also reveal that Krajewska became thoroughly disenchanted with Austria-Hungary's policy of 'civilising' BH by 1908. At that point, she remarked that the civil officers coming to BH were, in fact, being abused by the AH authorities by contributing to a politically dubious project for little money (1). She remembered her time in Tuzla as a time of never-ending work, self-doubt, and feelings of loneliness and depression (1). When she first travelled to Sarajevo in 1898, she reports having been enthusiastic about its beauty, its urban character, its new hospital, and the presence of a Polish Club (1). Therefore, she accepted the offer to be transferred to the 1899-created position of an AH female health officer in Sarajevo without much hesitation.

Krajewska's Professional Activities in Sarajevo, 1899-1923

Krajewska was appointed the female health officer of Sarajevo on May 23, 1899 (33). After her transfer in the summer of the same year, she started to function as an official physician in Sarajevo on October 1, 1899 (34). In 1900, Krajewska – as with Bohuslava Kecková in Mostar – was appointed a school physician at the higher girls' school in Sarajevo where she gave hygiene lessons to fifth-grade students. She also taught hygiene at the Institute for Teacher Education and, later, at the local private Roman Catholic and Islamic girls' schools (18). As in Tuzla, her field of duties covered conducting clinics at the outpatient ward in the provincial hospital (*Landeskrankenhaus*) in Sarajevo where she was also involved in establishing a maternity department. She was charged with 'approaching' and visiting Muslim women in their home in order to advertise

hygiene and public health utilisation. She reported on the health and living conditions of the Muslim population in Sarajevo where she exhibited content illustrating that not only upper-class, but also middle-class Muslims had repudiated tradition (1, 36). Her memoirs contain the observation that affluent Muslim women, in fact, consulted male physicians, though in the company of a male relative who communicated with the doctor, a man who was not expected to administer any physical examinations (1). Her complaints on the 'dirt' and lack of hygiene and fresh air in the houses of poor urban and particularly rural Muslims resemble her reports on the living conditions in both Tuzla and the Tuzla district (35, 36). Her disinclination to touch poor rural women is made clear in her memoirs, in which she remarks that she had suggested the authorities assemble rural clients outdoors rather than in buildings, quite obviously because she suffered repeatedly from panic attacks when she was confronted with what she dubbed rural women's 'evaporations' (1).

In 1899, she treated no more than 128 patients in Sarajevo from October to December because the AH administration had ordered her to combat a smallpox epidemic, the focus of which was considered *Derventa*, immediately upon her starting work. She was responsible for the vaccination campaign in the districts of Sarajevo and Travnik from 1900 to 1902. In the first half of 1902, she vaccinated 2,912 people in Sarajevo and its rural surroundings (18). From 1902, she was assigned to visit the rural regions of the district in order to examine the village women for endemic syphilis. When she visited the mountainous quarters of Sarajevo or rural villages, she rode a Bosnian horse in the warm seasons but had to travel by foot or carriage during the winter (1). From 1900, she treated far more than 1,000 patients every year, more than two thirds of whom were Muslim women and children

(34). When she decided to return to Poland in 1928, the city council awarded her a prize for her many years of work as an official doctor in Sarajevo (13). Back home in Warsaw, however, she expressed her deep regret to have left Bosnia in a letter to Zdenka Marković⁸ in Zagreb: 'My work bound me to Bosnia and filled me with the enthusiasm without which I cannot live.'

Krajewska's Research and Publishing Activities

Krajewska was the first female physician in the AHE, and probably in Europe, to publish in a medical journal and participate in medical congresses. Her memoirs clearly demonstrate that she would have much preferred to keep her research position at Geneva University if she had had the choice (1). One of the research activities she pursued in BH was volunteering to document the cases of leprosy in the Tuzla district. Leprosy was considered of particular interest by the AH authorities due to fact that the Vienna School of Medicine had advanced the theory that syphilis was a transformative form of leprosy and had not been introduced as a new disease from the Americas in the 1500s, as a hegemonic French theory suggested (38). In April 1898, she received a commendation for her leprosy research (33) which, however, was not published under her name. The focus of her own research was the discovery that osteomalacia was widespread in the districts of Tuzla and Sarajevo (35, 36, 39, 40). Osteomalacia had been identified correctly as 'adult rickets' by Francis Glisson's (1597?–1677) in the 17th century but became confused with osteoporosis as a form of malacia in the 19th century, when the disease's description as a female disorder probably related to the ovaries became intensely debated.

At that point, malacia meant the advanced demineralisation of the bones that forced the diseased to crawl on all fours or to stay in bed and was frequently accompanied by 'osteomalacic cachexia' (wasting syndrome), leading to death within 6 to 10 years. In Central Europe, around 1860, this advanced form of osteomalacia was called 'puerperal' and defined as a disorder of women of child-bearing age whose condition did not remain restricted to severe pains in the costal and sacral regions as was observed in male cases. The disorder was depicted as being exacerbated by repeated pregnancies, births, and breastfeeding of infants, and was said to be accompanied by a progressive softening and deformation of the pelvis and bones in general, forensically visible in the severely deformed femurs, and a loss in body length of up to 20 centimetres or more (41). Advanced osteomalacia frequently resulted in a pelvis fracturing during childbirth and made delivery a deadly risk. The disease which was considered to occur 'rarely' and locally endemically became a vehicle to promote gynaecological surgery, from Caesarian sections to Porro operations and ovariectomies (42). However, the total number of regularly discussed single and endemic cases all over Europe between 1750 and 1900 did not exceed approximately 300 (42). Around 1900, however, the case descriptions multiplied in Austria, Hungary and particularly in BH, where Krajewska and her colleagues, Gisela Januszewska, née Rosenfeld (Banjaluka), and Bohuslava Kecková (Mostar), were confronted with the most extensive osteomalacia 'endemics' ever observed.

Krajewska reports that, on her first official trip to Zvornik, Srebrenica and Vlasenica as a female health officer, she found no less than 22 cases of osteomalacia in some mountainous rural localities and gorges. She states that male AH doctors would not have discovered them because they were not allowed to see Muslim women, who were

⁸ Zdenka Marković, Croatian writer and translator (Pozega, 10 January 1884 - Zagreb, 14 October 1974).

captive in their homes (1, 35) In 1900, Krajewska provided in 'Wiener Medizinische Wochenschrift' a case description concerning 50 occurrences of osteomalacia in the district of Tuzla (39). In 1909, she reported, at the Medical Congress in Budapest, 150 cases of osteomalacia in Sarajevo and its surrounding district, 116 of which she considered 'puerperal' (40, 36). She had found the advanced cases to occur particularly on the slopes of Mount Trebević, in the 'hills of Mahmutovac, Begovac and Berkusa', in Fojnica and in Rudo (40). She stated both in 1900 and 1909 that only Muslim women suffered from osteomalacia, though in 1901 the disease was described as also being endemic in neighbouring Croatia (43). Drawing heavily on Orientalist stereotyping, Krajewska mentioned the causes of osteomalacia as being, in addition to the 'damp climate,' 'lack of sun,' poverty, and malnutrition, 'Muslim customs' such as early marriage, veiling, extended lactation periods, and too much time indoors (35, 36, 39, 40). In 1909, she examined the hypothesis of a correlation between osteomalacia and the involuntary contraction of muscles (tetany) as another affliction occurring among poor women, predominantly in the cold season. Since tetany is, in fact, commonly caused by a deficiency of calcium, Krajewska was able to verify the thesis (40).

Following Austrian medical doctrine, Krajewska rejected the hypothesis that osteomalacia was an effect of a 'malfunction of the ovaries'. However, deviating from this doctrine, she viewed, 'gravity' and 'other functions of the sexual sphere (sexual intercourse, menstruation, lactation)' as causes of osteomalacia (39). As suggested by French and Austrian doctrines, she administered phosphorus in cod liver oil, stating that this medication was much requested even by women she saw for the first time (40). Her assumption of the exacerbation of osteomalacic suffering by the excessive sex-

ual demands of Muslim husbands was new and quite probably inspired by contemporary feminist discourse. Obviously, Krajewska drew on a pro-birth control discourse that claimed that 'hypersexual' husbands were morally responsible for the exhaustion and early death of women who had to bear numerous children (44). Marrying this to bone disease, her report on osteomalacia in Bosnia can be read as a plea for birth control, contemporaneously advocated by Neo-Malthusians, feminists, and eugenicists (45). Regarding the then controversial debate concerning osteomalacia, Krajewska's contribution, might be considered substantial, however. Based on the unprecedented number of 200 cases, she had been able to demonstrate that the softening of bones was obviously a metabolic disorder caused predominantly by malnutrition and a lack of sunlight.⁹ The latter fact became to be accepted only 10 years later, when an osteomalacia 'endemic' occurred in Vienna after World War I (42). While Krajewska's work was much quoted and highly respected in Bosnia, she felt, as Tomasz Lis states (13), ignored by the international scientific community due to her gender.

Concluding Remarks

Teodora Krajewska, née Kosmowska, a young widowed Polish intellectual from Warsaw, made the unusual decision in 1882 not to remarry but to take up academic studies in Switzerland. She studied Natural Sciences and Medicine at the University of Geneva successfully, and was appointed an assistant to Moritz Schiff in 1890. From her memoirs, it can be concluded that she appreciated her research work and hoped to be promoted as the head of Schiff's laboratory.

⁹ However, Gisela Januszewska (official female physician in Banjaluka) cared for a locally even higher number of osteomalacia patients and came to the same conclusion (46).

However, she became bullied by her male colleagues, who did not tolerate a woman in an academic position. Lacking means, Polish friends succeeded in placing her into the position of an AH female health officer in Tuzla (1892-1899) who was transferred to Sarajevo (1899-1923). While she performed her numerous duties in an exemplary manner and did not voice her bias against (poor and rural) Muslims in public, she privately expressed her antipathy to her clients due to the Social Darwinist and eugenicist attitude she had quite probably adopted as a natural scientist and feminist of her time (47, 48). Despite her substantial workload, she pursued research on ('puerperal') osteomalacia as a disorder widespread locally in BH. Her research, however, did not bring her any laurels internationally, her memoirs revealing her permanent frustration concerning discrimination against 'intelligent' women as professionals (1). Krajewska who lived and worked for 35 years in BH was, however, highly respected as an official doctor and medical practitioner in the districts of Tuzla and Sarajevo. Additionally, at the fin-de-siècle, she was the first female medical scientist in BH and in the AHE.

Authors' Contributions: Conception and design: BF and HT; Acquisition, analysis and interpretation of data: BF and HT; Drafting the article: BF and HT; Revising it critically for important intellectual content: BF and HT; Approved final version of the manuscript: HT and BF.

Conflict of Interest: The authors declare that they have no conflict of interest.

References

1. Krajewska Teodora z Kosmowskich: Diary (prepared for print by Bogusława Czajecka) [in Polish]. Cracow: Krajowa Agencja Wydawnicza; 1989.
2. Krajewska T. Letters from a Bosnian doctor [in German]. Wiener Frauen-Blatt. 1893; 17(206) and 20(207).
3. MD Theodora Krajewska [in German]. Deutsche Hausfrauen-Zeitung. 1897;24(15).
4. SR, i.e. Schoenflies R. Women's lives [in German]. Der Bazaar. Illustrierte Damen-Zeitung (Berlin). 1897;43(22):FF267-8.
5. Kuhnow A. Practicing female doctors in the present [in German]. Illustrierte Zeitung (Leipzig/Berlin). 1898;111(2872).
6. Kállay V. Female physicians in Bosnia [in German]. Frauen-Werke. 1899;6(3):4-6.
7. Brod B. A visit to MD Theodora Krajewska in Sarajevo [in German]. Dokumente der Frauen. 1901;5(8):260-4.
8. Dr. Theodora Krajewska, official female doctor in Sarajevo [in German]. Daheim. 1902;38(16):7.
9. Lipinska M. Female physicians [in French]. Revue Universelle. 1901;51.
10. Baschkopf J. Experiences from the practise of a female doctor in Bosnia [in Polish]. Nowiny Lekarskie. 1905;17(1/9):57-61.
11. Nečas C. MD Teodora Krajewska. An official female doctor in Tuzla and Sarajevo [in Polish]. Archiwum Historii i Filozofii Medycyny. 1987;50(1):75-98.
12. Czajecka B. Biography [in Polish]. In: Krajewska, Teodora z Kosmowskich: Pamiętnik (przygotowała do druku Bogusława Czajecka). Cracow: Krajowa Agencja Wydawnicza; 1989. p. 5-22.
13. Lis TJ. Teodora Krajewska – a Bosnian dr Quinn [in Polish]. [updated 2014 March 28; accessed 2019, Nov 9]. Available from: <http://o-historii.pl/teodora-krajewska-bosniacka-dr-quinn/>.
14. Danielák Z. Krajewska z Kosmowskich Teodora (1854-1935) [in Polish]. Polski Słownik Biograficzny, vol. XV. Wrocław: Zakład Narodowy Imienia Ossolińskich, Wydawnictwo Polskiej Akademii Nauk. 1970; p. 101-3.
15. Krajewska, Teodora (1854-1935). In: Windsor, Laura Lynn, editor. Women in Medicine. An Encyclopedia, Santa Barbara: Clio; 2002. p. 122.
16. Mackiewicz J. The first women with a MD diploma in Russia- and Austria-ruled Poland [in Polish]. Medycyna Nowozytna. Studia nad Kulturą Medyczną. 1999;6(2):79-98.
17. Bojczuk H. Female doctors in the Medical Society of Warsaw 1875-1939 (first part, 1875-1905) [in Polish]. Medycyna Nowozytna. 2008;15(1):139-57.
18. Nečas C. Among Muslim Women. The Female Health Officers in Bosnia and Herzegovina 1892-1918 [in Czech]. Brno: Masaryk-University; 1992.
19. Kállay V. To our women's world [in Bosnian]. Nada. 1895;1(10):188-9.
20. Weiss O, Preindlsberger J. Obstetrics – Gynaecological Division [in German]. In Jahrbuch Bosn.-Herzeg. Landesspitales in Sarajevo: Sarajevo: Landesdruckerei; 1903. p. 473-529.

21. Jeremić R. Contributions to the History of Health and Medical Opportunities in Bosnia and Herzegovina under Turkey and Austria-Hungary [in Serbian]. Beograd: Naučna Knjiga; 1951.
22. Karahasanović A. Tuzla hospital and its first doctors [in Serbian]. *Srp Arh Celok Lek.* 1958;10:1-5.
23. Azabagić S. One hundred years of health service in Tuzla [in Bosnian]. *Acta Med Sal.* 1974;3(2):5-20.
24. Berić MB. The Importance and Role of Polish Physicians in the Development of Obstetrics and Gynecology in the Yugoslav Countries by 1918 [in Serbian]. *Acta hist med stom pharm med vet.* 1986;26(1-2):63-70.
25. Ibrahimagić OC, Zukić S, Čustović A. Health Care in Tuzla and Tuzla Area in the Second Half of the Nineteenth Century. *Acta Med Sal.* 2009, 38(1):1-5.
26. Alispahić N. Theodora Krajewska: First female doctor – gynecologist in Tuzla and Bosnia and Herzegovina [in Bosnian]. [S. l. : s. n.]; 2016.
27. Lis TJ. Contribution of Poles to the modernization of Bosnia and Herzegovina during the Austro-Hungarian period (1878-1918) [in Polish]. In: *Studia Migracyjne – Przegląd Polonijny.* 2014;40(4, 154):109-24. Available from: <http://cejsh.icm.edu.pl/cejsh/element/bwmeta1.element.desklight-62e203f6-3a23-417a-b3ac-921bd4609318?q=bwmeta1.element.desklight-6de933b2-c248-43a2-9b95-001bb6f4fe6a;5&qt=CHILDREN-STATELESS>.
28. Alispahić N. A bow for Mrs. Krajewska [in Bosnian]. In: *Leda Saliniana: Kulturna hronika Tuzle.* Tuzla: Radio Kameleon; 1997. p. 424-26.
29. Markovit (Marković) Z. What we women have made to the Croatian-Polish rapprochement [in Croatian]. *Marulić.* 1976;9(4)323-38.
30. Trifković D. Polish women in Tuzla [in Bosnian] In: Trifković D, editor. *Tuzlanski vremoplov III.* Tuzla: Universal; 1988. p. 35-7.
31. Pioneers of women's academic education in Austria [in German]. In: *Jahresbericht des Vereines für erweiterte Frauenbildung in Wien*, vol. VIII, Oct. 1895-Oct. Vienna: Gebr. Hollinek; 1896. p. 38-48.
32. Mysyrowicz L. Academia and Revolution. Eastern European students in Geneva at the time of Plekhanov and Lenin [in French]. In: *Schweizerische Zeitschrift für Geschichte.* 1975;25: 514-62.
33. Dienst- und Qualifikationstabelle of Krajewska, Dr. Theodora. *Archives of Bosnia and Herzegovina.*
34. Landesregierung für Bosnien und die Hercegovina (ed): *Public Health in Bosnia and Herzegovina 1878–1901* [in German]. Sarajevo: Landesdruckerei, 1903; Table XXV, p. 400-1.
35. Krajewska Th. Annual report of the official female physician MD T. Krajewska in Tuzla for 1897 [in German]. *Wiener Klinische Rundschau.* 1898;35:566-7, 581-2.
36. Krajewska Th. Annual report of the official female physician MD T. Krajewska in Sarajevo for 1902 [in German]. *Wiener Medizinische Wochenschrift.* 1903;38:1778-82, 1829-31, 1872-6, 1926-30.
37. Krajewska Th. The experience of a female physician's in Dolnja Tuzla (Bosnia) [in French]. In: Schoenflies R, Morgenstern L et al., editors. *Der Internationale Kongress für Frauenwerke und Frauenbestrebungen in Berlin*, 10. bis 26. Sept. 1896, Berlin: Hermann Walther; 1897. p. 185-90.
38. Zeissl H. Textbook of syphilis and the related local venereal diseases [in German], vol. II, Erlangen: Enke; 1872.
39. Krajewska Th. Osteomalacia in Bosnia (district of Donja Tuzla) [in German]. *Wiener Medizinische Wochenschrift.* 1900;50: 1785-1788, 1824-8, 1893-6, 1930-15, 1982–16, 2022-4, 2074-8, 2134-8.
40. Krajewska Th. The tetany of osteomalacic women [in French]. *CVIe Congrès international de médecine Budapest, Aout-Septembre 1909 – Compte rendue*, p. 418-28.
41. Gelpke L. Osteomalacia in the valley of Ergolz [in German], Basel/Liestal: Druck von Gebr. Lüdi; 1891.
42. Fuchs B. Osteomalacia: Femininity and the “Softening of the Bones” in Central European Medicine (1830–1920). In: *Light TP, Mitchinson W, Brooks B, editors. Bodily Subjects: Essays on Gender and Health, 1800–2000.* Montreal: McGill Queen's University Press; 2014. p. 123-51.
43. Vrbanić L. Osteomalacia in Croatia [in German]. *Centralblatt für Gynäkologie.* 1901;25:1; 922-4.
44. Bergmann A. Controlling sexuality. The beginnings of modern birth control [in German]. Hamburg: Rasch & Röhring Verlag, 1992.
45. Allen AT. *Feminism and Motherhood in Western Europe 1890–1970: The Maternal Dilemma.* Basingstoke: Palgrave Macmillan, 2005.
46. Januszewska G. On Osteomalacia (including a supplement on tetany) [in German]. *Klinisch-therapeutische Wochenschrift.* 1910;17(21):503-10.
47. Valverde M. „Racial Poison“. Drink, male vice, and degeneration in first-wave feminism. In: Fletcher IC, Nym Mayhall L, Levine P, editors. *Women's Suffrage in the British Empire. Citizenship, Nation, and Race.* London/New York: Routledge; 2000. p. 33-50.
48. Richardson A. The Birth of National Hygiene and Efficiency: Women and Eugenics in Britain and America 1865–1915. In: Heilmann A, Beetham M, editors: *New Woman Hybridities. Femininity, Feminism and International Consumer Culture.* London/New York: Routledge; 2004. p. 240-62.

To Save a Corpse from Decomposition – the Purpose of Petrification in the Second Half of the 19th Century

Marta Licata¹, Chiara Rossetti¹, Chiara Tesi¹, Omar Larentis¹, Roberta Fusco¹, Rosagemma Ciliberti²

¹Centre of Research in Osteoarchaeology and Paleopathology, Department of Biotechnology and Life Sciences, University of Insubria, Varese, Italy, ²Section of Forensic Medicine and Bioethics, Department of Health Sciences, University of Genoa, Genoa, Italy

Correspondence:

marta.licata@uninsubria.it

Tel.: + 39 0332217534

Fax.: + 39 0332217534

Received: 23 February 2019; Accepted: 3 October 2019

Abstract

We present this interesting note on the petrification of corpses, published in 1890 in the Italian Journal of Natural Sciences. After a brief review of the oldest forms of embalming, the author, Michele Martone, presents petrification as the only way to obtain the perfect conservation of the corpse. **Conclusion.** This scientific note presents some considerations regarding the constant search of humanity to arrest, if not the death of a person, the decomposition of their body.

Key Words: Petrification of the Corpse ▪ Michele Martone ▪ Italian Journal of Natural Sciences.

Introduction

“Gentlemen, from today I am available to those who care about their dead, and I am sure that with an invitation, even if telegraphic, to my address, I will arrive in time

to save the spoiling of your loved ones from corruption for the total expense of 1000 Lira for my travel expenses”.

With this invitation, Professor Michele Martone, Principal of the Technical Institute of Catanzaro and then Professor of Science at the Royal Technical Institute of Reggio Calabria, closed his interesting contribution with the title *On the conservation and petrification of corpses*, published in 1890 in the Italian Journal of Natural Sciences (1). Unfortunately, we do not have biographical information about the author. Looking in the various issues of the Italian Journal of Natural Sciences, we find the name of Michele Martone only in the issue published in 1892, in which the author requested: “to exchange beetles and Lepidoptera or minerals of any kind, as well as offering birds in exchange [...], with mammals or reptiles of any kind” (1).

In his brief but interesting article, Martone recalls that there were many in the past who had speculated from ancient times in the positive sciences about how to stop the decay of corpses, furthermore reiterating that the remedies to save the dissolution of the body in the past did not care about the “flattering sentence ... let nature complete its evolution because life is born from death”. However, the constant search, since ancient civilizations, for practices aimed at preserv-

ing dead bodies from the inexorable course of the decomposition process, attests how man has always been attracted by the bodily remains of a life now over, and by the constant desire to free himself from every temporal constraint (2).

We present and discuss the article published in 1890 by Michele Martone in the Italian Journal of Natural Sciences.

Presentation and Comment on Michele Martone's Article

In particular, we would like to focus the attention of our readers on this very interesting note in which the author supported the practice of petrification by intra-arterial injection. Firstly, Prof. Martone recalls the oldest forms of embalming from reports on the mummified remains of the Egyptians, witnessed by the archaeological excavators of the Egyptian tombs, and the descriptions of Herodotus, Diodorus of Sicily and Porphyrus, who told of the Egyptian funerals and their embalming techniques (3, 4).

He recalls that in the 15th century, in the Canary Islands, the indigenous Berber Guanche people practiced embalming corpses through the evisceration of the organs. This treatment was also present among the Jews, Greeks and Romans without having, however, the same meaning that it had for the Egyptians, whose religion required of them the duty to embalm the deceased (5). He then reports that historians recalled that embalming was also practiced among the Persians, Arabs and Ethiopians for their kings, princes and magnates. Publius Papinius Statius, in some of his verses, reports how the body of the famous Alexander the Great was rubbed with honey, because this substance was attributed with the property of "not corrupting" (1, 6).

The professor also recollects that his colleague Angelo Comi, at the last medical congress held in Perugia, attributed this prop-

erty to honey because the animal substances immersed in it, after putrid fermentation, mummified naturally when exposed to the air. However, Martone argues that he himself repeated the experiment on anatomical pieces but did not obtain mummification.

In his narrow historical review, he concludes by saying that the art of embalming fell into disuse from the Roman era up to the seventeenth century when the practice of preserving the corpse was resumed for anatomical research. In particular, he cites the research of the famous Dutch anatomists Swammerdam and Ruysch. The professor recalls that from the seventeenth century onwards embalming was practiced with very different recipes, without logic, and was often ineffective. Evisceration was practiced and the tongue was removed. In this way the corpses of Henry III, the king of France, Pope Alexander VI, Louis XVIII and other well-known personalities of that time were embalmed. This system was progressively discontinued after Tranchina's discovery in 1835 in Naples. Also Gannal and Sucquet in France began to inject a liquid preserver through a main artery: "With a simple incision of about ten centimeters it is sufficient to operate to preserve the dear departed".

The method of dissection of Tranchina, Gannal and Sucquet was performed by the author who, after completion, was not satisfied with the results because it caused disfigurement (1). The author believed that the only way for conservation to be perfect and lasting was petrification. Unfortunately, the author does not mention the technique used but well distinguishes mummification and other types of embalming from petrification. In this regard, he cites Girolamo Segato and Paolo Gorini, although he complains that their techniques were never disclosed (7, 8). For this reason, we think that Martone approached this type of preservation of bodies using a technique based on injections

of biological liquids with chemical preservatives (9-14).

After all these considerations, Martone said that he had devoted himself completely to petrification of cadavers and described that the corpse, after a few hours of corruption, in a short time assumed the consistency of stone, indefinitely preserving itself without being deformed by dissection. Finally, the author reports that on February 19th, 1889, the corpse of Dr. Giuseppe Piccolo was petrified by him, and even though it was in an advanced state of putrefaction he managed to preserve the body. It is interesting to report the emotional motivations that the author describes in the act of preserving the remains of loved ones.

“Who can deny that we always want to see a dear deceased person again? Does not a mother have it on her heart to see the remains of her dead baby or those of her adult son whose education did not spare her efforts? And would not a son like to look at his lost parents who in his life were not always lavish with care and kindness?” (1). “And if you allow me to express it this way: death makes us more disgusting, there are more weaknesses, because we think of the debacle and putrefaction which the body must undergo, including such pitiful feelings, so for several years I have studied the great problem of embalming”.

It is clear that the thoughts expressed by Martone were born in a time in which people lived daily with death. The possibility of preserving loved ones with all their physical features could allow the continuity of sharing life with the deceased. Currently, plastination, developed at the University of Heidelberg by the German anatomist Gunther von Hagens in 1977, replaces water and fats in anatomical tissues with plastic polymers (such as resin, silicone and polyester), allowing for the indefinite preservation of bodies in their entirety, as individual body parts or

as cross-sectional slices of individual body parts (15).

This revolutionary technique has proven very helpful for several human and animal medical disciplines (anatomy, neuroanatomy, pathology, histology, surgery, etc.) and the plastinated material is highly valued for educational purposes, research and educational display for the public. A plastinated body can be preserved in perfect condition for a very long time, challenging the natural transient condition of the human body. If, in petrification, we think that the procedure was carried out without any involvement of the person and, therefore, without consent, the strict procedures of plastination ensure that each body so treated belonged to an individual who voluntarily left his mortal remains for scientific purposes. Apart from the ethical, cultural and legal questions regarding respect for the dignity of the deceased and their body (16, 17), plastination reveals the constant and incessant search of humanity to arrest, if not the death of the person, the integrity of the body (18). As Freud claims, “no one believes in his own death, or to put the same thing another way, in the unconscious, every one of us is convinced of his own immortality” (19).

Conclusion

The myth of immortality (to continue to exist even after the end of our lives) that the Polish writer Stanisław Jerzy Lec denounced in the famous aphorism “The first condition of immortality is death”, is intensified in the desire to move to eternity with the solemnity that enhances the dynamism and vitality of your body, rather than its consumption under the earth. And yet the vivid immobile gazes coming from the bodies treated by Dr. Von Hagens are not very different from what the mummified or petrified face of a corpse returns to us.

The images tell us that they were like us and that we will be like them.

What Is Already Known on this Topic:

Knowledge about petrification of bodies in the second half of the nineteenth century is very limited. Among the most famous Italian scientists who worked in this field were Girolamo Segato and Paolo Gorini.

What this Study Adds:

This study focuses attention on an interesting note on the petrification of corpses, underlining the importance that was still attributed to the conservation of bodies at the end of the nineteenth century.

Authors' Contributions: Conception and design: ML and RC; Acquisition, analysis and interpretation of data: OL and CT; Drafting the article: CR and RF; Revising it critically for important intellectual content: ML and RC; Approved final version of the manuscript: ML, CR, CT, OL, RF and RC.

Conflict of Interest: The authors declare that they have no conflict of interest.

References

- Martone M. On the conservation and petrification of corpses [in Italian]. *Riv It Sci Nat.* 1890;10(5):49-52.
- Licata M, Borgo M, Armocida G, Nicosia L, Ferioli E. New paleoradiological investigations of ancient human remains from North West Lombardy archaeological excavations. *Skeletal Radiol.* 2016;45(3):323-31.
- Erodoto. *Histories*, book II [In Italian]. Milano: Edizioni Sugarco; 1994:85-90.
- Siculus D. *Library of history*, Loeb classical library edition, translated by Oldfather CH. Book I. Harvard University Press: Cambridge; 1933. p. 91.
- Licata M, Tosi A, Larentis O, Rossetti C, Lorio S, Pinto A. Radiology of Mummies. *Semin Ultrasound CT MR.* 2019;40(1):5-11.
- Stazio PP. *Publio Papinio Stazio's books with the translation and notes of various (Silvarum liber III) [In Italian]*. Venezia: Tip. Giuseppe Antonelli; 1840.
- Licata M, Larentis O, Ventura F, Ciliberti R. Mummified remains in the field of forensics. The comparison of a 19th century case report with current cases. *Med Histor.* 2019;3(2):99-104.
- Rossetti C, Licata M, Carli A, Birkhoff JM, Piombino-Mascoli D, Fulcheri E. The "petrified corpse". The first study on the preservation status of skin. *J Am Acad Dermatol.* 2019 Mar 23. [Epub ahead of print].
- Lippi D, Weber D. Between horrid and science. Girolamo Segato's strange anatomy (1792-1836). *J Morphol Sci.* 2014;31(1):51-3.
- Piombino-Mascoli D. Giovan Battista Rini and Paolo Gorini: A comparison of two characters. [In Italian]. *AMHA.* 2018;16(1):145-56.
- Piombino-Mascoli D. *The Master of Eternal Sleep*. Presentation by Arthur C. Aufderheide. Preface of Albert R. Zink [in Italian]. Palermo: Edizioni La Zisa; 2009.
- Marinozzi S. Bodies, mummies and texts for an history of embalming in Italy [in Italian]. *Med Secoli.* 2013;25(1):167-204.
- Piombino-Mascoli D. Oreste Maggio, a "petrifier" of Palermo [in Italian]. *Med & Stor.* 2008;8(16):169-77.
- Piombino-Mascoli D. Stone bodies. In: Cenzi I, editor. *The petrifier [in Italian]*. Modena: Logos edizioni; 2018. p. 3-4.
- Singh D, von Hagens G. Scientist or showman? *BMJ.* 2003;326(7387):468.
- Monza F, Licata M. Anatomical preparations in museums a special category of cultural heritage. *Med Secoli.* 2015;27(2):615-28.
- Licata M, Monza F. Ethical issues in paleopathological and anthropological research experiences. *Acta Biomed.* 2017;88(3):315-8.
- Bianucci R, Soldini M, Di Vella G, Verzé L, Day J. The Body Worlds Exhibits and Juvenile Understandings of Death: Do We Educate Children to Science or to Voyeurism? *Clin Ter.* 2015;166(4):264-8.
- Freud S. *Reflections on War and Death*. New York: Moffat, Yard & Co; 1918.

Carl Ferdinand von Arlt, Ritter von Bergschmidt (1812-1887): A Pioneer in Ophthalmology

Konstantinos Laios¹, Antonis Charalampakis², Evangellos Mavrommatis³,
Konstantinos Manes³, Efstathia Lagiou⁴, Pavlos Lytsikas – Sarlis³, Marilita M. Moschos¹

¹First Ophthalmological Department, Medical School, National and Kapodistrian University of Athens, Greece, ²Lieutenant colonel, Dental Surgeon, 401 Army General Hospital of Athens, Greece. ³Surgical Department, “Konstantopoulio” General Hospital, Athens, Greece, ⁴Ophthalmological Department, General Hospital of Aigion, Aigion, Greece

Correspondence:

konstlaios@gmail.com
Tel.: + 30 694 709 1434
Fax.: + 30 210 347 4338

Received: 3 May 2019; Accepted: 25 November 2019

Abstract

Carl Ferdinand von Arlt, Ritter von Bergschmidt (1812-1887) was a pioneer in ophthalmology. The purpose of our paper is to highlight his scientific work. He did not only introduce new surgical techniques and invent new instruments in ocular surgery, but also influenced the development of ophthalmology in the 19th century. He was an excellent and reputable professor of ophthalmology, and his students became very respected figures in ophthalmology.

Key Words: Carl Ferdinand von Arlt ■ Ocular Surgery ■ Innovations ■ Famous Students.

Introduction

Carl Ferdinand von Arlt, Ritter von Bergschmidt (1812-1887) is considered one of the most important figures in ophthalmology

from the 19th century (Figure 1). He had a high reputation among scholars, not only as an innovative ocular surgeon, but also as an excellent researcher, whose achievements influenced the development of ophthalmology. He was an excellent and renowned professor of ophthalmology, and his students became very respected figures in ophthalmology.

The purpose of our paper is to highlight his scientific work.

Short Biography

Carl Ferdinand von Arlt was born in Horní Krupka Obergraupen, Bohemia, on April 18th 1812. He was the son of an Austrian blacksmith. He attended elementary and high school in Leitmeritz, where he met his future wife, the daughter of his physics teacher. He initially studied theology, but from 1833 to 1839 he studied medicine at the Karl-Ferdinand-Universität, University of Prague. On 30th November 1839 he was appointed Doctor of Medicine and Surgery, and then Master of Arts in Ophthalmology. From 1840 to 1842 he was assistant to Johann Nepomuk Fischer (1777-1847) at the Ophthalmological Clinic of Prague. Until 1843 he was an intern at the Krumauer Kreisphysikate.

After the death of Fischer's assistant in the spring of 1844, von Arlt became an administrator at Fischer's clinic. In 1845 he



Figure 1. Carl Ferdinand von Arlt, Ritter von Bergschmidt (1812-1887). Source: Von Arlt F and Becker O. *Meine Erlebnisse* (My Experiences). Wiesbaden; Bergmann: 1887 p. X).

qualified in ophthalmology, and in 1847 in pathological anatomy. From 1846 to 1849 he was Associate Professor in the department specializing in diseases of the eye at the University of Prague, and from 1849 to 1856 he was Full Professor in the same department. In 1856 he moved to the University of Vienna, where he taught as Professor of Ophthalmology, succeeding Anton von Rosas (1771-1855), until his retirement in 1883. After he retired he worked as a private ophthalmologist until his death due to senile gangrene on 7th March 1887. He had three children, two daughters, and a son who also became an ophthalmologist (1).

Publications

Arlt was a prolific writer and his publications had a significant influence on other physicians worldwide. Among his works,

his important treatises on various fields of ophthalmology stand out. His doctoral thesis was presented in 1839 at the University of Prague under the title: '*Von Arlt F. Dissertatio inaug, medica sistens historias Amauroseos e vitiis organicis cerebri quatuor adnexis similibus, quotquot innotuere autorum varior. Observationibus. Pragae: Haase*' (Dissertation on Diseases of the Brain, Observations by the author (2)). In 1846 he published his study: 'Care for the eyes in healthy and diseased conditions, with a note on eye glasses' which received an updated edition in 1868 (3). In this study he expressed the idea that the physician should himself perform the refraction, not leaving this assignment to opticians. His main treatise was 'Eye diseases for practical physicians' in three volumes, with the first published in 1850, the second in 1853 and the third in 1856 (4). In 1876 he published his study, 'About the causes and origins of short-sightedness' (5) and in 1881, 'Clinical presentation of diseases of the conjunctiva, cornea and dermis, then the iris and ciliary body' (6). In 1875 he published the study, 'About eye injuries, with particular reference to their judicial appraisal' (6), which had a French (7) and an English (8) translation. From 1855 he became joint editor of Friedrich Wilhelm Ernst Albrecht von Graefe's (1828-1870) '*Archiv für Ophthalmologie* (Ophthalmology Archives)'. In this series his most celebrated work was his 'Operationlehre', Graefe-Saemisch, '*Handbuch der gesamten Augenheilkunde* (Handbook of collected Ophthalmology)', Vol. III, Part 2, Leipzig, 1874. He published numerous articles in various journals such as: '*Anzeiger der k. k. Gesellschaft der Ärzte in Wien* (Board of the Society of Physician of Vienna)', '*Mitteilungen des Vereines der Ärzte in Niederösterreich* (Communications of the Association of Physicians in Lower Austria)', '*Prager Medizinische Wochenschrift* (Prague Medical Weekly)', '*Prager Vierteljahresschrift* (Prague quarterly)', '*Wiener*

Medizinische Wochenschrift (Vienna Medical Weekly), Zeitschrift der k. k. Gesellschaft der Ärzte (Journal of the Society of Physicians)' (1).

Innovations in Ophthalmology

Arlt presented many innovations in ocular surgery and ocular clinical practice. It is important to remember that ophthalmologists still perform ocular surgeries according to the surgical techniques Arlt introduced in order to treat *trichiasis* and *pterygium*. However, surgical techniques have become less traumatic today. Enucleation to treat serious *endophthalmitis* or an incurable painful eye remains an unpleasant surgical procedure, and Arlt's enucleation technique is still in use. In 1859 he proposed a method for enucleation of the eye. In this operation a *strabismus* hook it is not used, as was advised at the time after the introduction of Ferral-Bonnet's enucleation method, but an incision on the conjunctiva is made two to three millimeters behind the limbus, which is slightly retracted. The surgeon first intersects the lateral and then the medial rectus but leaving a small stump on the bulb to serve as a handle. After a cross section of the superior and the inferior rectus muscles is made, the bulb is pulled horizontally by the clamp to either the inner or outer canthus, and the scissor blades are inserted above the rear portion of the sclera to the optic nerve, which is transected with the scissors near the sclera. The bulb is pulled toward the rectus muscles, which have not been transected. The insertion of the oblique is cut, as the vessels and nerves in the posterior part of the bulb are also cut. Finally, the insertion of the last rectus muscle is performed together with the overlying conjunctiva from the sclera (9).

Arlt also proposed a method for *medial tarsorrhaphy*. According to his method a narrow strip of skin is resected from around

the inner *canthus*, with the surgeon paying attention not to traumatize the underlying canaliculi, and the edges of this wound are spliced by fine sutures. After a few days the sutures are removed (10).

Another form of surgery he developed was the Jaesche-Arlt operation for trichiasis. He further developed a basic operation which was introduced by Georg Emanuel Jaesche (1815-1876). As described by Wood, in this operation: "An intermarginal incision is made along the whole length of the lid, following the gray line on the free border. This incision should be 3 or 4 mm. in depth, and should be so placed that all the lashes will be in the anterior layer, which is separated from the tarsus. A fold of skin is next removed from the anterior surface of the lid in the following manner. An incision is made in the skin parallel to the free border and about 4 mm from it; above this and joining it at each end, there is made a curved incision through the skin, which marks out a crescentic area of skin that at its widest part at the middle of the lid is about 8 mm. This crescentic piece of skin is then dissected off with blunt pointed scissors or a scalpel, care being taken not to buttonhole it, and not to remove the subjacent fibers. The gap produced by the excision of this piece of skin is then closed by five or six sutures. The sutures are not cut off, but are drawn upwards to cause the cilia border to take its new position higher up on the tarsus, and are secured to the forehead over the brow by an adhesive strip..." (11).

Arlt's method for excision of pterygium was considered one of the cleanest methods for treatment of this ocular pathology. According to his method, a Graefe knife and broad-toothed forceps are used. The neck of the pterygium is grasped by the forceps and cut by the knife. Then the pterygium bed is cut by small, straight, blunt-pointed scissors. Two incisions are made with the scissors at the upper and lower margins of the pterygi-

um. Two others are made, starting from the end of previous two, also using the scissors, following the median line near canthus on the conjunctiva. A quadrilateral piece of the pterygium is thus removed, leaving a similar area of the sclera to be covered by the conjunctiva drawn from above and below. A cut is made under the conjunctiva, in order to avoid tension, and the wound is stitched (11).

Furthermore, Arlt's surgery for treatment of symblepharon was the most common in use after its introduction. According to this method, a portion of the adhesion is grasped with sharp-toothed forceps and dissected using a keen-edged scalpel. Instead of forceps a double-armed suture may be used. The adhesion is abscised from the globe by blunt curved scissors, and the scar tissue is also removed by two incisions made from its apex to its base. Then the flap is stitched with sutures passing out through the entire thickness of the lids, which are tied over a small roll of gauze or piece of rubber tubing. The bulbar wound is stitched with silk sutures (10).

Arlt also modified epicanthus or rhinorrhaphy surgery. He excised the two semilunar pieces of integument comprising the greater portion of the epicanthal folds themselves. Sometimes he also excised a flap, making a median ellipse from the nose. The sutures had an X-shaped form. This operation is also known as *lateral rhinorrhaphy* (10).

His innovations in ocular surgery were not limited to new surgical techniques, but he also introduced new surgical instruments. Arlt's scalpel is a modification of the general surgeon's scalpel, having an elongated blade with a central point. The scalpel is 3.5 centimeters long and at its greatest width 5 to 6 millimeters. This scalpel could be used in various operations, giving the surgeon great flexibility, because it could create a pouch at its point, cut and be inserted to the orbit or the bulb at many angles.

Arlt also introduced a new loop for extraction of the lens during a cataract operation. His loop is elongated and has teeth in order to facilitate grabbing the lens, whereby the teeth make it more secure, and to ease the insertion of the instrument due to its elongated form. However, his best known instruments are the iris scissors. He invented this instrument for excising a piece of occluding pupillary membrane and the iris attached to it. After the initial incision using a keratome, the instrument is inserted into the anterior chamber, and when the blades are opened the iris diaphragm is located between the two blades. Firm pressure is exerted and the diaphragm is punched out. Therefore the instrument has blades like scissors for *iridectomy*, with a 45 degree inclination, where the upper blade is blunt and concave on its inner face, and the lower blade is a slightly pointed (11).

Arlt also modified the ocular 'orthoscope' (for revealing the visible fundus oculi a water-box was used to neutralize the corneal curvature) invented by Johann Nepomuk Czermak (1828–1873). He made it from soft rubber and he placed glass to one side. The glass eliminated the corneal curvature and could be applied close to the eye (12).

Arlt made also his name in the field of ocular pharmacy by introducing an ointment as an analgesic and counter-irritant for ocular inflammations, such as scleritis and iritis, and for blepharospasm in phlyctenular keratitis. It was applied three to four times a day and consisted of 5 grams of unguentum hydrargyri cinerei or ammoniati and 0.5 grams of belladonnae extract. This ointment was used more in America than in Germany (13).

Conclusion

Arlt was an ingenious ophthalmologist and ocular surgeon, and an esteemed professor of ophthalmology. His name is used for the linear scar which is present in the sul-

cus subtarsalis in Chlamydia trachomatis infection (Arlt's line), the contagious eye infection caused by Chlamydia trachomatis (Arlt's syndrome), and the keratic precipitate distributed in the wedge-shaped area on the inferior corneal endothelium (Arlt's triangle). His students were among the most significant figures in ophthalmology, such as Friedrich Wilhelm Ernst Albrecht von Graefe (1828-1870), Otto Heinrich Enoch Becker (1828-1890), August von Reuss (1841-1924), Vilmos Schulek (1843-1905), Hubert Sattler (1844-1928), Otto Bergmeister (1848-1918), Leopold Königstein (1850-1924), Ernst Fuchs (1851-1930), Friedrich Dimmer (1855-1926) Hans Adler (1843-1923) and Oskar Heifelder (dates unknown). Arlt did not live long enough to complete his autobiography, which was completed and published after his death by Otto Heinrich Enoch Becker (1).

Authors' Contributions: Conception and design: KL; Acquisition, analysis and interpretation of data: KL; Drafting the article: KL, EM, KM, EL, PLS and AC; Revising it critically for important intellectual content: KL; Approved final version of the manuscript: KL and MMM.

Conflict of Interest: The authors declare that they have no conflict of interest.

References

1. Von Arlt F, Becker O. My life [in German]. Wiesbaden: Bergmann; 1887.
2. Von Arlt F. Dissertation. The histories of the faults of the organs of the brain about amaurosis. Observations of the author [in Latin]. Prague: Haase; 1839.
3. Von Arlt F. Care of the eyes in a healthy and diseased state calls for an attachment over eye glasses [in German]. Prague: Gerzabek; 1846.
4. Von Arlt F. Illnesses of the eye for practical physicians. Vol. 1-3 [in German]. Prague: Credner; 1850-1856.
5. Von Arlt F. About the causes and the development of myopia [in German]. Vienna: W. Braumüller; 1876.
6. Von Arlt F. Clinical presentation of diseases of the conjunctiva, cornea and chorioidea, then the iris and the ciliary body [in German]. Vienna: Braumüller; 1875.
7. Von Arlt F. Injuries of the eye and their medico-legal aspect. Philadelphia: Claxton, Remsen & Haffelfinger; 1878.
8. Von Arlt F. Injuries to the eye from a practical and forensic point of view [in French]. Paris: Baillière; 1877.
9. Von Arlt F. Surgical Textbook for all ocular diseases. Graefe A and Saemisch T. [in German]. 1st ed. Vol. III, 1. Leipzig: Wilhelm Engelmann; 1874.
10. Beard CH. Ophthalmic surgery; a treatise on surgical operations pertaining to the eye and its appendages, with chapters on para-operative technic and management of instruments. Philadelphia: P. Blakiston's son & co.; 1910.
11. Wood CA. A System of Ophthalmic Operations. Vol. I-II. Chicago: Cleveland Press; 1911.
12. Wood CA, editor. American Encyclopedia and Dictionary of Ophthalmology. Vol. 1. Chicago: Cleveland press; 1913-21.
13. Wood CA. A system of ophthalmic therapeutics; being a complete work on the non-operative treatment, including the prophylaxis, of diseases of the eye. Chicago: Cleveland Press; 1909.

Dr. Anna Bayerova: Female Pioneer of Medicine in Bosnia and Herzegovina¹

Omer Ć. Ibrahimagić

Department of Neurology, University Clinical Center Tuzla and School of Medicine, University of Tuzla, 75000 Tuzla, Bosnia and Herzegovina

Correspondence:

omeribrahimagic@yahoo.com

Tel.: + 387 35 25 53 41; + 387 61 67 01 67

Received: 1 December 2019; Accepted: 15 December 2019

Dear Dr. Tahirović,

I read the article written by Fuchs and Tahirović in the first issue of *Acta Medica Academica* in 2019 with great attention (1). This excellent article about the history of medicine evaluates the life and enormous, but brief work of Dr. Anna Bayerova in Tuzla, Sarajevo, and Bosnia and Herzegovina.

The interesting fact is that for a quite long time it was not known precisely who was the first to start working in Tuzla and Bosnia and Herzegovina – a Czech or Polish female doctor? A few written documents show that Polish doctors were the first to start. According to Azabagić and Prašek-Calczynska, they were Dr. Teodora Krajewska and Dr. Jadwiga Olaszewska (2, 3). According to Karahasanović, there was no female doctor in Bosnia and Herzegovina before Dr. Krajewska arrived in Tuzla (4). Dr. Anna Bayerova's time in Bosnia

and Herzegovina was slightly longer than a year. This is probably the prime reason why she is not known so well.

In contrast, Fuchs and Tahirović, as well as Nečas, state that Anna Bayerova was in fact the first female doctor in Bosnia and Herzegovina (1, 5). According to Nečas, she was born in Vojtjehovo, near Prague, so perhaps not in Melnik. She ended her medical education due to her unfavorable material situation. Finally, she received her diploma after submitting her dissertation entitled: "Über die Zahlenverhältnisse der rothen und weissen Zellen im Blute vom Neugeborenen und Säuglingen" (*About the ratio of red and white cells in the blood of newborns and infants*) (5).

After careful analysis of the historical documents, it is clear that Teodora Krajewska was not the first official female doctor in Bosnia and Herzegovina. Without any doubt, Dr. Anna Bayerova was the female pioneer of medicine in Bosnia and Herzegovina. Furthermore, Dr. Bayerova had to promise not to get involved in any sort of political work in Bosnia and Herzegovina (6). Her medical work was not solely based in Tuzla, in fact, it was in Brčko, Gračanica and Derventa (7). Her success was even a surprise to the finance minister, Benjamin Kallay. After Dr. Bayerova heard that her work had been spoken of positively, she

¹ Comment on Article: Dr. Anna Bayerova: The First Official Female Doctor in Bosnia and Herzegovina.

wrote: “The news that the administrators in Vienna are satisfied by my work caught my attention – I can’t say I was ecstatic. I am so pleased by the grateful looks of my Muslim women and by their pleasure at being treated fairly and honestly, to the point where I lose interest in everything else” (8).

Key Words: Anna Bayerova ■ Tuzla ■ Bosnia and Herzegovina.

Conflict of Interest: The author declares that he has no conflict of interest.

References

1. Fuchs B, Tahirović H. Dr. Anna Bayerova: The First Official Female Doctor in Bosnia and Herzegovina. *Acta Med Acad.* 2019;48(1):121-6. DOI:105644/ama2006-124.249.
2. Azabagić S. One hundred years of health service in Tuzla [in Bosnian]. *Acta Med Sal.* 1974;3(2):520.
3. Prašek - Calczyńska B. MD Teodora Krajewska – The first official female doctor in Bosnia [in Croatian]. In: *Memoari jedne liječnice.* Zagreb: Durieux; 1997. p. 103-16.
4. Karahasanović A. Tuzla hospital and its first doctors [in Serbian]. *Srp Arh Celok Lek.* 1958;10:1-5.
5. Nečas C. Work of official female doctors in Bosnia and Herzegovina 1892-1918 [in Bosnian]. In: *Istorijski zbornik.* Banjaluka: Institut za istoriju. 1988;9:91-110.
6. Anonymous. The first official state female doctor in Europe [in Czech]. *Ženske listy.* 1892;20:35-6.
7. Ibrahimagić OČ, Zukić S, Čustović A. Health care in Tuzla and Tuzla area in the second half of the nineteenth century [in Bosnian]. *Acta Med Sal.* 2009;38(1):1-5.
8. Honzakova A. MD Anna Bayerova 1853-1924: The first Czech female doctor in Switzerland [in Czech]. Prague: *Ženska narodni rada;* 1937. p. 25.

ISSN 1840-1848



9 771840 184007