ISSN:2601-6877

2018 | Volume 1 | Issue 1

## ACTA STOMATOLOGICA MARISIENSIS Journal

Acta Stomatologica Marisiensis is an official journal of the University of Medicine and Pharmacy of Tirgu Mures

Acta Stomatologica Marisiensis (ISSN: 2601-6877) is published by University Press Tirgu Mures

**Corespondence:** Acta Stomatologica Marisiensis University of Medicine and Pharmacy of Tirgu Mures 38, Gh. Marinescu St., 540139, Tirgu Mures, Romania



## ACTA STOMATOLOGICA MARISIENSIS

### **EDITORIAL BOARD**

**Mircea SUCIU** *Editor-in-Chief* University of Medicine and Pharmacy of Tirgu Mures, Romania

### Mariana PĂCURAR

*Deputy Editor* University of Medicine and Pharmacy of Tirgu Mures, Romania

### Edwin Sever BECHIR

Managing Editor University of Medicine and Pharmacy of Tirgu Mures, Romania

### Emanuel BRATU (Romania)

"Victor Babeş" University of Medicine and Pharmacy, Timişoara, Romania

### Alexandru BUCUR (Romania)

"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

### Radu Septimiu CÂMPIANU (Romania)

"Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

## Maria Cristina FIGUEIREDO POLLMANN

(Portugal) University of Porto, Portugal

Norina Consuela FORNA (Romania) "Gr. T. Popa" University of Medicine and Pharmacy, Iași, Romania

### Tomasz GHEDRANGE (Germany) Technische Universität, Dresden, Germany

Francesco INCHINGOLO (Italy) Universita degli Studi di Bari "Aldo Moro", Bari, Italy Liran LEVIN (Canada) University of Alberta, Edmonton, Canada Krisztina MARTON (Hungary)

Semmelweis University, Budapest, Hungary

Romania Joseph NISSAN (Israel) University of Tel Aviv, Israel Raul Mihai POPESCU (Romania) University of Medicine and Pharmacy Craiova, Romania Nachum SAMET (USA) Harvard University, USA Anton SCULEAN (Switzerland) University of Bern, Switzerland Andreas STAVROPOULOS (Sweden) Malmö University, Sweden Roxana STEGAROIU (Japan) Niigata University, Japan Stefan Ioan STRATUL (Romania) "Victor Babes" University of Medicine and Pharmacy, Timișoara, Romania Mihail TÂRCOLEA (Romania) Polytechic University of Bucharest, Romania

University of Medicine and Pharmacy, Tirgu Mures,

Monica MONEA (Romania)

### SECTION EDITOR

Implantology and Oral Surgery Horia Mihail BARBU "Titu Maiorescu" University, Bucharest, Romania

Prosthetic Dentistry Liana LASCU "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

### Orthodontics

Krisztina MARTHA University of Medicine and Pharmacy, Tirgu Mures, Romania

#### Paedodontics

Cristina Ioana BICĂ University of Medicine and Pharmacy Tirgu Mures, Romania

Preventive Dentistry Codruta Angela PODARIU "Victor Babeş" University of Medicine and Pharmacy, Timişoara, Romania

Endodontics Monica MONEA University of Medicine and Pharmacy, Tirgu Mures, Romania

**Odontology** Sorin ANDRIAN "Gr. T. Popa" University of Medicine and Pharmacy, Iași, Romania

**Statistics Editor** 

Dana GHIGA University of Medicine and Pharmacy Tirgu Mures, Romania

Technical Editor Cristina MOLNAR-VARLAM

University of Medicine and Pharmacy Tirgu Mures, Romania

Parodontology Silvia MÂRȚU "Gr. T. Popa" University of Medicine and Pharmacy, Iași, Romania

Dental Tehnology Melinda SZEKELY University of Medicine and Pharmacy, Tirgu Mures, Romania

Dental Materials Anamaria BECHIR "Titu Maiorescu" University, Bucharest, Romania

### Oral Pathology/Oral Dermatology

Ovidiu Simion COTOI University of Medicine and Pharmacy, Tirgu Mures, Romania Horea Silviu MORARIU University of Medicine and Pharmacy, Tirgu Mures, Romania

Biotechnology, Medical Engineering Monica COMĂNEANU "Titu Maiorescu" University, Bucharest, Romania

### Dental Imaging

Mihaela HEDEȘIU "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

Acta Stomatologica Marisiensis is indexed in the following international databases:

.

Last update: June 10, 2018

Copyright © 2018 by Acta Stomatologica Marisiensis. All rights reserved.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise without either the prior written permission of the Publisher. **Disclaimer** 

Although each paper has been reviewed by a peer-reviewer, the authors take full responsibility for the scientific content. The views expressed in this journal represent those of the authors or advertisers only. In no way can they be construed necessarily to reflect the view of either the Editors or Publishers.

### **AIMS AND SCOPE**

Acta Stomatologica Marisiensis is an official Journal of the University of Medicine and Pharmacy Tirgu Mures, Romania, and is published twice a year.

Acta Stomatologica Marisiensis is an international journal dedicated to publishing high-quality peer-reviewed articles about all fields of dental medicine. The important topics covered by the journal refer to the complete, complex and interdisciplinary treatment of the patient with dental problems. This involves addressing all branches of dental medicine and does not exclude research in the field of nanomaterials, biotechnology or medical engineering.

By focusing on the publication of new documents and evidence of high quality research, Acta Stomatologica Marisiensis aims to improve research and clinical practice of dental medicine at an international level.

The journal focuses on the publication of quality medical research articles that bring new insights into dental medicine from the perspective of diagnosis and treatment methods as well as the materials used. No less important are presentations of interesting clinical cases that can bring new light into diagnosis and treatment methods or interdisciplinary therapeutic approaches or collaborations with various fields of engineering for the development of innovative new technologies.

Acta Stomatologica Marisiensis addresses the entire community of dental specialists or related specialties at national and international level and aims to provide studies and materials for a better understanding of diseases and treatments in the sphere of dental medicine.

The Journal emphasis is primarily on original high-quality medical research but also accepts manuscripts relating to the basic sciences, review articles, systemic reviews and meta-analysis, case reports, and observational studies of all types, including randomised control trials, editorial commentary and opinions covering the entire spectrum of research in dental medicine.

The role of the Journal is to inform its readers of ideas, opinions, developments and key issues concerning dental medicine, stimulating interest, debate and discussion amongst dental medicine colleagues and those of related disciplines.

Acta Stomatolocica Marisiensis has institutional support from the University of Medicine and Pharmacy Tirgu Mures, the owner of the journal.

### **INFORMATION ABOUT THE JOURNAL**

ASMJ is an official Journal of the University of Medicine and Pharmacy Tirgu Mures, Romania, and is published twice a year. Annual subscription rate

Annual subscription rate is 50 Euros for individuals and 100 Euros for institutions (or RON equivalent). Prices include postage and are subject to change.

Methods of payment:

Payments should be made by bank transfer to one of the following accounts:

• in Euros, in the following account:

Universitatea de Medicină și Farmacie (UMF) Tîrgu Mureș, str. Gheorghe Marinescu 38, Mureș, Romania, CF 4322742, Banca Comercială Română, București, b-dul Regina Elisabeta 5, COD IBAN: RO92RNCB0193015967800002, for: Banca Comercială Română, Sucursala Central Tîrgu-Mureș, Piața Trandafirilor nr. 26.

in RON, in the following account:

RO29TREZ47620F331600XXXX, Trezoreria Tîrgu Mureş, for: Universitatea de Medicină și Farmacie Tîrgu-Mureş, CF 4322742, Str. Gh. Marinescu nr. 38, Mureş.

- On the bank transfer please mention: name/name of the institution; subscription ASMJ.
- Cheques are not accepted.

#### **Publication fee**

This journal does not charge for any fees for the publication of articles

#### Authors reprints

For all queries in connection with author reprints, contact: asmj@umftgm.ro

Supplements are normally supplied to subscribers without any extra charge. Single back issues from current or recent volumes are available at the current single issue price of 20 Euros/issue from the University Press Publishing House.

Methods of payment: see annual subscription rate

#### Digital object identifier

For information about DOIs, please visit http://www.doi.org/ Derivative work

Subscribers may reproduce tables of contents and prepare lists of articles including abstracts for internal use within their own institutions. However, permission from the Publisher is required for resale or distribution of the above mentioned materials outside the institution and for all other derivative works, including compilation and translation.

#### Environmental policy

The journal is printed on environmentally-friendly ECF (elemental chlorine free) wood-free paper.

#### Electronic storage and Usage

Permission from the publisher is required to store or use electronically any material contained in this journal.

#### Advertising inquires

Advertising inquires should be addressed to: asmj@umftgm.ro **Drug disclaimer** 

Any method or technique described, which involves the use of any kind of drug should be interpreted only in accordance to the drugs manufacturer's own published literature. The mention of trade names or commercial products does not imply any endorsement by the journal. The editorial board takes the necessary precautions to verify drug names and dosage, the results of the studies published in the journal and their clinical implications, however the responsibility for the use and dosage of drugs mentioned in the article lies with the medical practitioners.

#### Material disclaimer

Statements or opinions expressed in ASMJ reflect the view of the authors, who undertake the full responsibility for their work. The editorial board will carefully organize and supervise the entire process of manuscript verification and review to make sure that no inaccurate or misleading data are published in the journal. However, the data and opinion appearing in an article are the responsibility of the contributing authors. Accordingly, the journal accepts no liability for the consequences of such inaccurate or misleading data, opinion or statement. Any kind of scientific misconduct including plagiarism will be immediately reported according to international regulations. **Funding body agreements and policies:** 

Authors are requested to indicate in the manuscript the source of funding.

#### Photocopying

Single photocopies of single articles may be made for personal use as allowed by national and international copyright laws. Multiple or systematic copies, copying for promotional or advertising purposes require prior permission from the publisher.

## CONTENTS

<b>EDITORIAL</b> The need for multidisciplinarity in modern dentistry <i>Mircea Suciu</i>	7
<b>REVIEW</b> Combination therapeutic strategies to improve the outcomes of reconstructive periodontal surgery <i>Richard J. Miron, Anton Sculean</i>	9
<b>ORIGINAL PAPER</b> Oral health among children with cardiovascular disease and risk of infective endocarditis <i>Adriana Craciun, Diana Cerghizan, Cristina Bica</i>	27
Thermal regime effect on the structure of metal component in metal-ceramic prosthesis Raluca Monica Comăneanu, Costin Coman, Oana Botoacă, Adi Lorean	32
Efficacy of associated therapy in the treatment of temporomandibular disorders Edwin Sever Bechir, Farah Curt-Mola, Mircea Suciu, Claudiu Horga, Carmen Biriş, Anamaria Bechir, Liran Levin	39
Clinical-statistical analysis of correlations between caries risk indicators and the prevalence of maxillary dental anomalies in a group of children from Tirgu Mures Mariana Păcurar, Eugen Bud, Haj Alexandra, Manuela Chibelean, Maria Cristina Figueiredo Pollmann	48
Comparative effectiveness of alternative medication in minor aphtous stomatitis Farah Curt-Mola, Mircea Suciu, Ilinca Suciu, Anamaria Bechir, Lelia Laurenta Mihai, Alexandru Burcea, Edwin Sever Bechir	55
Efficacy of periodontal debridement using an Erbium YAG laser: A scanning electron microscopic study Alexandra Stoica, Soos Reka, Tudor Hănțoiu	64
The influence of cervical finish line and type of cement on microleakage Adriana Elena Crăciun, Vodă Roxana, Janosi Kinga, Cerghizan Diana	69
Possibilities in alleviation of dentin sensitivity in vital abutments Anamaria Bechir, Violeta Hancu, Gabriela Ciavoi, Doina Lucia Ghergic, Valentin Pribac, Cherana Gioga, Claudia Florina Andreescu, Farah Curt-Mola	74
<b>CASE REPORT</b> Prosthodontic rehabilitation of a patient with osteoporosis and bisphosphonates treatment	82
Ciprian-Emanuel Rusu, Serfözö Norbert Erich, Andrei Petruț, Carmen Biriș, Claudiu Horga	

Acta Stomatologica Marisiensis

### **EDITORIAL**

## The need for multidisciplinarity in modern dentistry

Mircea Suciu<sup>1</sup> Editor-in-Chief <sup>1</sup>University of Medicine and Pharmacy of Tirgu Mures, Romania

It is a privilege to introduce to you Acta Stomatologica Marisiensis Journal a new international journal under the authority of University of Medicine and Pharmacy of Tirgu Mures whose purpose is to promote the topical issues of modern dentistry.

ASMJ wants a multidisciplinary journal that publishes high quality articles in all areas of dentistry, covering a complex area, from cariology to orthodontics, implant dentistry or nanotechnology and medical bioengineering.

A top priority and topical issue for all medical fields is to look at the human body as a unitary complex of biological systems that depend on each other and which are regulated by intrinsic neuroendocrine mechanisms and function as a whole as a computer to maintain the human body's homeostasis [1].

This requires a multidisciplinary approach and thinking for any disease and supports the detection of risk factors with pathogenic potential, capable of generating the appearance of morbid entities of the stomatognomic ensemble that is manifested by polymorphism, often placing physicians in difficulty in formulating correct diagnoses. These are clearly necessary to establish a proper treatment for each patient.

This approach to dental medicine opens the way for elaborate interdisciplinary collaborations when dealing with a complex oral rehabilitation of clinical cases.

The major objective of oral rehabilitation is the complete and complex approach of patients based on a rational diagnostic and therapeutic protocol, approached from gnatological, bio-prophylaxis and multidisciplinary perspective, the balance of the oral cavity being part of the general homeostasis of the human body. The physician and the patient must go through a logical succession of diagnosis and treatment throughout the complex oral rehabilitation, multidisciplinary in the field of dental medicine, correlated and integrated with those related to the general health of the human body. The end of this logical stepping is in most cases is prosthodontics which, however, cannot be achieved without going through the preparatory pre-and proprosthetic steps.

If in the past the approach to dental prosthodontics was focused on its major branches, physiology, dental materials, dental occlusion or clinical cases, today, due to technological advancement, research ideas in prosthetic dentistry expanded to a multidisciplinary science that includes digital dentistry or regenerative dentistry with a biological basis [2].

A conclusive example of these changes that demonstrate the way to multidisciplinarity is the evolution over time of the treatment of perhaps the most widespread clinical situation among the population: complete edentoulism. If in the past the solution for the increase of stability was the use of the complete denture made in gold palate and ivory teeth like Washington's complete dentures in 1795 [3], complete denture on maxilla with a suction cup, or a multi-cup dentures described by Jermyn in 1967 which requires a team consisting of a dentist and a dental technician [4], today a complete denture support on provide comfort implants, that and improvement of the quality of life, need for its realization two different dental specialties, implantologist and prosthodontist.

Another remarkable example that revolutionized the therapeutic decision in dentistry is the discovery of Branemark, the

7

implant. Since then, the vision of treatment opportunities has changed radically. This is an example of a multidisciplinary team that has made a medical breakthrough to significantly discard the evolution of dentistry.

On the other hand, if we refer to the means of investigation in dentistry, we find an astonishing evolution of them since 1895 when Roentgen discovered x-rays, until today when conical-beam tomography (CBCT) often makes wonders in the diagnosis and treatment of patients, being used in all clinical branches of dentistry.

These are some examples that prove the usefulness of multidisciplinary approaches in dentistry. Everything is done for the benefit of the patient's health.

If you persuaded yourself to do so, please believe that the purpose of our journal is to cover research topics that will contribute in the future to transforming daily dental practice into that of the future, the modern one.

We all know that we need to contribute to the evidence base necessary to improve medical practice [5] and that's why by launching the ASMJ we want to contribute actively to the field of dentistry at national and international level.

We thus invite you to publish your relevant research, clinical or theoretical, in ASMJ order to assist the growth of this journal together, and share together the joy of our success.

### **Conflict of interest:** None to declare.

### References

- Ieremia L, Bratu D, et al. Viziunea intersistemică in medicina dentară. Tirgu Mures: Editura Universității Petru Maior; 2006. P. 19-31
- 2. Kaku M. Prosthodontics: A multidisciplinary field in dentistry. J Prosthod Res. 2016;60(3):143-4.
- Sognnaes RF. President Washington's most famous dentures stolen from the Smithsonian. JADA 1983;106(2):216-8.
- Boucher CO. Complete denture prosthodonticsthe state of the art. J Prosthet Dent. 1975;34(4):372-83.
- 5. Azamfirei L. Critical Thinking for Critical Care. JCCM 2015;1(1):3-4

### Corresponding author:

Mircea Suciu

University of Medicine and Pharmacy of Tirgu Mures, 38 Gheorghe Marinescu street, Tirgu Mures, 540139, Romania Email: suciu.mircea@umftgm.ro

Received: April 29, 2018 / Accepted: May 15, 2018

### **REVIEW**

# Combination therapeutic strategies to improve the outcomes of reconstructive periodontal surgery

Richard J. Miron<sup>1</sup>, Anton Sculean<sup>1</sup> School of Dentistry, University of Bern, Switzerland

### Abstract

Substantial evidence from the literature indicates that following active periodontal therapy, persisting deep ( $\geq$  6mm) residual periodontal pockets associated with bleeding on probing are risk factors for tooth loss. Therefore, from a clinician's point of view, the main goal of periodontal therapy is considered to be the presence of shallow pockets (≤ 5 mm) and absence of bleeding on probing, preferably with limited or no soft tissue recession. Deep periodontal pockets are frequently associated with intrabony defects which, in most cases, do not completely resolve following non-surgical or conventional surgical therapy. Even though periodontal infection can be successfully treated by means of nonsurgical therapy, intrabony defects often remain as a sequellae and are associated with deep localized residual pockets. Despite the fact that resective surgery can be successfully used to completely eliminate intrabony defects, these techniques are inevitably associated with substantial loss of hard and soft tissues leading to impaired esthetics, chewing comfort and increased hypersensitivity. Thus, the ideal goal of treating intrabony defects is the regeneration of the tooth's supporting structures (i.e. formation of new root cementum with functionally orientated inserting periodontal ligament fibers connected to new alveolar bone), which should manifest clinically in shallow pockets, absence of bleeding on probing and no or minimal soft tissue recession. Over the past 20 years, many advancements including biologics, membranes and bone grafting materials have been made to predictably regenerate intrabony defects to additionally improve the clinical outcomes obtained with conventional periodontal surgery. Recent evidence indicates that the combination of different regenerative materials may additionally improve the clinical outcomes in defects with a complicated anatomy. The aim of the present review article was to summarize the potential additional effects of various combination procedures used in reconstructive periodontal surgery of intrabony defects as compared with those obtained with conventional flap procedures or monotherapies on periodontal pockets associated with intrabony lesions. The data appear to indicate that in defects with a complicated anatomy, certain combination approaches such as: bone grafting materials and biologics (i.e. enamel matrix proteins or recombinant platelet derived growth factor) or bone grafting material and membranes may not only result in periodontal regeneration but also in additional clinical improvements in terms of pocket depth reduction and clinical attachment gain compared to conventional periodontal surgery or the use of mono-therapies.

**Keywords:** Intrabony defects, periodontal regeneration, intrabony defects, enamel matrix derivative, EMD, growth factors, guided tissue regeneration

### Introduction

Periodontal disease, which begins as superficial inflammation of the gingiva without attachment or bone loss (gingivitis) and later progresses to attachment loss with subsequent bone destruction (periodontitis), is one of the leading infectious diseases known to mankind. Results from a national survey conducted in the United States in 2010 analyzing the distribution of the disease found that over 47% of the adult population was affected [1]. Furthermore, 38.5% of the population had either moderate or severe forms of periodontitis, which are more difficult and cost-intensive to handle due to the advanced loss of the tooth's supporting apparatus and

subsequently resulting niches that make infection control challenging [1]. Thus, it becomes vital for healthcare providers to diagnose the disease as early as possible and provide appropriate treatment. It has been extensively documented that periodontal infections can be successfully treated by nonsurgical and surgical periodontal therapy associated with meticulous oral hygiene. Moreover, longitudinal studies have provided conclusive evidence on the effectiveness of periodontal therapy in the presence of a rigorous maintenance program demonstrating successful outcomes over 30 years [2]. On the other hand, substantial evidence indicates that persistence of residual periodontal pockets of

9

 $\geq$  6 mm and presence of bleeding on probing following completion of active (non-surgical or surgical) periodontal therapy is associated with an increased risk of attachment and tooth loss [3,4].

Even though periodontal infection can be successfully treated by means of non-surgical therapy, intrabony defects often remain as a sequellae and are associated with deep localized residual pockets [5,6]. Moreover, periodontal pockets presenting with intrabony defects have been shown to deteriorate long-term tooth prognosis and, when left untreated, to increase tooth-mortality [7]. Despite the fact that various conventional surgical techniques have been successfully used to completely eliminate or reduce intrabony defects, such approaches are inevitably associated with significant gingival recession leading to impaired aesthetics and root hypersensitivity [8]. Therefore, the ideal goal of treating intrabony defects is the regeneration of the tooth's supporting structures (i.e. formation of root cementum with functionally orientated inserting periodontal ligament fibers connected to new alveolar bone), which should manifest clinically in shallow pockets ( $\leq 5$ mm), absence of bleeding on probing and no or minimal soft tissue recession [9]. Recent evidence indicates that the combination of different regenerative materials may additionally improve the clinical outcomes in defects with a complicated anatomy [9].

The aim of the present review article was to provide the biologic rationale and the clinical relevance in terms of pocket reduction/resolution of using various approaches in the regenerative therapy of intrabony defects.

### **Biologic Agents/Growth Factors**

It has long been speculated that the use of agents/growth biological factors could accelerate wound healing and tissue regeneration [10]. A variety of novel research in the mid-1990s attempted to achieve these goals utilizing growth factor delivery. Due to their fluid consistency, growth factors are utilized in conjunction with various types of carriers or scaffolds such as bone grafts or collagens and therefore, these effects are discussed later in this manuscript [11].

## Role of grafting materials in Periodontal Regeneration

Substantial literature is available on the role of various types of bone grafting materials for supporting periodontal regeneration in intrabony defects and decreasing or eliminating residual pockets [12,13]. Originally grafts were developed to serve as a passive, structural supporting network with the main criteria being biocompatibility. Advancements in tissue engineering have allowed for a large array of bone grafting materials, each possessing various advantages and disadvantages. It is now estimated that the global market for bone grafting procedures has surpassed \$2.5 billion with over 2.2 million procedures performed annually [14]. As such, the need for better biomaterials becomes vital due to the aging population and the number of bone grafting procedures for diseases such as osteoporosis, arthritis, tumors or trauma performed worldwide each year [15]. Bone grafting materials are typically classified under 3 main areas, that of osteoconduction, osteoinduction and osteogenesis [11]. However, it is important to point out that human histologic evidence has shown high variability among the various types of bone grafts in promoting regeneration of periodontal ligament, root cementum and bone [12]. While certain types of grafts such as autogenous bone, allografts or certain types of xenografts have been shown to support, at least to a certain extent, the healing process, synthetic grafts such as hydroxyapatite, beta tricalcium phosphate, polymers or bioactive glasses appear to have limited to no biologic effects when used in periodontal pockets associated with intrabony defects [12]. The data from human histological studies are in line with the findings from randomized controlled clinical studies evaluating the additional effect of various type of grafting materials in conjunction with open flap debridement (OFD) over the use of OFD alone and have demonstrated a high degree of heterogeneity (varying from 0.04 mm obtained with coralline calcium carbonate, to 0.41 mm with allografts, 0.60 mm with bioactive glass and 0.98 mm with hydroxyapatite) [16]. Therefore at present, it is difficult to draw any conclusion on the biological and clinical benefit of using grafting

materials alone to improve the results obtained with OFD in intrabony defects [16]. Therefore, it has to be understood that the main rationale for using grafting materials for reconstructive surgery is not necessarily to promote periodontal regeneration "per se", but rather to provide a carrier for biologic molecules/growth factors, to prevent flap collapse, and to enhance wound stability.

## Role of barrier membranes in Periodontal Regeneration

Guided tissue regeneration (GTR) is one of the more thoroughly documented techniques in reconstructive periodontal surgery. By of either non-bioresorbable means or bioresorbable barriers, the epithelial and gingival connective tissue cells are excluded from the wound area, thus enabling periodontal ligament and bone cells to selectively repopulate the root surfaces and the bony defects [17]. Furthermore, the GTR barrier will stabilize the blood clot and support the regeneration process [18]. Evidence from systematic reviews indicates that GTR promotes periodontal regeneration in humans [12] and has a greater effect on probing measures of periodontal treatment than open debridement, flap including improved attachment gain, reduced pocket depth, less increase in gingival recession and more gain in hard tissue probing at re-entry surgery. The additional use of a barrier membrane has vielded about 1.21 mm higher probing depth reduction than the use of flap surgery alone [19].

# Enamel Matrix proteins with bone grafting materials

The most widely utilized biologic agent for regeneration of intrabony defects is via the use of enamel matrix proteins (EMPs). Substantial evidence is available demonstrating that EMPs affects cells earlier in their differentiation process [20] and has various roles on the multilineage differentiation of periodontal ligament cells in vitro [21,22]. Since enamel matrix proteins are known to contribute to root development during tooth formation, the biological effects of EMPs on PDL, bone, cementum and gingival connective tissue cells have been shown to promote regeneration of intrabony defects [22].

An extensive systematic review on the topic showed that EMPs possesses a significant influence on cell behavior of many cell types by mediating cell attachment, spreading, proliferation and survival as well as expression of transcription factors, growth factors, cytokines, extracellular matrix constituents and other molecules involved in the regulation of bone remodeling [23]. EMPs further possesses the ability to reduce tissue inflammation and improve soft tissue wound healing [24] The use of EMPs in conjunction with OFD has been shown to promote periodontal regeneration of intrabony defects in humans [12] while clinically EMPs treated sites displayed statistically significant higher CAL gains (mean difference 1.1 mm, 95% CI 0.61 to 1.55) and PPD reductions (0.9 mm, 95% CI 0.44 to 1.31) when compared to OFD alone or placebo [25,26,27,28,29,30,31,33,34].

To date, a large number of clinical studies have evaluated the combination of EMPs with a bone grafting material when compared to either bone grafting material alone or EMPs alone (Table 1). Large variability exists and while the reasons are difficult to explain, they may at least in part be due to the defect anatomy and the utilized grafting material. Two separate studies have investigated the effects of EMPs + autogenous bone [35,36]. In a parallel study of 28 intra-osseous lesions, EMPs did not offer a statistically significant advantage when compared to EMPs alone for mean PD and CAL, however EMPs significantly improved healing in pockets greater than 6mm, and significantly increased recession coverages [35]. Yilmaz et al. also studied this combination and found that the combination approach led to statistically superior results in all areas measured including CAL gains and PD reductions [36].

The combination of allografts (either DFDBA or FDBA) with EMPs has been investigated in 5 clinical studies. In a split mouth study of 40 patients, Gurinsky et al found that EMPs + DFDBA offered no statistical difference in mean PD or CAL levels after a 6 month healing period. However, in the same study it was found statistically significant improvements in bone fill, crestal resorption and percentage of sites gaining greater than 50% and 90% bone fill when compared to EMPs alone (P < 0.001) [37]. Hoidal et al. validated this finding in a parallel study with 32 patients and found that the combination approach did not lead to any significant changes after a 6 month healing period when compared to the control group receiving DFDBA alone [38]. Contrary to these results, Aspriello et al. found in a parallel study with 56 intra-osseous defects that the combination of

DFDBA with EMPs led to significant improvements in mean CAL and PD reduction after 6 months of healing [39]. Recently, Ogihara and Tarnow found that the combination of either DFDBA or FDBA in combination with EMPs led to significant improvements in PD and CAL changes when compared to EMPs alone with no differences observed between either DFDBA + EMPs or FDBA + EMPs [40].

Author & Year	Study Desing & Patient Number	Clinical Defects	Healing Period	Treatment Groups	Mean PD change (mm)	P value	Mean CAL Change (mm)	P value
Lekovic,	Split mouth 42	42 intrabony		EMPs	1.91		1.71	
2000	with 21 patients	defects > 6 mm	6 months	EMPs + DBBM	3.43	<0,001	3.31	<0,001
Velasquez-	Split mouth	32 intrabony		EMPs	3.8		2.9	
Plata, 2002	16 patients	defects≥5 mm	6-8 months	EMPs + DBBM	4.0	n.s.	3.4	n.s.
Sculean,	Parallel 24	24 intrabony	12 months	DBBM	6.5		4.9	
2002	patients	defects	12 months	DBBM+ EMPs	5.7	n.s.	4.7	n.s.
Scheyer,	Split mouth	34 intrabony		DBBM	3.9		3.7	
2002	with 17 patients	defects ≥ 5 mm	6 months	DBBM + EMPs	4.2	n.s.	3.8	n.s.
Sculean,	Parallel	28 intrabony	nv	BG 4.22		3.07		
2002	with 28 patients	defects ≥ 6 mm	12 months	EMPs + BG	4.15	n.s.	3.22	n.s.
Zucchelli,	Parallel	16 intrabony		EMPs	5.8		4.9	
2003	with 16 patients	defects > 5 mm	12 months	EMPs + DBBM	6.2	n.s.	5.8	<0,01
Gurinsky,	Split mouth	67 intrabony		EMPs	4.0		3.2	
2004	with 40 patients	defects ≥ 3 mm	6 months	EMPs + DFDBA	3.6	n.s.	3.0	n.s.
Sculean,	Parallel	Parallel30with 30intrabonypatientsdefects ≥ 6mm12 months	le	EMPs	4.5		3.9	
2005			12 months	EMPs + BG	4.2	n.s.	3.2	n.s.
	Parallel	Parallel 23 intrabony		EMPs	5.03		4.06	
Kuru, 2006	with 23 patients	defects ≥ 6 mm	8 months	EMPs + BG	5.73	<0,05	4.17	<0,05

Table 1. Human clinical studies utilizing a combination approach including bone grafting material + EMPs

	1			1		1	1	1				
Bokan, 2006	Bokan, 2006 With 56 defe	56 intrabony	12 months	EMPs	3.9	n.s.	3.7	n.s.				
		detects > 3		EMPs + β-TCP	4.1		4.0					
Guida, 2007	Guida. 2007 Parallel : 27	28 intra- osseous	12 months	EMPs	5.6	n.s.	4.6	n.s.				
	patients	lesions		EMPs + AB	5.1		4.9					
Jan 2000	Parallel	73 intrabony	C as suth s	EMPs	2.55		1.83					
Jepsen, 2008	with 73 patients	defects ≥ 4 mm	6 months	EMPs + BCP	1.93	n.s.	1.31	n.s.				
	Parallel	41 intrabony		DFDBA	2.45		1.63					
Hoidal, 2008	2008 with 32 defects ≥ 3 mm	6 months	DFDBA + EMPs	2.56	n.s.	1.47	n.s.					
Yilmaz, 2010	D10 Parallel : 40 patients 40 2,3 wall intrabony defects	parallel : 40 intrabony	arallel: 40 intrabony		EMPs	4.6	<0,001	3.4	<0,001			
				EMPs + AB	5.6	I	4.2					
Aspriello,	Parallel with 56	ch 56 osseous					12 months	DFDBA	3.75	<0,05	3.5	<0,05
2011	2011 patients			DFDBA + EMPs	5.0		4.0					
Maula 2011	Parallel intrabony	el intrabony	12 months	EMPs	2.9		1.9	n.s.				
Meyle, 2011	with 73 patients	defect≥4 mm	12 months	EMPs + BC	2.8	n.s.	1.7					
	Parallel	30 class II	12	DFDBA + GTR	0.81	10.05	1.5	-0.05				
Jaiswal, 2013	with 30 furcatio patients defects			· ·		12 months	DFDBA + GTR + EMPs	1.74	<0,05	2.12	<0,05	
De	Parallel	34 intrabony		EMPs	3.51		2.73					
Leonardis, 2013	with 34 patients	defects ≥ 3 mm	defects ≥ 3	12 months	EMPs + HA/β- TCP	4.00	<0,001	3.47	<0,001			
Ogikara	Darallah CO	69	12.20	EMPs	1.91		3.04					
Ogihara, 2014	patients defec	cients defects > 6	12-36 months	EMPs + DFDBA	3.7	<0,001	3.52	<0,001				
		mm		EMPs + FDBA	3.26		4.14					

The combination of xenografts (DBBM) with EMPs has been investigated in 5 clinical studies. It was first demonstrated by Lekovic et al. in a split mouth study with 21 patients having intrabony defects > 6 mm that the combination of EMPs with DBBM led to statistically improved mean PD and CAL change after a 6 month healing period when compared to EMPs alone [41]. Since then, 1 other study showed significant advantages for the combination approach whereas 3 others no statistically significant demonstrated advantage for the combination approach [42,43,44,45]. Zucchelli et al. found that EMPs + DBBM showed statistically significantly greater CAL gains, radiographic bone level gains and less gingival recessions following a combination therapy with EMPs + DBBM [45].

The use of EMPs in combination with synthetic materials including Bioglass, (BG),  $\beta$ -Tricalcium phosphate ( $\beta$ -TCP), biphasic calcium phosphate (BCP), and hydroxyappatite (HA) has led to variable results for the regeneration of human intrabony defects. In 2 parallel studies evaluating the combination of EMPs with BG, no significant change in mean PD or CAL were observed when compared to either BG alone or EMPs alone following a 12 month healing period [46,47]. In contrast, Kuru et al. found after an 8 month healing period that a statistically significant increase in PD reduction and CAL was observed when compared to EMPs alone [48]. The combination of EMPs with  $\beta$ -TCP was investigated by Bokan et al. who showed that no statistical difference in mean PD change and CAL was observed after a 12 month healing period [49]. Similar results were also found for the combination of EMPs with BCP following a 6 and 12-month healing period [50,51]. A study combining  $HA/\Box$  -TCP with EMPs found that EMPs statistically improved the mean PD and CAL change for intrabony defects greater or equal to 3mm [52]. Moreover, the combination of EMPs and various types of grafting materials has provided evidence for periodontal regeneration in animal and humans, thus justifying its biologic rationale in reconstructive periodontal surgery [53,54,55-57].

In a recent systematic review including meta-analysis, Matarasso et al. found that the combination of EMPs + grafting material resulted in additional clinical improvements in terms of CAL gain and PD reduction compared with those obtained with EMPs alone [58]. Mean CAL gain amounted to 3.76 ± 1.07 mm (median 3.63 95% CI: 3.51-3.75) following treatment with a combination of EMPs and bone graft and to 3.32±1.04 mm (median 3.40; 95% CI 3.28; 3.52) following treatment with EMPs alone. Mean PD reduction measured 4.22±1.20 mm (median 4.10; 95%CI3.96-4.24) at sites treated with EMPs and bone graft and yielded 4.12±1.07 mm (median 4.00; 95% CI 3.88-4.12) at sites treated with EMPs alone. A clinical case is demonstrating provided periodontal regeneration following application of DBBM + EMPs.

On the other hand, a large variability amongst the studies was found which was partly explained by the fact that reconstructive surgery was performed in defects with different types of morphology (i.e. contained 2 and 3 walled defects and non-contained 1 and -2 walled ones), using different types of grafts and surgical techniques. Interestingly, the potential influence of the used graft or the surgical procedure (i.e. the used flap design) on the clinical outcomes is unclear. Furthermore, no differences in terms of tooth survival rate were found between the combination approach and EMPs (i.e. both approaches yielding 100% tooth survival) and none of them reported on the outcomes in terms of residual pockets  $\geq 5$ mm. Furthermore, no data on the costeffectiveness of using the combination approach is available.

## Combination of PDGF with bone grafting materials

The second most utilized biological growth factor for intrabony defect regeneration has been Platelet Derived Growth Factor (PDGF). Initially it was used as a concentrated form isolate from platelets by isolating autologous blood followed by centrifugation allowing super-physiological concentrations [59,60]. Following rigorous preclinical testing, recombinant human PDGF (rhPDGF) was granted FDA approval as the first such growth factor of its kind built from recombinant proteins [61,62]. Its main action is derived following injury by promoting rapid cell migration, proliferation and angiogenesis to defect sites [63]. Three different isoforms PDGF-AA, PDGF-AB and PDGF-BB are available [64].

The use of rhPDGF with a bone grafting carrier system has been investigated in comparison to bone grafting material alone in 4 different human randomized clinical studies. In the first study investigating the use of rhPDGF-BB in combination with a synthetic beta-TCP for the healing of advanced periodontal osseous defects, 11 clinical centers enrolled 180 subjects with 4mm or greater intrabony defects. It was found that PDGF at a concentration of 0.3 mg/ml led to significantly improved CAL gain and percentage of bone fill at 3 months following surgery when compared to beta-TCP alone; however, this difference was no longer significant at 6 months [65]. Nevertheless, on a long-term basis (up to 36 months), a consistent improvement in CAL gain was observed compared to the baseline. Moreover, the regenerative technique yielded significantly higher clinical improvements in terms of bone fill compared to the control (i.e. synthetic beta-TCP).

In a second double blinded, prospective, parallel, randomized multi-center clinical trial of 54 patients, it was found that rhPDGF-BB+ $\beta$ -TCP also performed better than  $\beta$ -TCP alone [66]. Thakare and Deo also found that following 12 months of healing, а concentration of 0.3 mg/ml was able to significantly improve CAL and PD reductions when compared to the bone grafting material utilized alone [67]. Furthermore, it was also concluded in a split mouth study comparing the regenerative potential of intrabony defects that rhPDGF-BB+β-TCP led to significantly higher CAL and PD reduction when compared to of  $\beta$ -TCP alone [68]. Despite a small number of clinical trials with appropriate controls, there have been numerous other case reports and retrospective studies that have demonstrated that PDGF-BB in combination with a bone grafting material is capable of periodontal regeneration of intrabony defects and therefore, it could be suggested that it remains a viable treatment option[69,70-72,73,74-76,77,78].

Furthermore, studies have also confirmed the ability for rhPDGF + bone grafting material histologically to demonstrate periodontal regeneration in humans [73,79]. However, despite the fact that the use of rhPDGF + bone grafting is based on a biologic rationale and has provided evidence for periodontal regeneration in humans, no data are available on the potential beneficial effect of this approach over the outcomes obtained with OFD alone (i.e. without any grafting material). Moreover, the effect of this treatment on minimizing the number of sites < 6 mm has not yet been reported and requires further studies.

# Combination of PRP with bone grafting materials and membranes

Platelet Rich Plasma (PRP) is an autologous concentration of growth factors derived from typical platelets following centrifugation to reach super-natural concentrations [80,81]. It was first introduced in the 1970s as a fibrin glue and has since exploded in popularity for a variety of dental treatments and procedures. Since 1990, the understanding of concepts involved in tissue repair have demonstrated the ability for several key factors found in blood that improve the speed and quality of wound healing. PRP has since been utilised by many oral surgeons for extensive dental procedures [82,83,60]. Its main drawback includes the use of anticoagulants which has been shown to limit the natural healing process despite containing a number of growth factors implicated in tissue repair [80,81]. As PRP is a blood concentrate, its main use has been in combination with a bone grafting material.

The combined use PRP and several bone grafts for the treatment of intrabony human defects has been documented in several randomized controlled clinical trials [84,85, 86, 87, 88, 89-91, 92, 93-95, 96, 97, 98, 99] (Table 2) with contradictory conclusions. Five of the studies have investigated the additional effect of PRP in conjunction with bovine porous bone mineral (BPBM) and only two have reported positive results. Also, four studies have used β-TCP in combination with PRP and just one has claimed adjunctive beneficial effect of PRP. Furthermore, another study failed to show a positive result when PRP was added to bioglass (BG). On the other hand, five studies have claimed an additional effect of PRP when it combined with autograft (AUG), DFDBA or hydroxyapatite (HA).

In summary, despite a number of the available studies showing a tendency to indicate that the use of PRP may improve the CAL in the treatment of intrabony human defects, there is no solid evidence regarding the potential of PRP application. Additionally, although more than half of these studies reported a positive additional effect of PRP on the treatment of the intrabony defects, this effect was minimal to modest in the most of them. Nevertheless, the use of PRP was demonstrated by all selected RCTs to be entirely safe, without causing complications or adverse events and postoperative healing was uneventful in all RCTs. Despite its common use, to date there are no human histological studies documenting the use of PRP for periodontal regeneration and animal histological evidence is also quite limited.

Regarding the combined use of PRP with GTR, only few randomized controlled clinical trials are available [100,101,102-104,105] (Table 2). The majority of the studies (five out

of six) used the combination GTR plus bone graft as control vs. PRP plus GTR plus bone graft as test group. In summary, when platelet concentrates are used in conjunction to GTR, no adjunctive effect can be detected after 6 to 12 months. Among the six human studies using GTR, none accomplished to report any significant positive adjunctive effect of PRP. A possible explanation is that the proven efficacy of GTR in regenerative periodontal procedures could mask the potential effect of the platelet concentrate. Unfortunately, the vast majority of the selected RCTs provide no scientific data on whether the adjunctive use of PRP was associated with lower incidence of exposure of and resorbable non-resorbable barrier membranes, improved aesthetics, higher progression of soft and hard tissue healing or improved clinical handling of the combinations of PRP with various regenerative materials [106]. Furthermore, to date, no clinical investigation has evaluated this combination approach with human histology, thus it remains to be determined what type of regeneration/reparation is occurring following periodontal regenerative therapy.

In addition, a few studies have compared the effects of PRP + bone grafting material + barrier membrane [100,103,104,99]. YassibagBerkman et al. compared three groups on intrabony defect regeneration including, 1) graft alone (beta-TCP), 2) graft + PRP, and 3) graft + PRP + collagen membrane. No statistically significant difference could be observed between the groups [99]. Dori et al. investigated PRP in a study containing twentyfour patients with advanced chronic periodontal disease and displaying one intrabony defect whom were randomly treated with a combination of either PRP + DBBM + GTR or DBBM + GTR [103]. No difference in any of the investigated parameters including plaque index (PI), gingival index (GI), bleeding on probing (BOP), PD, GR and CAL was observed [103]. Furthermore, Dori et al. also investigated the same combination approach with beta-TCP [20]. Once again no significant difference could be observed for any of the measured parameters [104]. Camargo et al. compared twenty-three paired intrabony defects treated with DBBM + GTR + PRP or [100]. No significant DBBM + GTR differences could be observed [100]. Therefore, the additive effect of combining 3 therapies including barrier membrane + bone grafting material + PRP did not lead to significant clinical improvements in any of the above mentioned studies.

Author & Year	Study Desing, patient number	Healing Period	Treatment Groups	Mean PD change (mm)	<i>P</i> value	Mean CAL Change (mm)	<i>P</i> value	
	RCT/split-mouth, 13		BPBM	2.5 ± 1.0		2.3 ± 1.2	0.026	
Hanna et al. 2004	patients	6 months	BPBM+PRP	3.5 ± 1.2	0.033	3.2 ± 1.0		
Okuda et al. 2005	RCT/parallel, 70 patients	12 months	НА	3.7 ± 2.0	<0.05	2.0 ± 1.2	<0.001	
	Nell'parallel, 70 patients	12 11011013	HA+PRP	4.7 ± 1.6	<0.05	3.4 ± 1.7		
Ouwang & Oian 2000	RCT/mixted, 10 patients	12 months	BPBM	3.5 ± 0.4	<0.01	2.9 ± 0.8	<0.01	
Ouyang & Qiao 2006			BPBM+PRP	4.8 ± 1.0		4.5 ± 1.1		
Vasilas Darlinas et al. 2007	RCT/mixted, 25 patients	12 months	b-TCP	4.1	n.s.	2.4	n.s.	
Yassibag-Berkman et al. 2007			bTCP+PRP	3.6		2.1		
Demir et al. 2007	RCT/parallel, 29 patients	9 months	BG	3.3 ± 0.5	n.s.	2.9 ± 0.4	n.s.	
Denni et al. 2007			BG+PRP	3.6 ± 0.5		3.1 ± 0.5		
Döri et al. 2008	RCT/parallel, 26 patients	12 months	BPBM/EMPs	5.9 ± 1.3		5.0±0.9	n.s.	
Don et al. 2008			BPBM/EMPs+PRP	5.8 ± 1.8	n.s.	4.8±1.3		
	RCT/parallel, 60 patients	12 months	DFDBA	3.5 ± 1.9	<0.05	2.4 ± 2.2	<0.001	
Piemontese et al. 2008			DFDBA+PRP	4.6 ± 1.3	<0.05	3.6 ± 1.8		
Döri et al. 2009	PCT/parallel 20 patients	12 months	12	BPBM	5.3±1.7		4.7±1.6	n.s.
Don et al. 2009	09 RCT/parallel, 30 patients		BPBM+PRP	5.2±1.6	n.s.	4.6±1.7	11.5.	

				1					
Harnack et al. 2009	RCT/split-mouth, 22	6 months	b-TCP	0.4	n.s.	0.3	n.s.		
	patients	omonths	bTCP+PRP	0.8	11.5.	0.1			
Parimala & Mehta 2010	RCT/split-mouth, 14	9 months	BPBM	6.2±1.4	n.s.	4.1±1.1	n.s.		
	patients	9 11011115	BPBM+PRP	6.6±1.4	11.5.	4.7±0.8			
Kaushish at al. 2011	RCT/split-mouth, 10	6 months	HA/b-TCP	3.3±0.8	0.03	2.9±0.7	0.002		
Kaushick et al. 2011	patients	6 months	HA/b-TCP+PRP	4.3±0.9	0.03	4.4±0.8			
C-:-: -+ -  2011	RCT/split-mouth, 20 patients	3 months	b-TCP	2.2±0.2	0.036	1.1±0.2	0.042		
Saini et al. 2011		3 months	bTCP+PRP	2.8±0.3		1.8±0.3			
Ozdemir & Okte 2012	RCT/split-mouth, 14 patients	6 months	b-TCP	3.0 ±1.3	n.s.	2.0 ±1.3	n.s.		
Ozdemír & Okte 2012			bTCP+PRP	3.0 ±1.3		2.0 ±2.0			
	RCT/split-mouth, 12	12	AUG	4.4	.0.01	2.9	.0.01		
Hassan et al. 2012	patients	12 months	AUG+PRP	5.0	<0.01	3.8	<0.01		
Curta 2014	RCT/split-mouth, 10	12 months	HA	1.9	10.05	1.2	<0.05		
Gupta 2014	patients		HA+PRP	3.4	<0.05	3.1			
A	RCT/split-mouth, 24	12 months			DFDBA	2.7 ± 0.4	10.05	2.4 ± 0.6	10.05
Agarwal & Gupta 2014	wal & Gupta 2014 patients 12		DFDBA+PRP	3.3 ± 0.5	<0.05	3.2 ± 0.5	<0.05		

Taken together, the additional use of PRP to various types of grafting materials used in conjunction with EMPs or membranes, did not reveal statistically or clinically significant benefits in terms of CAL gain and PPD reduction. Moreover, the additional efforts and costs related to the use of PRP (i.e. sampling blood, use of various centrifuges and anticoagulants) along with patient centred outcomes have has not yet been evaluated. Since at present no data on the effect of various combination modalities including PRP on reducing periodontal pockets are available and as such, its clinical benefit appears to be more than questionable.

# Combination of biologic agents/growth factors and membranes

The use of barrier membranes has been demonstrated to provide additional spacemaintenance for the regrowth of periodontal tissues [107]. The rationale behind a combination strategy is based on the fact that while the barrier membrane is able to create additional space for the repopulation of periodontal tissues, the additional use of a growth factor is then capable of speeding their regeneration by either providing faster cell repopulation or influencing their differentiation towards specialized tissues [107]. While less studies with appropriate controls have investigated this combination, it does possess theoretical advantages when

compared to the use of membranes alone or growth factors alone. Below the use of EMPs are discussed in combination with a barrier membrane for their possible improvement of periodontal regeneration of intrabony defects.

### **Combination EMPs + Membrane**

An animal study was first investigated following surgically created intrabony defects in monkeys. Treatment groups included 1) OFD + GTR, 2) OFD + EMPs, 3) OFD + EMPs + GR or 4) OFD alone (control) [108]. The results from this histological investigation demonstrated that although OFD + EMPs + GTR may enhance new attachment and bone, the results were not superior to those found in OFD + EMPs alone or OFD + GTR alone [108].

In the first human study analyzing this combination, a series of 56 patients were either assigned to 1) OFD, 2) EMPs alone, 3) GTR alone or 4) EMPs + GTR [31]. Mean PD change and CAL were investigated. No significant difference between treatment sites receiving EMPs + GTR, EMPs alone or GTR alone could be observed [31]. Furthermore, a second parallel study and a split mouth study no preferential regeneration found of periodontal tissues for the combination of EMPs + GTR when compared to EMPs alone, or GTR alone (Table 3) [62,108]. Furthermore, no human histological study has investigated this combination.

No of Studies	no of teeth	CAL gain range	tooth survival	follow up time
9	126	2.0 ± 0.4 - 5.9 ± 1.2	100%	6 - 12 m
9	134	2.0 ± 1.4 - 5.4 ± 1.7	100%	6 - 12 m
8	137	2.1 ± 1.1 - 3.0 ± 2.0	81.8% - 100%	3 - 10 y
4	56	2.3 ± 2.1 - 4.1 ± 1.6	90.9% - 100%	6 – 10 y
	9 9 8	9 126   9 134   8 137	9 126 2.0 ± 0.4 - 5.9 ± 1.2   9 134 2.0 ± 1.4 - 5.4 ± 1.7   8 137 2.1 ± 1.1 - 3.0 ± 2.0	9 126 2.0 ± 0.4 - 5.9 ± 1.2 100%   9 134 2.0 ± 1.4 - 5.4 ± 1.7 100%   8 137 2.1 ± 1.1 - 3.0 ± 2.0 81.8% - 100%

Table 3. Results from clinical short-term (6 - 12 months) and long-term (3 - 10 years) studies. (adapted and amended from Murphy & Gunsolley 2003 (short-term studies) and Figueiro et al. 2014 (long-term studies))

Taken together with the additional histological evidence from animals and humans, it can be concluded that the combination of EMPs with a GTR barrier membrane provides little to no additional support for the regeneration of intrabony defects.

## Combination of grafting materials with membranes

А critical factor for periodontal regeneration is provision of adequate space for new tissue formation during healing [111,112]. Since the majority of currently available membranes consist of supple materials, there is an inherent risk for membrane collapse in cases of non-supportive defect anatomy, i.e., the membrane collapses/falls (partially or totally) into the defect and/or towards the root surface, thus physically reducing the space available for new tissue invasion. Indeed, reduced amounts of periodontal regeneration, and of new bone formation in particular, due to membrane collapse was noticed in several preclinical in vivo studies on GTR [113,114,115,116]. Haney et al. [115] observed a statistically significant correlation between the space provided by the membrane and the amount of regenerated alveolar bone using a supra-alveolar defect model in dogs. Similarly, in the clinic, Cortellini et al. reported that application of self-supporting (reinforced with titanium strips) e-PTFE membranes, which could be positioned more coronally than

e-PTFE ordinary membranes, vielded statistically significant more CAL gain in intrabony defects [117]. In a subsequent publication, a retrospective analysis of the results of this study showed that the most significant factor associated with the amount of regenerated tissue was the amount of space available under the membranes, and not the type of membrane [118]. Thus, membranes have often been combined with the use of particulated bone grafts and substitutes, with the aim to support the membrane and assure space provision, and thereby enhance the histological and clinical outcome of GTR treatment.

Almost all available bone graft and substitute materials have been combined with GTR membranes for the treatment of periodontal intrabony defects [119,120].

Murphy & Gunssoley, in a systematic review, evaluated all randomized control studies, cohort studies, and case-control studies on GTR (both non-resorbable and resorbable barriers) in combination with bone grafts/substitutes [121]. The review identified studies providing direct comparisons 7 between intrabony defects treated with membranes in combination with bone grafts/substitutes and defects treated with membranes only. Significant clinical improvements, i.e. CAL gains (average range 2.0-5.4 mm) and PD reduction (average range 2.3-5.8 mm), were observed in sites treated with the combination approach (Table 4).

	√o of Studies	No of Teeth	Defect depth (mm)	Osseouswal Is	CF (%)	NC (%)	NB (%)	JE (%)
Animal								
GTR	18	201	$4.9 \pm 0.9$	1-3	43 ± 29	66 ± 25	58 ± 25	25 ± 17
GTR+BG/BS	14	95	5.2 ± 1.1	1-3	28 ± 20	64 ± 21	58 ± 6	15 ± 13
Human								
GTR	8	20	5.1 ± 2.5	1-3	3.1 ± 2.1	2.6 ± 1.6	1.7 ± 1.3	-
GTR+BG/BS	8	39	6.22 ± 2.04	1-3	0.47 ± 0.63	2.32 ± 1.94	2.41 ±1.61	2.53 ± 1.14

Table 4. Histomorphometric results of animal and human histological studies (Adapted from Ivanovic et al. 2014 (animal data) and Sculean et al. 2015 (human data)

However, the meta-analysis performed in that study failed to reveal any statistically significant or clinically meaningful differences between the two treatment modalities in any of the evaluated parameters; differences were in a range of magnitude 0.01-0.7 mm. On the same conclusion led the results of another very recent systematic review [122] which identified few studies providing onlv a direct comparisons between membranes with and without bone grafts/substitutes, that were published at a later time-point then those included in the former review [121]. For instance, Stavropoulos et al observed an average CAL gain and residual PD of 2.5 mm and 4.9 mm, respectively, in sites treated with a PLA/PGA membrane in combination with DBBM [123]. The corresponding values in sites treated only with membranes were 2.9 mm and 4.9 mm, respectively. Similarly, no significant difference was observed between the combination approach and the monotherapy, in terms of radiographic bone formation (2.8 mm and 3.1 mm, respectively). In this context, it has also to be remembered that DBBM is a radiopaque material, and thus radiographic bone fill in DBBM treated sites does not necessary imply bone and/or periodontal regeneration. On the other hand, human histologic evidence indicates that the combination of DBBM and membranes may not only result in substantial clinical and radiographic improvements, but may also promote periodontal regeneration in human intrabony defects [12].

Several randomized controlled clinical studies and systematic reviews have evaluated

the effects of combining DBBM and collagen membranes on the healing of intrabony defects. The available data indicate that in deep intrabony defects, this combination may lead to statistically and clinically higher improvements in terms of CAL gain and PD reduction compared to OFD alone (Sculean et al. 2003, 2005, Tonetti et al. 2004, Stoecklin-Wasmer et al. 2013). In a systematic review including meta-analysis Stoecklin-Wasmer et al. 2013 have shown that the combination of bone grafts and GTR with collagen membranes resulted in significantly higher CAL gain (i.e. weighted mean difference of 1.71 mm (95% CI, 1.26 to 2.15)) when compared with OFD. Despite the fact that the available studies did not clearly report the number of residual pockets  $\geq 6$  mm, the combination approach has led to statistically and clinically significantly higher PPD reduction compared to OFD alone (i.e. weighted mean difference of 1.44 mm (95% CI, 1.04 to 1.85)). Therefore, these data suggest that this combination approach is a valuable modality to promote periodontal regeneration and pocket closure at deep intrabony defects.

In context, in an earlier systematic review looking specifically on pre-clinical in vivo studies on combinations of barrier membranes and grafting materials, Sculean et al. concluded that clear additional benefits of combination treatments over the use of membranes alone were detected only in defects sites with nonsupportive anatomy [124]. Specifically, larger amount of periodontal regeneration were observed only in non-contained two-wall intrabony or supra-alveolar defects, i.e. in sites with a larger risk of membrane collapse [124]. These preclinical findings are in line with clinical data indicating that a combination of GTR and bone grafts may only bear certain advantages over the use of GTR alone in defects with а non-self-containing configuration (for example in one wall defects), whereas in 2 and 3-wall defects the advantages may be limited to non- existent (Stoecklin-Wasmer et al. 2013). This aspect needs to be carefully considered during the decision making process in treating intrabony defects in order to avoid overtreatment and limit the possibilities of complications such as infections that may occur once several biomaterials are used simultaneously.

One relevant aspect, in this discussion, is long-term outcome of treatment. the According to the results of a recent systematic review of controlled clinical studies [125] that identified 11 publications reporting on treatment outcomes after an observation period of 3 to 10 years post-operatively, the clinical improvements achieved at short-term after regenerative treatment with the use of membranes in combination with bone grafts/substitutes can in general be preserved on the long-term. In particular, the average CAL gain reported for sites treated with a membrane in combination with a bone graft/substitute was 2.3 - 4.1 mm (Table 4). However, this range of values was not much different from what it was observed for sites treated with only a membrane (2.1 - 3.0 mm). Most of the studies included in the review reported that only a small number of sites showed some CAL loss (mostly < 1 mm onaverage) between the short- and long-term evaluation time-point. Importantly, in one of the studies included in the review, specific analysis failed to show any association of DBB grafting (in combination with a resorbable membrane) with sites showing CAL loss within a 6-year period after treatment [126]. The results of Stavropoulos et al. [126] suggest, thus, that mere presence of bone graft substitute particles in the regenerated and/or repaired periodontal tissues may have no consequence per se on the stability of the improved clinical conditions as long as optimal plaque control is maintained.

Overall, treatment of periodontal intrabony defects with membranes in combination of bone grafts/substitutes may result, at least in part, in periodontal regeneration while clinically, the results are accompanied by significant clinical improvements evidenced by CAL gain and pocket closure [12]. These improvements are in general preserved on the long-term for the majority of cases, provided the patient performs adequate oral hygiene and receives supportive periodontal therapy. Nevertheless, it appears that this combination may bear clinical relevance in non-contained defects or defects with a complicated anatomy.

### Conclusions and future perspectives

Although numerous attempts and combination approaches have been made to enhance periodontal regeneration, it remains an optimistic future goal as complete periodontal regeneration at present is not predictably achievable.

Despite this, numerous combination approaches have been utilized to improve intrabony defect regeneration and decrease residual pockets around teeth. The available literature suggests that the combination of biologic agents/growth factors/GTR with bone grafting materials may possess a biologically sound rationale which also bears clinical relevance evidenced in superior clinical outcomes compared to treatment with OFD alone. However, it also appears that combination or biologic agents/growth factors or bone grafting materials and GTR may only bear certain clinical relevance in defects with a more complicated (i.e. so called non-selfcontaining defects) while in two or three wall defects no clear advantage is present. Furthermore, it might be speculated that the use of GTR barriers may be replaced by the use of biologic agents/growth factors when used in combination with bone grafting materials.

### **Conflict of interest:** None to declare.

### References

 Eke PI, Dye BA, Wei L, Thornton-Evans GO, Genco RJ, Cdc Periodontal Disease Surveillance workgroup: James Beck GDRP. Prevalence of periodontitis in adults in the United States: 2009 and 2010. J Dent Res 2012; 91: 914-920.

- 2. Axelsson P, Nystrom B, Lindhe J. The long-term effect of a plaque control program on tooth mortality, caries and periodontal disease in adults. Results after 30 years of maintenance. J Clin Periodontol 2004; 31: 749-757.
- 3. Claffey N, Egelberg J. Clinical indicators of probing attachment loss following initial periodontal treatment in advanced periodontitis patients. J Clin Periodontol 1995; 22: 690-696.
- Matuliene G, Pjetursson BE, Salvi GE, Schmidlin K, Bragger U, Zwahlen M, Lang NP. Influence of residual pockets on progression of periodontitis and tooth loss: results after 11 years of maintenance. J Clin Periodontol 2008; 35: 685-695.
- 5. Papapanou PN, Tonetti MS. Diagnosis and epidemiology of periodontal osseous lesions. Periodontology 2000 2000; 22: 8-21.
- Soder B, Jin LJ, Soder PO, Wikner S. Clinical characteristics of destructive periodontitis in a risk group of Swedish urban adults. Swed Dent J 1995; 19: 9-15.
- 7. Papapanou PN, Tonetti MS. Diagnosis and epidemiology of periodontal osseous lesions. Periodontol 2000 2000; 22: 8-21.
- Douglas de Oliveira DW, Oliveira-Ferreira F, Flecha OD, Gonçalves PF. Is surgical root coverage effective for the treatment of cervical dentin hypersensitivity? A systematic review. Journal of periodontology 2013; 84: 295-306.
- 9. Cortellini P, Tonetti MS. Clinical concepts for regenerative therapy in intrabony defects. Periodontol 2000 2015; 68: 282-307.
- Kaigler D, Avila G, Wisner-Lynch L, Nevins ML, Nevins M, Rasperini G, Lynch SE, Giannobile WV. Platelet-derived growth factor applications in periodontal and peri-implant bone regeneration. Expert Opin Biol Ther 2011; 11: 375-385.
- Miron RJ, Zhang YF. Osteoinduction: a review of old concepts with new standards. J Dent Res 2012; 91: 736-744.
- 12. Sculean A, Nikolidakis D, Nikou G, Ivanovic A, Chapple IL, Stavropoulos A. Biomaterials for promoting periodontal regeneration in human intrabony defects: a systematic review. Periodontol 2000 2015; 68: 182-216.
- 13. Trombelli L. Which reconstructive procedures are effective for treating the periodontal intraosseous defect? Periodontol 2000 2005; 37: 88-105.
- 14. Giannoudis PV, Dinopoulos H, Tsiridis E. Bone substitutes: an update. Injury 2005; 36 Suppl 3: S20-27.
- 15. Place ES, Evans ND, Stevens MM. Complexity in biomaterials for tissue engineering. Nat Mater 2009; 8: 457-470.
- 16. Trombelli L, Bottega S, Zucchelli G. Supracrestal soft tissue preservation with enamel matrix

proteins in treatment of deep intrabony defects. J Clin Periodontol 2002; 29: 433-439.

- 17. Karring T, Nyman S, Gottlow J, Laurell L. Development of the biological concept of guided tissue regeneration--animal and human studies. Periodontol 2000 1993; 1: 26-35.
- Susin C, Fiorini T, Lee J, De Stefano JA, Dickinson DP, Wikesjo UM. Wound healing following surgical and regenerative periodontal therapy. Periodontol 2000 2015; 68: 83-98.
- 19. Needleman IG, Worthington HV, Giedrys-Leeper E, Tucker RJ. Guided tissue regeneration for periodontal infra-bony defects. Cochrane Database Syst Rev 2006: Cd001724.
- 20. Miron RJ, Caluseru OM, Guillemette V, Zhang Y, Gemperli AC, Chandad F, Sculean A. Influence of enamel matrix derivative on cells at different maturation stages of differentiation. PLoS One 2013; 8: e71008.
- 21. Amin HD, Olsen I, Knowles JC, Dard M, Donos N. Effects of enamel matrix proteins on multi-lineage differentiation of periodontal ligament cells in vitro. Acta Biomater 2013; 9: 4796-4805.
- 22. Miron RJ, Sculean A, Cochran DL, Froum S, Zucchelli G, Nemcovsky C, Donos N, Lyngstadaas SP, Deschner J, Dard M, Stavropoulos A, Zhang Y, Trombelli L, Kasaj A, Shirakata Y, Cortellini P, Tonetti M, Rasperini G, Jepsen S, Bosshardt DD. 20 years of Enamel Matrix Derivative: The past, the present and the future. J Clin Periodontol 2016.
- 23. Bosshardt DD. Biological mediators and periodontal regeneration: a review of enamel matrix proteins at the cellular and molecular levels. J Clin Periodontol 2008; 35: 87-105.
- 24. Miron RJ, Dard M, Weinreb M. Enamel matrix derivative, inflammation and soft tissue wound healing. J Periodontal Res 2014.
- 25. Esposito M, Grusovin MG, Papanikolaou N, Coulthard P, Worthington HV. Enamel matrix derivative (Emdogain(R)) for periodontal tissue regeneration in intrabony defects. Cochrane Database Syst Rev 2009: Cd003875.
- 26. Froum SJ, Weinberg MA, Rosenberg E, Tarnow D. A comparative study utilizing open flap debridement with and without enamel matrix derivative in the treatment of periodontal intrabony defects: a 12-month re-entry study. J Periodontol 2001; 72: 25-34.
- 27. Heijl L, Heden G, Svardstrom G, Ostgren A. Enamel matrix derivative (EMDOGAIN) in the treatment of intrabony periodontal defects. J Clin Periodontol 1997; 24: 705-714.
- 28. Okuda K, Momose M, Miyazaki A, Murata M, Yokoyama S, Yonezawa Y, Wolff LF, Yoshie H. Enamel matrix derivative in the treatment of human intrabony osseous defects. J Periodontol 2000; 71: 1821-1828.

- 29. Pontoriero R, Wennstrom J, Lindhe J. The use of barrier membranes and enamel matrix proteins in the treatment of angular bone defects. A prospective controlled clinical study. J Clin Periodontol 1999; 26: 833-840.
- 30. Rosing CK, Aass AM, Mavropoulos A, Gjermo P. Clinical and radiographic effects of enamel matrix derivative in the treatment of intrabony periodontal defects: a 12-month longitudinal placebo-controlled clinical trial in adult periodontitis patients. J Periodontol 2005; 76: 129-133.
- 31. Sculean A, Windisch P, Chiantella GC, Donos N, Brecx M, Reich E. Treatment of intrabony defects with enamel matrix proteins and guided tissue regeneration. A prospective controlled clinical study. J Clin Periodontol 2001; 28: 397-403.
- 32. Silvestri M, Ricci G, Rasperini G, Sartori S, Cattaneo V. Comparison of treatments of infrabony defects with enamel matrix derivative, guided tissue regeneration with a nonresorbable membrane and Widman modified flap. A pilot study. J Clin Periodontol 2000; 27: 603-610.
- 33. Tonetti MS, Lang NP, Cortellini P, Suvan JE, Adriaens P, Dubravec D, Fonzar A, Fourmousis I, Mayfield L, Rossi R, Silvestri M, Tiedemann C, Topoll H, Vangsted T, Wallkamm B. Enamel matrix proteins in the regenerative therapy of deep intrabony defects. J Clin Periodontol 2002; 29: 317-325.
- 34. Zucchelli G, Bernardi F, Montebugnoli L, De SM. Enamel matrix proteins and guided tissue regeneration with titanium-reinforced expanded polytetrafluoroethylene membranes in the treatment of infrabony defects: a comparative controlled clinical trial. J Periodontol 2002; 73: 3-12.
- 35. Guida L, Annunziata M, Belardo S, Farina R, Scabbia A, Trombelli L. Effect of autogenous cortical bone particulate in conjunction with enamel matrix derivative in the treatment of periodontal intraosseous defects. J Periodontol 2007; 78: 231-238.
- 36. Yilmaz S, Cakar G, Yildirim B, Sculean A. Healing of two and three wall intrabony periodontal defects following treatment with an enamel matrix derivative combined with autogenous bone. J Clin Periodontol 2010; 37: 544-550.
- 37. Gurinsky BS, Mills MP, Mellonig JT. Clinical evaluation of demineralized freeze-dried bone allograft and enamel matrix derivative versus enamel matrix derivative alone for the treatment of periodontal osseous defects in humans. J Periodontol 2004; 75: 1309-1318.
- Hoidal MJ, Grimard BA, Mills MP, Schoolfield JD, Mellonig JT, Mealey BL. Clinical evaluation of demineralized freeze-dried bone allograft with and

without enamel matrix derivative for the treatment of periodontal osseous defects in humans. J Periodontol 2008; 79: 2273-2280.

- 39. Aspriello SD, Ferrante L, Rubini C, Piemontese M. Comparative study of DFDBA in combination with enamel matrix derivative versus DFDBA alone for treatment of periodontal intrabony defects at 12 months post-surgery. Clin Oral Investig 2011; 15: 225-232.
- 40. Ogihara S, Tarnow DP. Efficacy of enamel matrix derivative with freeze-dried bone allograft or demineralized freeze-dried bone allograft in intrabony defects: a randomized trial. J Periodontol 2014; 85: 1351-1360.
- 41. Lekovic V, Camargo PM, Weinlaender M, Nedic M, Aleksic Z, Kenney EB. A comparison between enamel matrix proteins used alone or in combination with bovine porous bone mineral in the treatment of intrabony periodontal defects in humans. J Periodontol 2000; 71: 1110-1116.
- 42. Scheyer ET, Velasquez-Plata D, Brunsvold MA, Lasho DJ, Mellonig JT. A clinical comparison of a bovine-derived xenograft used alone and in combination with enamel matrix derivative for the treatment of periodontal osseous defects in humans. J Periodontol 2002; 73: 423-432.
- 43. Sculean A, Chiantella GC, Windisch P, Gera I, Reich E. Clinical evaluation of an enamel matrix protein derivative (Emdogain) combined with a bovinederived xenograft (Bio-Oss) for the treatment of intrabony periodontal defects in humans. Int J Periodontics Restorative Dent 2002; 22: 259-267.
- 44. Velasquez-Plata D, Scheyer ET, Mellonig JT. Clinical comparison of an enamel matrix derivative used alone or in combination with a bovine-derived xenograft for the treatment of periodontal osseous defects in humans. J Periodontol 2002; 73: 433-440.
- 45. Zucchelli G, Amore C, Montebugnoli L, De Sanctis M. Enamel matrix proteins and bovine porous bone mineral in the treatment of intrabony defects: a comparative controlled clinical trial. J Periodontol 2003; 74: 1725-1735.
- 46. Sculean A, Barbe G, Chiantella GC, Arweiler NB, Berakdar M, Brecx M. Clinical evaluation of an enamel matrix protein derivative combined with a bioactive glass for the treatment of intrabony periodontal defects in humans. J Periodontol 2002; 73: 401-408.
- 47. Sculean A, Pietruska M, Schwarz F, Willershausen B, Arweiler NB, Auschill TM. Healing of human intrabony defects following regenerative periodontal therapy with an enamel matrix protein derivative alone or combined with a bioactive glass. A controlled clinical study. J Clin Periodontol 2005; 32: 111-117.

- 48. Kuru B, Yilmaz S, Argin K, Noyan U. Enamel matrix derivative alone or in combination with a bioactive glass in wide intrabony defects. Clin Oral Investig 2006; 10: 227-234.
- 49. Bokan I, Bill JS, Schlagenhauf U. Primary flap closure combined with Emdogain alone or Emdogain and Cerasorb in the treatment of intrabony defects. J Clin Periodontol 2006; 33: 885-893.
- 50. Jepsen S, Topoll H, Rengers H, Heinz B, Teich M, Hoffmann T, Al-Machot E, Meyle J, Jervoe-Storm PM. Clinical outcomes after treatment of intrabony defects with an EMD/synthetic bone graft or EMD alone: a multicentre randomized-controlled clinical trial. J Clin Periodontol 2008; 35: 420-428.
- 51. Meyle J, Hoffmann T, Topoll H, Heinz B, Al-Machot E, Jervoe-Storm PM, Meiss C, Eickholz P, Jepsen S. A multi-centre randomized controlled clinical trial on the treatment of intra-bony defects with enamel matrix derivatives/synthetic bone graft or enamel matrix derivatives alone: results after 12 months. J Clin Periodontol 2011; 38: 652-660.
- 52. De Leonardis D, Paolantonio M. Enamel matrix derivative, alone or associated with a synthetic bone substitute, in the treatment of 1- to 2-wall periodontal defects. J Periodontol 2013; 84: 444-455.
- 53. Ivanovic A, Nikou G, Miron RJ, Nikolidakis D, Sculean A. Which biomaterials may promote periodontal regeneration in intrabony periodontal defects? A systematic review of preclinical studies. Quintessence Int 2014; 45: 385-395.
- 54. Sculean A, Chiantella GC, Arweiler NB, Becker J, Schwarz F, Stavropoulos A. Five-year clinical and histologic results following treatment of human intrabony defects with an enamel matrix derivative combined with a natural bone mineral. Int J Periodontics Restorative Dent 2008; 28: 153-161.
- 55. Sculean A, Windisch P, Keglevich T, Chiantella GC, Gera I, Donos N. Clinical and histologic evaluation of human intrabony defects treated with an enamel matrix protein derivative combined with a bovine-derived xenograft. Int J Periodontics Restorative Dent 2003; 23: 47-55.
- 56. Sculean A, Windisch P, Keglevich T, Gera I. Clinical and histologic evaluation of an enamel matrix protein derivative combined with a bioactive glass for the treatment of intrabony periodontal defects in humans. Int J Periodontics Restorative Dent 2005; 25: 139-147.
- 57. Sculean A, Windisch P, Szendroi-Kiss D, Horvath A, Rosta P, Becker J, Gera I, Schwarz F. Clinical and histologic evaluation of an enamel matrix derivative combined with a biphasic calcium phosphate for the treatment of human intrabony periodontal defects. J Periodontol 2008; 79: 1991-1999.

- 58. Matarasso M, Iorio-Siciliano V, Blasi A, Ramaglia L, Salvi GE, Sculean A. Enamel matrix derivative and bone grafts for periodontal regeneration of intrabony defects. A systematic review and metaanalysis. Clin Oral Investig 2015; 19: 1581-1593.
- 59. El-Sharkawy H, Kantarci A, Deady J, Hasturk H, Liu H, Alshahat M, Van Dyke TE. Platelet-rich plasma: growth factors and pro- and anti-inflammatory properties. J Periodontol 2007; 78: 661-669.
- 60. Marx RE, Carlson ER, Eichstaedt RM, Schimmele SR, Strauss JE, Georgeff KR. Platelet-rich plasma: Growth factor enhancement for bone grafts. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998; 85: 638-646.
- 61. Steed DL, Donohoe D, Webster MW, Lindsley L. Effect of extensive debridement and treatment on the healing of diabetic foot ulcers. Diabetic Ulcer Study Group. J Am Coll Surg 1996; 183: 61-64.
- 62. Wieman TJ, Smiell JM, Su Y. Efficacy and safety of a topical gel formulation of recombinant human platelet-derived growth factor-BB (becaplermin) in patients with chronic neuropathic diabetic ulcers. A phase III randomized placebo-controlled doubleblind study. Diabetes Care 1998; 21: 822-827.
- 63. Ronnstrand L, Heldin CH. Mechanisms of plateletderived growth factor-induced chemotaxis. Int J Cancer 2001; 91: 757-762.
- 64. Alvarez RH, Kantarjian HM, Cortes JE. Biology of platelet-derived growth factor and its involvement in disease. Mayo Clin Proc 2006; 81: 1241-1257.
- 65. Nevins M, Giannobile WV, McGuire MK, Kao RT, Mellonig JT, Hinrichs JE, McAllister BS, Murphy KS, McClain PK, Nevins ML, Paquette DW, Han TJ, Reddy MS, Lavin PT, Genco RJ, Lynch SE. Plateletderived growth factor stimulates bone fill and rate of attachment level gain: results of a large multicenter randomized controlled trial. J Periodontol 2005; 76: 2205-2215.
- 66. Jayakumar A, Rajababu P, Rohini S, Butchibabu K, Naveen A, Reddy PK, Vidyasagar S, Satyanarayana D, Pavan Kumar S. Multi-centre, randomized clinical trial on the efficacy and safety of recombinant human platelet-derived growth factor with beta-tricalcium phosphate in human intra-osseous periodontal defects. J Clin Periodontol 2011; 38: 163-172.
- 67. Thakare K, Deo V. Randomized controlled clinical study of rhPDGF-BB + beta-TCP versus HA + beta-TCP for the treatment of infrabony periodontal defects: clinical and radiographic results. Int J Periodontics Restorative Dent 2012; 32: 689-696.
- 68. Maroo S, Murthy KR. Treatment of periodontal intrabony defects using beta-TCP alone or in combination with rhPDGF-BB: a randomized controlled clinical and radiographic study. Int J Periodontics Restorative Dent 2014; 34: 841-847.

- 69. Khoshkam V, Chan HL, Lin GH, Mailoa J, Giannobile WV, Wang HL, Oh TJ. Outcomes of Regenerative Treatment with rhPDGF-BB and rhFGF-2 for Periodontal Intrabony Defects: A Systematic Review and Meta-analysis. J Clin Periodontol 2015.
- 70. McGuire MK, Kao RT, Nevins M, Lynch SE. rhPDGF-BB promotes healing of periodontal defects: 24month clinical and radiographic observations. Int J Periodontics Restorative Dent 2006; 26: 223-231.
- 71. McGuire MK, Scheyer ET, Schupbach P. Growth factor-mediated treatment of recession defects: a randomized controlled trial and histologic and microcomputed tomography examination. J Periodontol 2009; 80: 550-564.
- 72. McGuire MK, Scheyer T, Nevins M, Schupbach P. Evaluation of human recession defects treated with coronally advanced flaps and either purified recombinant human platelet-derived growth factor-BB with beta tricalcium phosphate or connective tissue: a histologic and microcomputed tomographic examination. Int J Periodontics Restorative Dent 2009; 29: 7-21.
- 73. Nevins M, Camelo M, Nevins ML, Schenk RK, Lynch SE. Periodontal regeneration in humans using recombinant human platelet-derived growth factor-BB (rhPDGF-BB) and allogenic bone. J Periodontol 2003; 74: 1282-1292.
- 74. Nevins M, Hanratty J, Lynch SE. Clinical results using recombinant human platelet-derived growth factor and mineralized freeze-dried bone allograft in periodontal defects. Int J Periodontics Restorative Dent 2007; 27: 421-427.
- 75. Nevins M, Kao RT, McGuire MK, McClain PK, Hinrichs JE, McAllister BS, Reddy MS, Nevins ML, Genco RJ, Lynch SE, Giannobile WV. Plateletderived growth factor promotes periodontal regeneration in localized osseous defects: 36month extension results from a randomized, controlled, double-masked clinical trial. J Periodontol 2013; 84: 456-464.
- 76. Nevins M, Nevins ML, Karimbux N, Kim SW, Schupbach P, Kim DM. The combination of purified recombinant human platelet-derived growth factor-BB and equine particulate bone graft for periodontal regeneration. J Periodontol 2012; 83: 565-573.
- 77. Rosen PS. Using recombinant platelet-derived growth factor to facilitate wound healing. Compend Contin Educ Dent 2006; 27: 520-525.
- 78. Rosen PS, Toscano N, Holzclaw D, Reynolds MA. A retrospective consecutive case series using mineralized allograft combined with recombinant human platelet-derived growth factor BB to treat moderate to severe osseous lesions. Int J Periodontics Restorative Dent 2011; 31: 335-342.
- 79. Ridgway HK, Mellonig JT, Cochran DL. Human histologic and clinical evaluation of recombinant

human platelet-derived growth factor and betatricalcium phosphate for the treatment of periodontal intraosseous defects. Int J Periodontics Restorative Dent 2008; 28: 171-179.

- 80. Del Corso M, Vervelle A, Simonpieri A, Jimbo R, Inchingolo F, Sammartino G, Dohan Ehrenfest DM. Current knowledge and perspectives for the use of platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) in oral and maxillofacial surgery part 1: Periodontal and dentoalveolar surgery. Curr Pharm Biotechnol 2012; 13: 1207-1230.
- 81. Simonpieri A, Del Corso M, Vervelle A, Jimbo R, Inchingolo F, Sammartino G, Dohan Ehrenfest DM. Current knowledge and perspectives for the use of platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) in oral and maxillofacial surgery part 2: Bone graft, implant and reconstructive surgery. Curr Pharm Biotechnol 2012; 13: 1231-1256.
- 82. Marx RE. Platelet-rich plasma (PRP): what is PRP and what is not PRP? Implant Dent 2001; 10: 225-228.
- 83. Marx RE. Platelet-rich plasma: evidence to support its use. J Oral Maxillofac Surg 2004; 62: 489-496.
- 84. Agarwal A, Gupta ND. Platelet-rich plasma combined with decalcified freeze-dried bone allograft for the treatment of noncontained human intrabony periodontal defects: a randomized controlled split-mouth study. Int J Periodontics Restorative Dent 2014; 34: 705-711.
- 85. Demir B, Sengun D, Berberoglu A. Clinical evaluation of platelet-rich plasma and bioactive glass in the treatment of intra-bony defects. J Clin Periodontol 2007; 34: 709-715.
- 86. Dori F, Kovacs V, Arweiler NB, Huszar T, Gera I, Nikolidakis D, Sculean A. Effect of platelet-rich plasma on the healing of intrabony defects treated with an anorganic bovine bone mineral: a pilot study. J Periodontol 2009; 80: 1599-1605.
- 87. Dori F, Nikolidakis D, Huszar T, Arweiler NB, Gera I, Sculean A. Effect of platelet-rich plasma on the healing of intrabony defects treated with an enamel matrix protein derivative and a natural bone mineral. J Clin Periodontol 2008; 35: 44-50.
- 88. Gupta G. Clinical and radiographic evaluation of intra-bony defects in localized aggressive periodontitis patients with platelet rich plasma/hydroxyapatite graft: A comparative controlled clinical trial. Contemp Clin Dent 2014; 5: 445-451.
- 89. Hanna R, Trejo PM, Weltman RL. Treatment of intrabony defects with bovine-derived xenograft alone and in combination with platelet-rich plasma: a randomized clinical trial. J Periodontol 2004; 75: 1668-1677.
- 90. Harnack L, Boedeker RH, Kurtulus I, Boehm S, Gonzales J, Meyle J. Use of platelet-rich plasma in periodontal surgery--a prospective randomised

double blind clinical trial. Clin Oral Investig 2009; 13: 179-187.

- 91. Hassan KS, Alagl AS, Abdel-Hady A. Torus mandibularis bone chips combined with platelet rich plasma gel for treatment of intrabony osseous defects: clinical and radiographic evaluation. Int J Oral Maxillofac Surg 2012; 41: 1519-1526.
- 92. Kaushick BT, Jayakumar ND, Padmalatha O, Varghese S. Treatment of human periodontal infrabony defects with hydroxyapatite + beta tricalcium phosphate bone graft alone and in combination with platelet rich plasma: a randomized clinical trial. Indian J Dent Res 2011; 22: 505-510.
- 93. Okuda K, Tai H, Tanabe K, Suzuki H, Sato T, Kawase T, Saito Y, Wolff LF, Yoshiex H. Platelet-rich plasma combined with a porous hydroxyapatite graft for the treatment of intrabony periodontal defects in humans: a comparative controlled clinical study. J Periodontol 2005; 76: 890-898.
- 94. Ouyang XY, Qiao J. Effect of platelet-rich plasma in the treatment of periodontal intrabony defects in humans. Chin Med J (Engl) 2006; 119: 1511-1521.
- 95. Ozdemir B, Okte E. Treatment of intrabony defects with beta-tricalciumphosphate alone and in combination with platelet-rich plasma. J Biomed Mater Res B Appl Biomater 2012; 100: 976-983.
- 96. Parimala M, Mehta DS. Comparative evaluation of bovine porous bone mineral. J Indian Soc Periodontol 2010; 14: 126-131.
- 97. Piemontese M, Aspriello SD, Rubini C, Ferrante L, Procaccini M. Treatment of periodontal intrabony defects with demineralized freeze-dried bone allograft in combination with platelet-rich plasma: a comparative clinical trial. J Periodontol 2008; 79: 802-810.
- 98. Saini N, Sikri P, Gupta H. Evaluation of the relative efficacy of autologous platelet-rich plasma in combination with beta-tricalcium phosphate alloplast versus an alloplast alone in the treatment of human periodontal infrabony defects: a clinical and radiological study. Indian J Dent Res 2011; 22: 107-115.
- 99. Yassibag-Berkman Z, Tuncer O, Subasioglu T, Kantarci A. Combined use of platelet-rich plasma and bone grafting with or without guided tissue regeneration in the treatment of anterior Sculean A, Nikolidakis D, Schwarz F. Regeneration of periodontal tissues: combinations of barrier membranes and grafting materials - biological foundation and preclinical evidence: a systematic review. J Clin Periodontol 2008; 35: 106-116.
- 100. Camargo PM, Lekovic V, Weinlaender M, Divnic-Resnik T, Pavlovic M, Kenney EB. A surgical reentry study on the influence of platelet-rich plasma in enhancing the regenerative effects of bovine porous bone mineral and guided tissue

regeneration in the treatment of intrabony defects in humans. J Periodontol 2009; 80: 915-923.

- 101. Christgau M, Moder D, Wagner J, Glassl M, Hiller KA, Wenzel A, Schmalz G. Influence of autologous platelet concentrate on healing in intra-bony defects following guided tissue regeneration therapy: a randomized prospective clinical split-mouth study. J Clin Periodontol 2006; 33: 908-921.
- 102. Dori F, Huszar T, Nikolidakis D, Arweiler NB, Gera I, Sculean A. Effect of platelet-rich plasma on the healing of intra-bony defects treated with a natural bone mineral and a collagen membrane. J Clin Periodontol 2007; 34: 254-261.
- 103. Dori F, Huszar T, Nikolidakis D, Arweiler NB, Gera I, Sculean A. Effect of platelet-rich plasma on the healing of intrabony defects treated with an anorganic bovine bone mineral and expanded polytetrafluoroethylene membranes. J Periodontol 2007; 78: 983-990.
- 104. Dori F, Huszar T, Nikolidakis D, Tihanyi D, Horvath A, Arweiler NB, Gera I, Sculean A. Effect of platelet-rich plasma on the healing of intrabony defects treated with Beta tricalcium phosphate and expanded polytetrafluoroethylene membranes. J Periodontol 2008; 79: 660-669.
- Keles GC, Cetinkaya BO, Albayrak D, Koprulu H, Acikgoz G. Comparison of platelet pellet and bioactive glass in periodontal regenerative therapy. Acta Odontol Scand 2006; 64: 327-333.
- 106. Kotsovilis S, Markou N, Pepelassi E, Nikolidakis D. The adjunctive use of platelet-rich plasma in the therapy of periodontal intraosseous defects: a systematic review. J Periodontal Res 2010; 45: 428-443.
- 107. Nyman S, Lindhe J, Karring T, Rylander H. New attachment following surgical treatment of human periodontal disease. J Clin Periodontol 1982; 9: 290-296.
- Sculean A, Donos N, Brecx M, Reich E, Karring T. Treatment of intrabony defects with guided tissue regeneration and enamel-matrix-proteins. An experimental study in monkeys. J Clin Periodontol 2000; 27: 466-472.
- 109. Minabe M, Kodama T, Kogou T, Takeuchi K, Fushimi H, Sugiyama T, Mitarai E. A comparative study of combined treatment with a collagen membrane and enamel matrix proteins for the regeneration of intraosseous defects. Int J Periodontics Restorative Dent 2002; 22: 595-605.
- 110. Sipos PM, Loos BG, Abbas F, Timmerman MF, van der Velden U. The combined use of enamel matrix proteins and a tetracycline-coated expanded polytetrafluoroethylene barrier membrane in the treatment of intra-osseous defects. J Clin Periodontol 2005; 32: 765-772.

- 111. Donos N, Kostopoulos L, Karring T. Augmentation of the mandible with GTR and onlay cortical bone grafting. An experimental study in the rat. Clin Oral Implants Res 2002; 13: 175-184.
- 112. Stavropoulos A, Wikesjo UM. Influence of defect dimensions on periodontal wound healing/regeneration in intrabony defects following implantation of a bovine bone biomaterial and provisions for guided tissue regeneration: an experimental study in the dog. J Clin Periodontol 2010; 37: 534-543.
- 113. Caton J, Wagener C, Polson A, Nyman S, Frantz B, Bouwsma O, Blieden T. Guided tissue regeneration in interproximal defects in the monkey. Int J Periodontics Restorative Dent 1992; 12: 266-277.
- 114. Gottlow J, Nyman S, Karring T, Lindhe J. New attachment formation as the result of controlled tissue regeneration. J Clin Periodontol 1984; 11: 494-503.
- 115. Haney JM, Nilveus RE, McMillan PJ, Wikesjo UM. Periodontal repair in dogs: expanded polytetrafluoroethylene barrier membranes support wound stabilization and enhance bone regeneration. J Periodontol 1993; 64: 883-890.
- 116. Sallum EA, Sallum AW, Nociti FH, Jr., Marcantonio RA, de Toledo S. New attachment achieved by guided tissue regeneration using a bioresorbable polylactic acid membrane in dogs. Int J Periodontics Restorative Dent 1998; 18: 502-510.
- 117. Cortellini P, Pini Prato G, Tonetti MS. Periodontal regeneration of human intrabony defects with titanium reinforced membranes. A controlled clinical trial. J Periodontol 1995; 66: 797-803.
- 118. Tonetti MS, Prato GP, Cortellini P. Factors affecting the healing response of intrabony defects following guided tissue regeneration and access flap surgery. J Clin Periodontol 1996; 23: 548-556.

- 119. Sculean A, Berakdar M, Chiantella GC, Donos N, Arweiler NB, Brecx M. Healing of intrabony defects following treatment with a bovine-derived xenograft and collagen membrane. A controlled clinical study. J Clin Periodontol 2003; 30: 73-80.
- Stoecklin-Wasmer C, Rutjes AW, da Costa BR, Salvi GE, Juni P, Sculean A. Absorbable collagen membranes for periodontal regeneration: a systematic review. J Dent Res 2013; 92: 773-781.
- 121. Murphy KG, Gunsolley JC. Guided tissue regeneration for the treatment of periodontal intrabony and furcation defects. A systematic review. Ann Periodontol 2003; 8: 266-302.
- 122. Kao RT, Nares S, Reynolds MA. Periodontal regeneration intrabony defects: a systematic review from the AAP Regeneration Workshop. J Periodontol 2015; 86: S77-104.
- 123. Stavropoulos A, Karring ES, Kostopoulos L, Karring T. Deproteinized bovine bone and gentamicin as an adjunct to GTR in the treatment of intrabony defects: a randomized controlled clinical study. J Clin Periodontol 2003; 30: 486-495.
- 124. Sculean A, Nikolidakis D, Schwarz F. Regeneration of periodontal tissues: combinations of barrier membranes and grafting materials biological foundation and preclinical evidence: a systematic review. J Clin Periodontol 2008; 35: 106-116.
- 125. Figueira EA, de Assis AO, Montenegro SC, Soares DM, Barros AA, Dantas EM, de Vasconcelos Gurgel BC. Long-term periodontal tissue outcome in regenerated infrabony and furcation defects: a systematic review. Clin Oral Investig 2014; 18: 1881-1892.
- 126. Stavropoulos A, Karring T. Guided tissue regeneration combined with a deproteinized bovine bone mineral (Bio-Oss) in the treatment of intrabony periodontal defects: 6-year results from a randomized-controlled clinical trial. J Clin Periodontol 2010; 37: 200-210.

### **Corresponding author:**

Anton Sculean

School of Dental Medicine, University of Bern, Freiburgstrasse 7, 3010 Bern, Switzerland Email: anton.sculean@zmk.unibe.ch

Received: April 30, 2018 / Accepted: May 29, 2018

## **ORIGINAL PAPER**

# Oral health among children with cardiovascular disease and risk of infective endocarditis

Adiana Craciun<sup>1</sup>, Diana Cerghizan<sup>1</sup>, Cristina Bica<sup>1</sup>

Faculty of Dental Medicine, University of Medicine and Pharmacy of Tirgu Mures, Romania

### Abstract

Objective: The purpose of our study was to assess the oral health of a sample of children with cardiovascular conditions who have been recommended to prevent infective endocarditis.

Methods: The prevalence of cavity in temporary and permanent dentition was assessed by determining the dmf-t index, DMF-T index and the analysis of their components (dt, mt, ft, DT, MT, FT). Inclusion in the study was based on two criteria: children at risk of developing infective endocarditis; age between 6 and 12, representing the period of mixed dentition.

Results: dmf-t index reaches the highest score around the age of 9 and the lowest score at the age of 10. For the DMF-T index, the highest scores are found in 10-year-old children and the lowest in 8-year-olds. The evolution of the DT and FT components has been emphasized. Compared to DT, which has scored above 0.5 in all ages except 6 years old, FT is very weakly represented, with very low scores (under 0.5) in only 3 of the 7 age groups.

Conclusions: Children with cardiac anomalies who follow chronic medicine treatment present a high risk of developing the dental cavity. In the context of preventing infective endocarditis, the monitoring of patients with cardiac conditions and the maintenance of rigorous oral hygiene are unsatisfactory.

Keywords: cardiovascular disease, endocarditis, cavity, temporary dentition, permanent dentition.

### Introduction

Congenital cardiac diseases are the most common and severe anomalies present at birth, with a significant impact on infant morbidity and mortality. In Romania, 1,500-1,600 babies with congenital cardiac diseases are born every year. Of these, 850-950 a year require surgical correction. Each of these babies' hospital discharge sheet recommends preventing infective endocarditis. For this reason, treating these patients is a challenge not just for pediatricians, but also for pediatric dentists or dentists in general. Firstly, these children are predisposed to developing infective endocarditis as a consequence of bacteremia induced by dental procedures.

Secondly, children whose health is severely affected can have a low tolerance to the stress induced by dental treatment. Thirdly, hematological, respiratory and neurological complications, as well as any chronic medication administered, must be taken into account when preparing a dental treatment plan for children with congenital cardiac conditions [1, 2]. Certain authors believed that the role of dental procedures in inducing infective endocarditis had been overestimated [3, 4]. The prevention of bacterial endocarditis in the case of children at risk involves both parents and pediatric dentists knowing the risks these children are exposed to, as well as the responsibilities they have.

One can often note the parents' lack of knowledge regarding bacterial endocarditis, even after they have been informed on it during the child's routine cardiology visit. Dentists also seem to present a knowledge deficit about indications and the regimen for administering antibiotic prophylaxis, required for the prevention of bacterial endocarditis [5].

The purpose of this study was to assess the oral health of a sample of children with cardiovascular conditions who have been recommended to prevent infective endocarditis. This study is cross-sectional, and it was carried out during 2014 and 2015, involving a group of 37 children 25 girls and 12 boys directly observed and treated in the Pediatric Cardiology Clinic of Tirgu Mures.

### Material and method

Inclusion in the study was based on two criteria: 1. Children at risk of developing infective endocarditis; 2. Age between 6 and 12, representing the period of mixed dentition. The study group consisted of 37 patients: 25 children with congenital cardiac anomalies, 7 presenting pulmonary hypertension and 5 with cardiomyopathy. The sample contained nine children aged 6 years, six children aged 7 years, five children aged 8 years, seven children aged 9 years, two children aged 10, three children aged 11 and five children aged 12. Their background was not a reference element for the study so that children from both rural and urban backgrounds were included in the study. The protocol involved a clinical examination as per the recommendations of World Health Organization. The results were recorded in specially designed sheets. The dental health indices were calculated to emphasize the patients' cavity experience and oral health. The prevalence of cavity in temporary dentition was assessed by determining the dmf-t index and analyzing its components (dt, mt, ft). The incidence of the cavity in permanent dentition was evaluated based on the DMF-T index and the analysis of its components (DT, MT, FT).

### Results

The age average was 8.43 years old, 6-yearolds being the most numerous. The *DMF-T index* reached scores from 0 to 6, except score 5, for which the number of patients was 0.



scores

The highest DMF-T average scores were found in subjects diagnosed with congenital cardiac anomalies, while the highest average More than half of the patients obtained a score of DMF-T = 0; the maximum index score was present in less than 3 cases (figure 1).

Concerning the *dmf-t index*, in our study, the index reached scores between 0 and 8; no patients achieve a 7. In the case of temporary teeth, most patients obtained a score of 0 (10 cases) or 1 (6 cases), and three patients a score of 8 (figure 2).

Depending on age, we assessed the evolution of the dmf-t index. It reaches the highest score around the age of 9, and the lowest at the age of 10. For the DMF-T index, the highest scores are found in 10-year-old children and the lowest in 8-year-olds.

The evolution of the DT and FT components according to age groups is illustrated in figure 3. Compared to DT, which has scored above 0.5 in all ages except six years old, FT is very weakly represented, with very low scores (under 0.5) in only 3 of the seven age groups.

In the case of temporary teeth, ft has scored only for the ages of 6 and 7, but even then, the scores are very low (<1). On the other hand, dt has high scores in all ages, up to and including 11, which is the age when the dt component reaches maximum level.



Figure 2. Distribution of patients with similar dmf-t scores

scores for the dmf-t index were recorded in subjects diagnosed with pulmonary hypertension.



Figure 3. The evolution of DT and FT indices according to age

### Discussion

The results of this study indicated a significant difference between scores obtained for dmf-t and DMF-T indices; the average score for dmf-t (=2.72) was almost double that for DMF-T (=1.40); therefore, the subjects of this study present a better state of oral health for their permanent dentition than for their temporary dentition. Stecksén-Blicks et al. obtained results in concordance with those of our study. In their study both the dmf-t (average score 5.2) and the DMF-T (average score 0.9) indices of the sample of children with cardiac conditions (obviously, the average dmf-t score > the average DMF-T score) have high levels compared to the control group [6].

Therefore, children diagnosed with cardiac conditions have a superior dental status in their permanent teeth compared to the temporary ones. The aspect can be explained by a series of situations which occur in the context of the general conditions these children suffer from, situations which may affect their dental health. For instance, many of the children have nutrition-related problems during their first year of life. Vomiting is a common problem, and to compensate this, they should frequently be fed, while nightly meals are often required to maintain the energy intake at an acceptable level. Moreover, some of the medication administered for cardiac diseases contains sugar and diuretics, which can cause xerostomia.

Infections last longer than in the case of healthy children; there is a high requirement for liquids, especially at night, when salivary protection is lower [6]. All these aspects have repercussions mainly on the health of temporary teeth.

The high incidence of the cavity in temporary teeth compared to permanent teeth in the case of children with cardiac conditions can also be explained by El-Hawary and his collaborators' conclusion: congenital cardiac conditions affect the chemical structure and composition of temporary teeth [7]. Enamel has a protective role for the tooth; loss of enamel exposes the sensitive dentine underneath. Once deteriorated, enamel is generally impossible to recover [8]. El-Hawary's study proves the occurrence of alterations in the enamel and dentine of temporary incisors in patients with congenital cardiac diseases. Changes were found both in ultrastructure and in mineral content (Ca and P) in the enamel and dentine [7]. Hallet et al. reached the same result in their study: the average score for dmf-t (=4.2) is higher than the DMF-T score (=0.9) in a sample of 39 children diagnosed with congenital cardiac conditions [1].

It is worthy of mention that, in the three studies mentioned above, it is in our study that dmf-t indices have the lowest scores. Stecksén-Blicks' study [6], performed on a sample of Swedish children, has the highest dmf-t scores (=5.2), followed by the sample of children from Northern Australia, examined by Hallet (=4.2). Romania, represented by a sample of children from TirguMures, has significantly lower dmf-t scores (=2.75).

There also are studies which did not find significant differences between the scores of the two indices, such as the study carried out by Talebi et al., involving a sample of children with cardiac conditions. Comparatively, they also studied a sample of healthy children, the results being similar to those obtained for the study sample [9]. The results obtained by Talebi et al. are related to two other studies in specialized literature [10, 11]. Silva et al. [3] obtained higher scores for DMF-T compared to dmf-t. However, it should be noted that their study aimed to establish oral health status in a sample of 104 children aged between 2 and 17. Thus, even if the sample consisted of children at risk of infectious endocarditis, the age groups studied by Silva et al. make it difficult to compare the results with those obtained in our study.

About average scores according to age groups, the results obtained in our study cannot be included in a specific pattern; average scores do not decrease or increase with age. Thus, the maximum average score for temporary teeth is found at the age of 9 (=4.14), and the minimum average score at the age of 10 (=1.00). At seven years of age, the average score is 3.60, while at 12 years of age it is 1.25. The same situation resulted in the case of permanent teeth; the maximum average score was recorded at the age of 10 (=4.00), and the minimum score at the age of 6 (=0).

A study carried out in Romania on a sample of children aged between 7 and 12 from rural areas in Dolj County, attracted our attention by its results, which we considered comparable to those of our study, even though the study in question was performed on a sample of clinically healthy children. Bătăiosu et al. [12] indicated that the average scores for temporary teeth decrease once the subject's age; average scores are directly proportional with age. The maximum score for the dmf-t index was found at the age of 7 (=4.11), and the minimum score at the age of 12 (=0.52). In the same study, the average scores of the DMF-T index followed age groups according to a specific pattern, like in our study, scores being directly proportional to age. Thus, the minimum average score for the index (=0.55) was recorded at the age of 7, and the maximum average score (=3.33) at the age of 11.

The average scores obtained by Bătăiosu and his collaborators are very close to the ones in our study: average score2.56 for dmf-t index and 1.87 for the DMF-T index, compared to an average score of 2.72 for the dmf-t index and 1.40 for the DMF-T index found in our study. It is essential to specify once more that Bătăiosu's [12] study sample consisted of healthy children, whereas our sample consisted of children with acute cardiac conditions. However, we can note that, in the case of permanent dentition, children with cardiac conditions have a dental health status superior to healthy children. Since this surprises us, we can ask whether the rural background of the healthy children may be the cause of these scores.

To be able to answer this question, we analyzed the results obtained by Fleancu [13], who studies the oro-dental status of primary school children in two schools in Sibiu. The schools were selected because they both had a dentist's practice. The DMF-T index had an average score of 1,71 for the entire sample, a score which is lower than that found for children in the rural environment (=1.87), but higher than the score obtained by children with cardiac conditions (=1.40).

Therefore, healthy children in urban schools which are equipped with dental practices have an inferior dental status to healthy children in the rural environment, but with insignificant differences, while the sample of children with cardiac conditions has a better dental status. It is important to note that antibiotics are prescribed for the prophylaxis of infective endocarditis, so it is possible that medication may induce a prophylactic effect on cavities [6].

Another explanation for the favorable dental status of subjects with cardiac conditions compared to healthy subjects may be the indication they have all received, namely the prophylaxis of bacterial endocarditis; in this context, regular dental check-ups and rigorous oral hygiene ensure an explanation to the situation.

Concerning parent knowledge on the prophylaxis of endocarditis, Balmer et al. specified that 64% of parents were aware of the relationship between their children's oral health and infective endocarditis [11]. Cheuk et al. [14] conclude that the parents of children with congenital cardiac conditions have essential knowledge gaps regarding their children's disease, and suggest that the current educational program is inadequate. The study performed by Nath et al. [15] reached similar conclusions, namely that only 8% of parents were aware of the importance of good oral and dental hygiene and the need to prevent infective endocarditis.

Another important aspect emphasized by our study was the scores reached by the components of the indices - dt, ft / DT, FT. The scores suggest that the rate of dental treatment is very low, both in the case of temporary dentition and permanent dentition, even though the need for treatment exists and is recommended.

### Conclusions

Children with cardiac conditions have a better state of oral health for permanent dentition than temporary dentition. Children with cardiac anomalies who follow chronic medicine treatment present a high risk of developing the dental cavity. In the context of preventing infective endocarditis, the monitoring of patients with cardiac conditions and the maintenance of rigorous oral hygiene are unsatisfactory.

Patients see a dentist only when forced by the imminence of heart surgery, to eliminate dental hotbeds. An effort is required on the part of pediatricians and pediatric cardiologists to make parents aware of the importance of oral hygiene and the necessity to prevent infections in children with cardiac conditions.

### **Conflict of interest:** None to declare.

### **References:**

- 1. Hallett K, Radford D, Seow K. Oral health of children with congenital cardiac diseases: a controlled study. Pediatric Dentistry 1992, 14: 224-230.
- Hurmuzache M. Contribuţii clinice şi terapeutice privind endocarditele infecţioase. Teză de doctorat, laşi, 2012.
- 3. Silva D, Souza I, Cunha M. Knowledge, attitudes and status of oral health in children at risk for

infective endocarditis. Int J Paed Dentistry, 2002, 12: 124–131.

- 4. American Dental Association. For the dental patient Antibiotics before dental treatment Preventing bacterial endocarditis. J Am Dent Assoc. 2002; 133:127.
- Hayes PA, Fasules J. Dental screening of pediatric cardiac surgical patients, ASDC Dent Child, 2001, 68: 255–8, 228.
- Stecksén-Blicks C, Rydberg A, Nyman L. Dental caries experience in children with congenital heart disease: a case-control study, Int J Paed Dent. 2004, 14(2): 94-100.
- El-Hawary YM, El-Sayed B, Abd-Alhakem G. Deciduous teeth structure changes in congenital heart disease: Ultrastructure and microanalysis. Interv Med Appl Sci. 2014, 6(3): 111–117.
- Atar M, Körperich EJ. Systemic disorders and their influence on the development of dental hard tissues: a literature review, J Dent. 2010, 38(4): 296-306.
- 9. Talebi M, Khordi Mood M, Mahmoudi M. et al. A Study on Oral Health of Children with Cardiac Diseases in Mashhad, Iran. J Dent Res Dent Clin Dent Prospects. 2007, 1(3): 114–118.
- 10. Sarheed M, Angeletou A, Ashley PF. An investigation of the oral status and reported oral care of children with heart and heart-lung transplants. Int J Paed Dent. 2000, 10(4): 298-305.
- 11. Balmer R, Bu'Lock FA. The experiences with oral health and dental prevention of children with congenital heart disease. Cardiol Young. 2003, 13(5): 439-43.
- Bătăiosu M, Moraru I, Dăguci C et al. Oro-dental status of school children aged between 7-12 years, in the rural areas of Dolj county. Int J Paed Dent. 2013, 3(2): 150-154.
- Fleancu A. Incidența cariei dinților permanenți la un lot de elevi ai claaselor I-IV din municipiul Sibiu, AMT, 2010, vol II(3): 127-130.
- 14. Cheuk DKL, Wong SMY, Choi YP. Parents' understanding of their child's congenital heart disease, Heart. 2004, 90(4): 435–439.
- 15. Nath P, KiranV, Maheshwari S. Awareness of infective endocarditis prophylaxis in parents of children with congenital heart disease: A prospective survey. Ann Pediatr Cardiol. 2008, 1(1): 54–55.

### **Corresponding author:**

### Diana Cerghizan

University of Medicine and Pharmacy of Tirgu Mures, 38 Gheorghe Marinescu street, Tirgu Mures, 540139, Romania Email: diana.cerghizan@umftgm.ro

Received: April 30, 2018 / Accepted: May 29, 2018

## **ORIGINAL PAPER**

## Thermal regime effect on the structure of metal component in metalceramic prosthesis

Raluca Monica Comăneanu<sup>1</sup>, Costin Coman<sup>1</sup>, Oana Botoacă<sup>1</sup>, Adi Lorean<sup>1</sup> <sup>1</sup>Faculty of Dental Medicine, Titu Maiorescu University, Bucharest, Romania

### Abstract

The success of dental restorations is dependent both on clinical phases of treatment to achieve fairness and on rigor to achieve technical phases. In our study we conducted research on metal parts microstructure of metal-ceramic dentures, to investigate the effect of reheating to successive deposits layers of ceramic. We analyzed molded samples and replicates on which were simulated ceramics firing. Applying such heat treatments have resulted in complete dissolution of intermetallic compounds and conducted to a homogeneous microstructure near to thermodynamic equilibrium, which leads to improved behavior in long-term operation of dental restorations. **Keywords:** dental alloys, microstructure, molding flaw.

### Introduction

The metal-ceramic fixed prosthetic restoration which reestablish the continuity of dental arches [1] are widely used in dentistry.

The alloys features needed for in metalceramic technology [2-4] are:

- high temperature resistance, which allow for no deformation during ceramics firing;
- melting temperature must be lower than 1300°C for an easy processing, and should be higher with about 150...200°C than sintering temperature interval of the ceramics which is in the range 850...1100°C;
- thermal expansion coefficient should be closed to the one of ceramic mass, to avoid share stress appearance in the interface alloy-ceramic durring prosthetic piece cooling;
- solidification shrinkage should be less than 2.5%;
- yield strength should be as high as possible;
- should allow on optimal adherence of the ceramics mass.

Dental materials interact with living tissues they come in contact with and generate local or systemic responses [5]. The biocompatibility of dental alloys is important and is considered a controversial problem for practitioner physicians [6].

Among the causes of metal-ceramic restorations failure are cited in literature:

degradation by corrosion of alloys, mechanical wear and fatigue fracture [7-9].

Corrosion is described as the destruction or damage of the material under the action of aggressive environment (atmosphere and oral fluids) [10].

Metal alloys based on Chromium and Cobalt are widely used in the dentistry field [11].

The Co-Cr or Ni-Cr alloys have good corrosion comportment because of Chromium presence, which forms a stable chromium oxide layer on the alloy surface [12-18]. In addition, the allergenic potential of Cr-Co based dental alloys is very small compared with the allergenic potential of the dental alloys based on Ni-Cr [18] in patients with allergic ground.

The corrosion behavior of cast alloys is considered to be the most relevant property that complies with safety biological material [19]. For the commercial alloys, the proportion of Cr and Mo ranges between 11...25 wt. % and respectively 0...10 wt. % [20].

Modern Ni-Cr alloys chemistry has mainly Ni (60-70%) and Cr (15-20%), with some content of Mo, Al, Mn, Be, Cu, Co, Fe, W, Ti or Nb.

Nickel reduces hardness, increases malleability and elasticity of the alloy. Generally, substituting some important percentages of Fe, any alloy gets better resistance to corrosion. Chromium improves mechanical properties, and the chromium oxide formed on the alloy surface has anticorrosive effect and offer good adhesion to ceramics. Oxidation improves the quality of metal-ceramic interface [21, 22].

Molybdenum (3-11 wt. %) increases corrosion resistance and has convenient influence on the thermal expansion coefficient. Addition of Mn, W, and Ti improves also corrosion resistance of the alloy. Beryllium addition in Ni-Cr alloys improves alloy fluidity in liquid state and increases adherence between porcelain and metal [21, 23-25].

Studies [26] showed that the corrosion products from dental alloys solubilized in adjacent gum tissues depends on the composition of the alloy restorations which influence the corrosion resistance [27-30], the structure formed during casting [20] and the subsequent combustion/firing protocols [ 20, 31].

Here we conducted research on components of metal alloys Co-Cr and Ni-Cr of the same shape/dimensions of metalceramic dentures, to investigate the effect of reheating the structure of alloys on the successive layers of ceramic deposited. We analyzed the samples comparing as cast dentures to same shape/dimensions dentures with simulated firing of the ceramics.

### **Experimental part**

In this study were considered three alloy types: A. Co-Cr based (wt. % Co 64, Cr 21, Mo 6, W 6, Fe, Mn and Si < 1); B. Ni-Cr based (wt. % Ni 58, Cr 27, Mo 8, Si 2); and C. Ni-Cr based (wt. % Ni 63, Cr 25, Mo 9, Si 2, Nb 1). For each alloy were made two samples, each consisting of two interlocked elements: a crown shell and a body bridge.

The samples were codified as follows:

- A1: dental alloy Co-Cr as cast
- A2: dental alloy Co-Cr after ceramic firing simulation through heat treatments
- B1: dental alloy Ni-Cr 1 as cast
- B2: dental alloy Ni-Cr 1 after ceramic firing simulation through heat treatments

- C1: dental alloy Ni-Cr 2 as cast
- C2: dental alloy Ni-Cr 2 after ceramic firing simulation through heat treatments.

All the 6 samples we embedded in acrylic resin and were prepared for metallographic observations.

Metallographic preparation consisted of successive polishing on sanding paper grit 180-320-500-800-1000-1200 mm, and suspension of diamond 5, 3 and 1 $\mu$ m on cloth. Subsequent the prepared surfaces were etched electrochemical in oxalic acid solution 5%, 5 sec at 2 V.

The metallographic observations, normal and DIC (Differential Interference Contrast) were made with an optical microscope Reichert Univar<sup>°</sup> from Biomaterials Research Centre UPB-BIOMAT<sup>°</sup>.

### **Results and discussions**

For samples A1 – as cast; crown and bridge - magnification  $200\times$ , the microstructure consists of solid solution and can be observed intermetallic compounds. In DIC image can observe slight tendency of dendrite formations in the crown and more relevant in the bridge (thicker and with more volume of material).

With magnification  $500 \times$  one can observe that inter-dendritic distances are in the range 14...25µm for the bridge sample. One can be noted the presence of intermetallic compounds (figure 1).

For samples A2 – firing simulation by heat treatments; crown and bridge – magnification 200× one can observe the slight dissolution of intermetallic compounds between interdendritic arms.

With magnification  $500 \times$  there are revealed that intermetallic compounds separations are discontinuous, also as a result of elements diffusion in solid state during heat treatments. The interdendritic distance is now 10...18 µm for the crown and 18...36 µm for the bridge. can observe that dendrites One are even if homogenized, there persist interdendritic intermetallic compounds (figure 2).

ISSN 2601-6877(print)/ISSN-L 2601-6877(online)



Bridge A1; 200×

Bridge A1; 500× Figure 1.

Bridge A1-DIC 500×

Now is clearly revealed the crystalline grains limits formation. Interdendritic segregation is less pronounced comparing with as cast microstructure, as an effect of solid state diffusion produced by heat treatments/firing.



Bridge A2; 200×

Bridge A2; 500× Figure 2.



Bridge A2-DIC 500×

For B1 samples, the interdendritic arms distance is in the range of 60...90 µm for the bridge. For the crown there are evident only

the solid solution non-homogeneous in as cast state. This dental alloy presents no intermetallic compounds (figure 3).

Acta Stomatologica Marisiensis 2018;1(1)32-38











Crown B1-DIC 500x



Bridge B1-DIC 500×

Bridge B1; 200×

Bridge B1; 500× Figure 3.

In DIC images one can observe more clear the solidification dendrites (in depth) and interdendritic zones (in relief).

For the bridge in sample B2 (heat treated), the distance between dendrite arms is in the

range 35...55 µm, and the crown is more homogenized. The primary dendrites are visible, but the secondary ones are hardly observed as a result of homogenization through heat treatments (figure 4).



Crown B2; 200×



Bridge B2; 200×

Crown B2; 500×



Bridge B2; 500×

Figure 4.



Crown B2-DIC 500×



Bridge B2-DIC 500×

With higher magnification  $(500\times)$ , one can observe the grain limits; so the microstructure of the casted material was clearly homogenized.

In casted samples C1, the distance between secondary dendritic arms is in the range  $30...35 \,\mu\text{m}$  for the crown and  $35...55 \,\mu\text{m}$  for the bridge. The corresponding alloy for these samples, even in as cast state, has a microstructure less segregated (figure 5).

For the C2 samples, one can be observed a good homogenization after firing simulations through heat treatments (figure 6).



Crown C1; 200×



Bridge C1; 200×



Crown C1; 500×



Bridge C1; 500× Figure 5.



Crown C1-DIC 500×



Bridge C1-DIC 500×





Bridge C2; 200×

simulation.

micro-cracks

It is obvious the formation of a new

In all these images the casting defects could

to

dendritic

generation of crystalline grains after firing

be pores due to solidifying contraction and

microstructures [32]. Only a few papers report

about the influence of metal casting process on

corrosion resistance of dental alloys [33, 34]. It

specific





Bridge C2; 500× Figure 6.



Bridge C2-DIC 500×

In our study, there were applied thermal regimes similar to ceramic firing cycles, and microstructural and compositional homogenization of the samples were examined.
According to the results obtained in other research [35], thermal cycles for firing the ceramics acts favorably to metal component and allow for the homogeneity of the restoration.

The homogenization of the products diminish the contours of the dendrites due to the diffusion carried out in the solid state during firing.

#### Conclusions

Application of a heat treatment (annealing for homogenization) will produce the complete dissolution of the intermetallic compounds and so is possible to obtain a microstructure of thermodynamic equilibrium. This correspond to the ideal shape of uniform crystalline grains, compositional and dimensional homogeneous.

Applying the firing cycles of the different ceramic layers it manages to produce approximately similar effect, which leads to improved operational behavior of dental restorations.

As a result of compositional and structural homogenization, dental restorations supports better the mechanical associated with thermal stress mechanical, and, especially, the combined effect of corrosive effect on metalceramic restorations in the oral cavity.

**Conflict of interest:** None to declare.

#### References

- Comaneanu RM, Hancu ID, Coman C, Hancu V, Barbu HM, Cotrut MC, Cernusca Mitariu M, Maris M, Comparative study on the corrosion of Ni-Cr and Co-Cr alloys in the presence of Ti6Al4V implant abutment. REV CHIM. (Bucharest), 2016;67(10):1940-4.
- Bratu D, Nussbaum R. Bazele clinice şi tehnice ale protezării fi×e. Bucureşti: Ed.Medicală; 2006. P.319-328.
- Leinfelder K.F., New developments in resin restorative systems J Am Dent Assoc. 1997;128(5):573-81.
- van Noort R, Brown D, Clarck EC, et al. Dental Materials: 1992 literature review. J.Dent. 1994;22(1):5-28.
- Hancu V, Comaneanu RM, Coman C, Filipescu AG, Ghergic DL, Cotrut MC. In vitro studies regarding the corrosion resistance of NiCr and CoCr types dental alloys. REV CHIM. (Bucharest), 2014;65(6):706-9.

- Mareci D, Sutiman D, Cretescu I, Cailean A, Rosca M. Electrochemical characterization of some cooper based dental materials in accelerated test solution. REV CHIM. (Bucharest), 2008;59(8):871-7.
- Schweitzer PA. Corrosion engineering Handbook. 2<sup>nd</sup> edition. New York: CRC Press; 2007.P 96.
- Shreir LL, Jarman RA, Burstein GT. Corrosion: Metal/Environment Reactions. Vol. 1. Boston:Newness-Butterworth; 2000. P. 237.
- Zamfir S, Vidu R, Brinzoi V. Coroziunea materialelor metalice. București:Ed. Didactică şi pedagogică RA;1994. P.201.
- Porojan S, Porojan L. Evaluation of Co-Cr dental alloys welds corrosion. REV CHIM. (Bucharest). 2015;66(3):357-9.
- Minciuna MG, Vizureanu P, Achitei DC, Ghiban N, Sandu AV, Forna NC. Structural characterization of some COCRMo alloys with medical applications. REV CHIM. (Bucharest). 2014;65(3):335-8.
- 12. Giacomelli FC, Giacomelli C, Spinelli A. Behavior of Co–Cr–Mo biomaterial in simulated body fluid solutions studied by electrochemical and surface analysis techniques. J. Braz. Chem. Soc. 2004;15 (4):541-7.
- 13. Hodgson AWE, Kurz S, Virtanen S, Fervel V, Olsson COA, Mischler S. Passive and transpassive behavior of CoCrMo in simulated biological solutions. Electrochimica Acta. 2004;49:2167 - 78.
- Hsu RW, Yang C, Huang C, Chen Y. Electrochemical corrosion studies on Co–Cr–Mo implant alloys. Mater. Chem. Phys. 2005;93:531 - 8.
- 15. Kelly JR, Rose TC. Non-precious alloys for use in fixed prosthodontics J Prosthet Dent. 1983;49: 363 7.
- 16. Kocijan A, Milosev I, Pihlar B. Cobalt-based alloys for orthopedic applications studied by electrochemical and ×PS analysis. J Mater Sci Mater Med. 2004;15:643 - 50.
- Metikos-Hukovic M, Babic R. Passivation and corrosion behaviors of cobalt and cobalt chromium–molibdenium. Corros Sci. 2007;49:3570 -9.
- Roberts HW, Berzins DW, Moore BK, Charlton DG. Metal–ceramic alloys in dentistry: a review. J. Prosthodont, 2009;18:188 - 94.
- 19. Wataha JC. Biocompatibility of dental casting alloys: A review. J. Prosthet. Dent. 2000;83:223 34.
- 20. Wylie CM, Shelton RM, Fleming GJ, Davenport AJ. Corrosion of nickel-based dental casting alloys. Dent Mater. 2007;23:714 - 23.
- 21. Anthony DH, Burnett AP, Smith DL, Brooks MS. Shear test for measuring bonding in cast gold alloyporcelain composites. J. Dent. Res. 1970;49:27 -33.

- 22. Johnson T, van Noort R, Stokes CW. Surface analysis of porcelain fused to metal systems. Dent. Mater. 2006;22:330 - 7.
- 23. Bezzon OL, de Mattos MG, Ribeiro RF, Rollo JM. Effect of beryllium on the castability and resistance of metal-ceramic bonds in nickelchromium alloys. J Prosthet Dent. 1998;80:570 - 4.
- 24. Reclaru L, Unger RE, Kirkpatrick CJ, Susz C, Eschler PY, Zuercher MH, Antoniac I, Lüthy H. Ni–Cr based dental alloys - Ni release, corrosion and biological evaluation. Mater Sci Engineer C. 2012;32:1452 -60.
- 25. Setcos JC, Babaei-Mahamani A, Di Silvio L, Mijör IA, Wilson NHF. The safety of nickel containing dental alloys, Dent. Mater. 2006;22(12):1163 - 68.
- Wataha JC, Lockwood PE, Schedle A. Effect of silver, copper, mercury, and nickel ions on cellular proliferation during extended, low-dose exposure. J Biomed Mater Res. 2000;52:360 - 4.
- 27. Ardlin BI, Dahl JE, Tibballs JE. Static immersion and irritation tests of dental metal-ceramic alloys. Eur J Oral Sci. 2005;113:83 9.
- 28. Elshahawy W, Watanabe I, Koike M. Elemental ion release from four different fixed prosthodontic materials. Dent Mater. 2009;25:976 81.

- 29. Hanawa T. Metal ion release from metal implants. Mater Sci Eng. 2004;24:745 - 52.
- 30. Huang TH, Ding SJ, Min Y, Kao CT. Metal ion release from new and recycled stainless steel brackets. Eur. J. Orthodont. 2004;26:171 - 7.
- 31. Lin HY, Bowers B, Wolan JT, Cai Z, Bumgardner JD. Metallurgical surface and corrosion analysis of Ni– Cr dental casting alloys before and after porcelain firing. Dent Mater. 2008;24:378 - 85.
- Fossati A, Borgiolo F, Galvanetto E, Bacci T. Corrosion resistance properties of plasma nitrided Ti6Al4V10 alloy in nitric acid solutions. Corrosion Sci. 2004;46:917 - 27.
- Kim SJ, Ko YM, Choe HC. Pitting corrosion of TiNi coated dental cast alloy with casting methods. Adv Mater Res. 2007;15(17):164 - 8.
- 34. Mulders C, Darwish M, Holze R. The influence of alloy composition and casting procedure upon the corrosion behaviour of dental alloys: An in vitro study. J Oral Rehab. 1996;23:825 - 31.
- 35. Hancu V, Comăneanu RM, Coman C, Târcolea M, Barbu HM, Bechir A, Miculescu F, Lorean A, Microstructure and Chemical Homogeneity of cast dental crowns made from CoCrMoW alloy and ceramic mass. REV CHIM. (Bucharest). 2015;66(9):1327-30.

#### **Corresponding author:**

Costin Coman

Titu Maiorescu University Bucharest, 67A Gh. Petrașcu, Bucuresti, 031593, Romania Email: costin\_coman@yahoo.co.uk

Received: April 28, 2018 / Accepted: May 29, 2018

# **ORIGINAL PAPER**

# Efficacy of associated therapy in the treatment of temporomandibular disorders

Edwin Sever Bechir<sup>1</sup>, Farah Curt-Mola<sup>1</sup>, Mircea Suciu<sup>1</sup>, Claudiu Horga<sup>1</sup>, Carmen Biriş<sup>1</sup>, Anamaria Bechir<sup>2</sup>, Liran Levin<sup>3</sup>

<sup>1</sup>Faculty of Dental Medicine, University of Medicine and Pharmacy of Tirgu Mures, Romania

<sup>2</sup> Faculty of Dental Medicine, Titu Maiorescu University of Bucharest, Romania

<sup>3</sup> Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Canada

#### Abstract:

The purpose of this clinical study was to assess the efficacy of low-level laser therapy (LLLT) as mono- and associated therapy, in temporomandibular disorders (TMDs).

In the randomized controlled clinical trial 123 patients with TMDs, pain in masticatory musculature and limited opening of the oral cavity were included. The patients were divided in 3 groups, the group of patients treated with LLLT as monotherapy (42), the group of patients treated with nonsteroidal anti-inflammatory and centrally acting muscle relaxant medication (40), and the group of patients which benefited by LLLT as associated therapy (41 patients, LLLT and medication). The parameters represented by the reductions in pain and the improvement of mouth-opening were assessed in 8 monitoring sessions. The intensity of pain was evaluated on the visual-analogue scale (VAS), ranging from 0 to 10, and the maximal opening capacity of oral cavity was measured in mm, by ruler, in the morning of the monitoring sessions.

According to the obtained results, the optimal modality with highest success rate is represented by the associated method, where the reductions in pain and the improvement of mouth-opening were significantly increased - in the third group, in comparison with the second and the first group of patients.

Based on the results, associated therapy in the treatment of TMDs should be considered as an alternative method to other monotherapies.

**Keywords:** painful TMDs, LLLT as mono- and associated therapy, pain reduction in masticatory musculature, improvement of mouth-opening

#### Introduction

Orofacial pain is manifested in the face or oral cavity area, and includes the disorders of TMJ [1]. Between 5-12% of adult people in the United States [2], 33% of the adult Chinese population in Hong Kong [3], and 33.3% of 2005 individuals in Italy [4], experience pain associated with disorders of the TMJ. The usual symptoms of myogenic temporomandibular disorders (TMDs) are represented by the facial pain, earaches or ringing of the ears, dull, chronic headaches, jaw locking, clicking or popping sounds in the jaw joint, a bite that feels uncomfortable or "off", neck, shoulder and back pain, and swelling on the side of the face [5-7]. The classical treatment used were injections, physical therapy, splints, anti-inflammatory medications (that could have side effects when used over long periods of time), to which have been added self-management strategies, laser

therapies and interventions based on cognitive behavioral approaches [8-10].

At present, a conservative treatment approach prevails over surgery, given it is less aggressive and usually results in satisfactory clinical outcomes in mild-moderate temporomandibular disorder (TMDs).

Nocturnal grinding is a detrimental motor activity, а self-destructive parafunction, characterized by "the consequences of a normal function used in abnormal condition". Differential diagnosis in nocturnal or daygrinding patients is realized according to the frequency of phenomenon, the destruction degree, the social discomfort and the manifested symptomatology. The morbid clinical entity of nocturnal-grinding is characterized by the existence of occlusal and TMJ disharmony determined by premature contact areas and by occlusal interferences, strong chaotic contractions of elevator muscles

of mandible, accentuated interdentally friction, etc. [11-13].

Inflammation is a complex, neurotropic, vascular and metabolic self-defense reaction, induced by the penetration of pathogen agents or of own degradation products into the healthy tissues of an organism and has some commune mechanisms with infections and allergies.

According to the therapeutic utilization, the anti-inflammatory medications are divided into four categories: anti-inflammatory with immediate effect. basic anti-rheumatic medication, anti-inflammatory and other adjuvant. All these therapeutical means have the purpose to suppress the infection, eluding the pain, functional improvement and maintenance of T.M.J. The treatment of TMJ disorders is a long-term treatment, motif which can determine the apparition of adverse effects/intolerances and drugs interactions [14-17].

Photobiostimulation with therapeutical laser is the use of low-energy laser light on tissues. to achieve a clinical effect. Biostimulation has been used clinically for pain reduction, wound healing and aid in physical therapy for temporomandibular joint disorders. The basic mechanism for biostimulation occurs at molecular level. Laser light penetrates through tissue and strikes a (photosensitive chromophore molecule), situated which is in mitochondria. Mitochondrial cytochromes are responsible for converting adenosine diphosphate (ADP) to adenosine triphosphate (ATP), thus supplying energy to the cell and driving cellular

metabolism. The ability of laser light to affect target molecules is dependent on the absorption spectra of biomolecules and tissue optics. With inflammation, the normal resting potential of nerve fibers is decreased, leading to hypersensitivity. Returning the resting potential to normal could decrease pain transmission. This area of biostimulation is clinically important in pain reduction. Biostimulation is also effective in increasing metabolism and cell replication in fibroblasts and endothelial cells [18-22].

Epic 10 diode lasers can be used too for temporary relief of minor pain, including pain associated with TMJ or other temporomandibular disorders, by providing a therapeutic and non-invasive way in treating pain. Using a special handpiece attachment, the Epic 10 laser is transformed in a device capable to reduce and manage oral and maxillofacial pain. Technical specifications of Epic 10 diode lasers are: laser classification IV (4); InGaAsP semi-conductor diode; 940 nm wavelength; 10 W peak power. The presentation mode of Epic 10 diode laser, of the handpiece and the method of use for the device in our study can be observed in figure 1 [23,24].

The pain therapy procedure with Epic 10 laser is the process by which tissue temperature is elevated for the temporary relief of minor pain, the temporary increase in local blood circulation, and the temporary relaxation of muscle. Affected muscles and/or joints have to be exposed to an adequate level of therapeutic energy over a short period of time, to provide effective therapeutic effects [26].



Figure 1. The presentation mode of Epic 10 diode laser (A), of deep tissue handpiece (B), and using method (C) [24, 25]

The visual analogue scale (VAS) is onedimensional psychometric response scale, which can be used for measuring the pain intensity in adult populations. VAS helps to assess the subjective pain intensity of the patient (before, during, and after the treatment), in questionnaires. VAS scale was noted between "no pain" (score of 0) and "pain as bad as it could be" (score of 10) (as none, mild, moderate, or severe). VAS scale has the advantage of easy and quick use, reduced time required to fill in the questionnaire, and of the low cost [27-29]. The VAS scale inserted in the questionnaire used in this study had the aspect presented in figure 2.



Fig. 2. The aspect of VAS inserted in the used questionnaire of study

The purpose of this study was to assess the effectiveness of low-level laser therapy (LLLT) as mono- and associated therapy, in temporomandibular disorders (TMDs).

#### Materials and method

The study was performed according to ethical principles and good clinical practice.

All participants signed written informed consent prior to the beginning of this study.

This randomized controlled clinical trial initially enrolled 155 patients. We excluded patients who were admitted as emergency patients and were in acute pain and dysfunction that required other forms of treatment, and thereafter those who were unable to cooperate within the studied requirements. The patients were selected after a detailed anamnesis and all patients presented painful cranio-mandibular dysfunctional syndrome and nocturnal bruxism. Also, the included 123 patients presented TMDs, pain in masseter and temporalis masticatory musculature and limited opening of the oral cavity. The participating dentists attended a training day to ensure consistency of examination and treatments. The patients were monitored during the period of 2012-2018 in the Dental Clinics of the Dental Medicine Faculties.

The inclusion criteria of patients were: an age range of 41-60 years, pain and muscle

fatigue in the TMJ area and in the masseter and temporal masticatory muscles, reduced opening of the oral cavity under 35 mm, no sensibility/ adverse effects/intolerances at anti-inflammatory drugs/medication, no allergic reactions, any other adverse reaction to anti-inflammatory medication, and without other acute or chronic, general or dental diseases (e.g. gastritis, digestive ulcer, gastrointestinal hemorrhages, liver- and renal disturbances, etc.) in personal antecedents. The mean ( $\pm$ SD) of selected patients' age was 50.5  $\pm$  9.5 years.

Prior to the start of therapy, professional oral hygiene was performed in all the patients.

The 123 eligible patients were randomized in three groups:

First group of patients (L group, n = 42, 24 females and 18 males) benefited from a series of 4 sessions LLLT as monotherapy, once every 2 days, with the Epic 10 laser device. Treatment takes 10 minutes for each site (left and right), to provide relief from disagreeable TMJ symptoms. The deep tissue handpiece with attached protective cover was used at the 30 mm spot size. Laser parameters was selected for pain therapy program. LLL treatment was performed by placing the handpiece with protective cover in the treated area, by using the red laser beam as reference for center of

the treatment location to position the handpiece, and by checking periodically the patients comfort during the use of the Epic 10 laser device. The eyes of patient and clinician were protected with colored in green plastic glasses, and the laser fascicle irradiated the skin surface. We seated the laser screen to the recommended initial power settings for therapeutic effect (at 4.0 W delivered over 10 minutes = 600 seconds of continuous treatment = CW). The patient response was monitored in order to adjust the needed power and/or distance for the patient comfort. Power frequency was 50-60 Hz magnetic field and 3 A/m in continuous level.

• The patients of second group (M group, n=40, 21 females and 19 males), were

Graph 1.

The distribution of the patients in

groups, after gender and the used

treatment

treated for 8 days with nonsteroidal local anti-inflammatory gel (by massaging 3 times a day with Fastum gel in the masseter and temporal muscles area) and centrally relaxant medication for muscles (2 tablets of Clorzoxazon of 250 mg 2 times a day, so 500 mg x 2 times a day).

Third group of patients (L+M group, n=41, 24 females and 19 males), benefited from associated therapy, LLLT (4 irradiation sessions) and the previously mentioned medication (nonsteroidal local anti-inflammatory gel Fastum gel) and centrally relaxant medication for muscles (Clorzoxazon tablets).

The distribution of the patients in groups, after gender and the used therapy, is presented in graph 1.



All patients were monitored to pursue the results. Before VAS evaluations of pain in TMJ area, were assessed the mouth opening variables with a ruler. VAS evaluations were based on the found pain level, after direct extraoral palpation of masseter and temporalis muscles. Both sides of the head were examined separately, to avoid confusion in the patient reactions. The parameters represented by the improvement of mouth-opening and the reductions in pain were assessed before (Ev.1) and after (Ev.2) the first applied treatment, in the third day (after the second session of LLLT = Ev.3), in the fifth day (after the third session of LLLT = Ev.4), in the seventh days (after the fourth session of LLLT = Ev.5), respectively after 3 months (Ev.6), after 6 months (Ev.7) and after 9 months (Ev.8). In total, 8 monitoring sessions were carried out on the effects of applied therapies in the selected patients.

#### **Result and Discussions**

In the first part of the assessment, the oral cavity opening (MO) was measured and recorded in all patients of the 3 groups.

In the first group of patients (L) (table 1):

- the highest number of patients presented the MO=24mm in Ev.1 (19.04%), MO=30mm in Ev.2 (19.04%), MO=38mm in Ev.3 (19.04%), MO=44mm in Ev.4 (19.04%), MO=46mm in Ev.5 (19.04%), MO=42mm in Ev.6 (19.04%), MO=40mm in Ev.7 (19.04%), and MO=38mm in Ev.8 (16.66%);
- minimum values of MO increased from Ev.1 (=18mm) to Ev.5 (=33mm), and then decreased in Ev.6 (=30mm), Ev.7 (=26mm) and at Ev.8 (=24mm);
- maximum values of MO increased from Ev.1 (=30mm) to Ev.6 (=54mm), and then decreased in Ev.7 (=48mm) and at Ev.8 (=44mm).

MO-mm	Ev. 1	Ev. 2	Ev. 3	Ev. 4	Ev. 5	Ev. 6	Ev. 7	Ev. 8
16	-	-	-	-	-	-	-	-
18	3	-	-	-	-	-	-	-
20	6	2	-	-	-	-	-	-
22	6	3	-	-	-	-	-	-
24	8	4	-	-	-	-	-	1
26	7	6	1	-	-	-	1	3
28	7	6	2	-	-		2	4
30	5	8	3	2	-	1	3	4
32	-	6	4	3	1	1	3	4
34	-	4	4	3	2	2	4	5
36	-	2	6	4	3	2	5	6
38	-	1	8	4	4	3	5	7
40	-	-	7	6	6	4	8	5
42	-	-	4	6	7	8	6	2
44	-	-	2	8	7	7	2	1
46	-	-	1	3	8	6	2	-
48	-	-	-	2	2	5	1	-
50	-	-	-	1	1	1	-	-
52	-	-	-	-	1	1	-	-
54	-	-	-	-	-	-	-	-
56	-	-	-	-	-	-	-	-

Table 1. Assessment of the opening of oral cavity, in first group (L) of 42 patients (in mm)

In the second group of patients (M) (table 2):

- the highest number of patients presented the MO=24mm in Ev.1 (20%), MO=26mm in Ev.2 (20%), MO=34mm in Ev.3 (17.5%), MO=36mm in Ev.4 (20%), MO=40mm in Ev.5 (17.5%), MO=38mm in Ev.6 (17.5%), MO=36mm in Ev.7 (15%), and MO=34mm in Ev.8 (17.5%);
- minimum values of MO increased from Ev.1 (=18mm) to Ev.5 (=28mm), and then decreased in Ev.6 (=26mm), Ev.7 (=24mm) and at Ev.8 (=22mm);
- maximum values of MO increased from Ev.1 (=30mm) to Ev.5 (=48mm), and then decreased in Ev.6 (=46mm), Ev.7 (=44mm) and at Ev.8 (=42mm).

In the third group of patients, with associated therapy (L+M) (table 3):

 the highest number of patients presented the MO=24mm in Ev.1 (19.51%), MO=32mm in Ev.2 (19.51%), MO=40mm in Ev.3 (19.51%), MO=44mm in Ev.4 (21.95%), MO=48mm in Ev.5 (19.51%), MO=46mm in Ev.6 (21.95%), MO=42mm in Ev.7 (19.51%), and MO=40mm in Ev.8 (19.51%);

- minimum values of MO increased from Ev.1 (=18mm) to Ev.5 (=36mm), and then decreased in Ev.6 (=30mm), Ev.7 (=28mm) and at Ev.8 (=26mm);
- maximum values of MO increased from Ev.1 (=30mm) to Ev.5 (=56mm), and then decreased in Ev.6 (=52mm), Ev.7 (=50mm) and at Ev.8 (=48mm).

The mouth opening (MO) in all the patients increased gradually during the therapy till Ev.5, and then decreased until the Ev.8. The yellow color of the boxes in the tables indicates the maximum number of patients.

MO-mm	Ev. 1	Ev. 2	Ev. 3	Ev. 4	Ev. 5	Ev. 6	Ev. 7	Ev. 8
16	-	-	-	-	-	-	-	-
18	3	2	-	-	-	-	-	-
20	5	4	-	-	-	-	-	-
22	6	7	1	-	-	-	-	1
24	8	7	1	-	-	-	1	2
26	7	8	4	3	-	1	3	4
28	6	6	5	3	2	2	3	4
30	5	4	6	5	3	3	4	4
32	-	2	6	6	4	4	5	5
34	-	-	7	6	4	4	5	7
36	-	-	4	8	4	5	6	5
38	-	-	3	3	6	7	5	5
40	-	-	2	2	7	6	4	2
42	-	-	1	2	5	5	2	1
44	-	-	-	1	2	2	2	-
46	-	-	-	1	2	1	-	-
48	-	-	-	-	1	-	-	-
50	-	-	-	-	-	-	-	-
52	-	-	-	-	-	-	-	-
54	-	-	-	-	-	-	-	-
56	-	-	-	-	-		-	-

Table 2. Assessment of the opening of oral cavity, in second group (M) of 40 patients (in mm)

Table 3. Assessment of the opening of oral cavi	ty, in third group (L+M) of 41 patients (in mm
)	

				)				
MO-mm	Ev. 1	Ev. 2	Ev. 3	Ev. 4	Ev. 5	Ev. 6	Ev. 7	Ev. 8
16	-	-	-	-	-	-	-	-
18	5	-	-	-	-	-	-	-
20	6	2	-	-	-	-	-	-
22	6	2	-	-	-	-	-	-
24	8	3	-	-	-	-	-	-
26	6	4	-	-	-	-	-	1
28	6	6	-	-	-		1	2
30	4	7	1	-	-	1	2	3
32	-	8	1	1	-	1	3	3
34	-	4	2	1	-	2	3	3
36	-	3	3	2	1	2	3	5
38	-	2	3	2	2	3	5	6
40	-	-	8	4	3	3	7	8
42	-	-	7	7	5	6	8	6
44	-	-	7	9	7	7	5	2
46	-	-	6	7	7	9	2	1
48	-	-	3	5	8	4	1	1
50	-	-	-	2	4	1	1	-
52	-	-	-	1	2	1	-	-
54	-	-	-	-	1	-	-	-
56	-	-	-	-	1	-	-	-

44

The mouth opening (MO) in all the patients increased gradually during the therapy till Ev.5, and then decreased until the Ev.8. The yellow color of the boxes in the tables indicates the maximum number of patients.

Table 4 presents the reported answers of pain intensity in all three groups of patients, in all eight evaluation sessions, according to the analogical visual scale (VAS) for pain. The reference points used in our study were: VAS 0-1 = no pain; VAS 2-3 = mild pain; VAS 4-5 = moderate pain; VAS 6-7 = severe pain; VAS 8-9 = very severe pain; VAS 10 = the most intense pain possible.

Studying the values of table 4, it is noticeable that the pain intensity reported by

the patients was decreased from Ev.1 (from the maximum "severe pain", VAS = 8-9) to Ev.5 (to minimum "no pain", VAS = 0).

On Ev.6, Ev.7 and Ev.8, it is noticeable that a new increase in pain appeared.

We underline that VAS values were the lowest in patients in the third group (L + M), thus patients who received associated therapy, followed by the VAS values of the first group of patients (L). VAS values in the second patient group (M) were higher than in the other two groups, throughout the applied therapies and monitoring sessions.

The yellow color of the boxes in the tables indicates the maximum number of patients.

Group	VAS	Ev. 1	Ev. 2	Ev. 3	Ev. 4	Ev. 5	Ev. 6	Ev. 7	Ev. 8
	0-1	-	-	1	11	12	12	10	8
	2-3	-	1	3	17	21	22	15	15
L 40	4-5	2	6	16	12	9	8	16	17
42 patients	6-7	15	18	11	2	-	-	1	2
patients	8-9	20	15	11	-	-	-	-	-
	10	5	2	-	-	-	-	-	-
	0-1	-	-	-	3	6	6	6	4
	2-3	-	-	2	6	9	9	8	7
<b>M</b> 40	4-5	1	1	4	8	11	9	9	8
patients	6-7	16	16	15	14	9	12	12	12
patients	8-9	19	20	17	9	5	4	6	9
	10	4	3	2	2	-	-	-	-
	0-1	-	3	5	15	17	18	14	8
1.84	2-3	-	7	11	17	15	16	16	16
<b>L+M</b> 41	4-5	2	6	13	9	9	7	11	15
41 patients	6-7	15	14	9	-	-	-	-	2
patients	8-9	19	1	3	-	-	-	-	-
	10	5	-	-	-	-	-	-	-

Table 4. Reported answers of pain intensity according to the Visual Analogue Scale (VAS)

According to the obtained results, the optimal modality with highest success rate is represented by the associated therapy, due to the improvement of the mouth-opening that was significant increased, and the pain intensities that were reduced in the patients of third group, in comparison with the patients of first and the second group.

The Epic 10 device in pain therapy determines local heating of treated tissues, which induce a temporary increase of the blood circulation, and temporary relaxation of the contracted muscles. [30].

The researches of Shukla et al [31], demonstrated that LLLT seems to be effective in the pain reducing of TMDs, and the treatment with soft lasers may be an option for the patients which are interested in noninvasive therapy. Leite et al [32] underlined that most studies about LLLT presented pain remission, but the standardization of used parameters (wavelength, output power, frequency) and defined protocols for the use of LLLT are necessary for an efficient treatment of TMDs. The studies of Melis [33], suggest that the use of LLL in the therapy of TMDs cannot be recommended. Kathuria et al [34], indicates that LLLT should be applied with great attention in the patients with malignancies and coagulation disorders. Eroglu et al [35], consider that extra-oral singlesessions with LLLT effectuated immediately after the extraction of impacted third molar can help patients be less affected by the postoperative trismus and swelling.

Currently, there is no consensus in the literature on the frequency and the number of LLLT sessions. [36].

#### Conclusions

- LLLT as monotherapy, proves its efficiency in comparison with medication therapy.
- The efficacy of associated therapy was demonstrated, the improving of the oral cavity opening was demonstrated and the time interval for pain disappearance of TMDs was shorter in patients with associated treatment, than in the other patients.
- Associated therapy in the treatment of TMJ disorders should be considered as an alternative method to monotherapies.
- The utilization of LLLT in the treatment of painful TMDs is a facile method, is easily performed, allows the patient increased comfort, and cuts patient's anxiety.
- If proper occlusal equilibration is not performed, regardless of the type of applied treatment, the pain in TMJ and the TMDs reappears.
- The present study did not evaluat the long term effect of applied treatments and there is need to design a study with longer followups. Moreover, controlled double-blind clinical trials and multicenter studies are necessary.

#### **Conflict of interest:** None to declare.

#### References

1. Zakrzewska J.M., Temporomandibular disorders, headaches and chronic pain. J Pain Palliat Care Pharmacother. 2015 Mar; 29(1):61-3

- 2. National Institute of Dental and Craniofacial Research. Prevalence of TMJD and Its Signs and Symptoms. July 18, 2013, <u>http://www.nidcr.nih.gov/DataStatistics/FindData</u> <u>ByTopic/FacialPain/PrevalenceTMJD.htm</u>
- Pow E.H., Leung K.C., McMillan A.S., Prevalence of symptoms associated with temporomandibular disorders in Hong Kong Chinese. J Orofac Pain. 2001 Summer; 15(3):228-34
- Mobilio N., Casetta I., Cesnik E., Catapano S., Prevalence of self-reported symptoms related to temporomandibular disorders in an Italian population.J Oral Rehabil. 2011 Dec; 38(12):884-90
- Nidal G., Concepts of TMD Etiology: Effects on Diagnosis and Treatment, IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), Vol. 15, Issue 6, Ver. II (June. 2016), p. 25-42
- 6. Dutton M., Dutton's Orthopaedic Examination, Evaluation, and Intervention, capter 26, The temporomandibular joint, 3 edition. McGraw-Hill Education / Medical, 2012
- 7. Sharav Y., Benoliel R., Orofacial Pain And Headache, Edinburgh London New York Oxford Philadelphia St Louis Sydney Toronto, Mosby, Elselvier, 2008, <u>https://archive.org/details/OrofacialPainAndHead</u> ache2008
- 8. Manfredini D. Current concepts on temporomandibular disorders. London, Berlin, Chicago: Quintessence Publishing, 2010
- Iserto D.M., Summers S., TMJ Temporomandibular Joint Dysfunction - Causes, Symptoms, Treatment, and Pain Relief For Your Jaw Pain, Amazon Digital Services LLC, 2014
- 10. Paço M., Peleteiro B., Duarte J., Pinho T., The effectiveness of physiotherapy in the management of temporomandibular disorders: a systematic review and meta-analysis. J Oral Facial Pain Headache. 2016;30(3):210–220
- 11. Reddy SV, Kumar MP, Sravanthi D, Mohsin AHB, Anuhya V. Bruxism: A Literature Review. Journal of International Oral Health : JIOH. 2014;6(6):105-109
- 12. Murali RV, Rangarajan P, Mounissamy A. Bruxism: Conceptual discussion and review. Journal of Pharmacy & Bioallied Sciences. 2015;7(Suppl 1):S265-S270.
- Dzingutė A, Pileičikienė G, Baltrušaitytė A, Skirbutis G. Evaluation of the relationship between the occlusion parameters and symptoms of the temporomandibular joint disorder. Acta Medica Lituanica. 2017;24(3):167-175
- 14. <u>https://www.sciencedirect.com/topics/neuroscie</u> <u>nce/anti-inflammatory</u>
- 15. <u>https://www.drugs.com/drug-class/nonsteroidal-anti-inflammatory-agents.html</u>

- 16. Chantaracherd P, John MT, Hodges JS, Schiffman EL. Temporomandibular Joint Disorders' Impact on Pain, Function, and Disability. Journal of Dental Research. 2015;94(3 Suppl):79S-86S
- 17. Das S, Gupta R, Dhyani M, Goel D. Headache secondary to sleep-related bruxism: A case with polysomnographic findings. Journal of Neurosciences in Rural Practice. 2015;6(2):248-251
- López-Ramírez M, Vílchez-Pérez MA, Gargallo-Albiol J, ArnabatDomínguez J, Gay-Escoda C (2012) Efficacy of low-level laser therapy in the management of pain, facial swelling, and postoperative trismus after a lower third molar extraction. A preliminary study. Lasers Med Sci 27:559–566
- 19. Maia ML, Bonjardim LR, Quintans Jde S, Ribeiro MA, Maia LG, Conti PC (2012) Effect of low-level laser therapy on pain levels in patients with temporomandibular disorders: a systematic review. J Appl Oral Sci 20:594–602
- 20. Herranz-Aparicio J, Vázquez-Delgado E, Arnabat-Domínguez J, España-Tost A, Gay-Escoda C. The use of low level laser therapy in the treatment of temporomandibular joint disorders. Review of the literature. Medicina Oral, Patología Oral y Cirugía Bucal. 2013;18(4):e603-e612.
- Huang Y.-F., Lin J.-C., Yang H.-W., Lee Y.-H., Yu C.-H., Clinical effectiveness of laser acupuncture in the treatment of temporomandibular joint disorder, Journal of the Formosan Medical Association, Volume 113, Issue 8, August 2014, p. 535-539
- 22. Cotler HB, Chow RT, Hamblin MR, Carroll J. The Use of Low Level Laser Therapy (LLLT) For Musculoskeletal Pain. MOJ orthopedics & rheumatology. 2015;2(5):00068.
- 23. www.biolase.com/procedures/hygienists/paintherapy/
- 24. <u>https://www.biolase.com/products/dental-lasers-</u> soft-tissue/epic-10/
- 25. <u>https://www.youtube.com/watch?v=pMLtbFAz13</u> <u>w</u>
- 26. <u>https://www.biolase.com/media/EPIC\_PainThera</u> py\_Brochure.pdf
- 27. Gouveia M.V.C., Barbalho J.C.M., Pereira Júnior E.D., Nascimento M.M.M., Vasconcelos B.C.E., Effectiveness and satisfaction evaluation of

patients submitted to TMJ arthrocenthesis: a case series, Braz Oral Res [online]. 2015;29(1):1-5

- 28. Klimek L, Bergmann K-C, Biedermann T, et al. Visual analogue scales (VAS): Measuring instruments for the documentation of symptoms and therapy monitoring in cases of allergic rhinitis in everyday health care: Position Paper of the German Society of Allergology (AeDA) and the German Society of Allergy and Clinical Immunology (DGAKI), ENT Section, in collaboration with the working group on Clinical Immunology, Allergology and Environmental Medicine of the German Society of Otorhinolaryngology, Head and Neck Surgery (DGHNOKHC). Allergo Journal International. 2017;26(1):16-24
- 29. Kersten P, White PJ, Tennant A. Is the Pain Visual Analogue Scale Linear and Responsive to Change? An Exploration Using Rasch Analysis. Mouraux A, ed. PLoS ONE. 2014;9(6):e99485.
- 30. <u>file:///C:/Users/user4/Desktop/Art%20rev%20Tg</u> <u>M%2015.05.2018/2.%20ATM%20disf/EPIC\_User</u> <u>Manual.pdf</u>
- Shukla D, Muthusekhar MR. Efficacy of low-level laser therapy in temporomandibular disorders: A systematic review. National Journal of Maxillofacial Surgery. 2016;7(1):62-66.
- 32. Leite P., Melo N., Silva P., Montenegro R., Bonan P., Batista A., Low-level laser therapy for temporomandibular disorders (tmd) treatment: a systematic review of randomized trials. Journal of Research in Dentistry, [S.I.], v. 2, no. 5, p. 376-387, 2014,

http://www.portaldeperiodicos.unisul.br/index.ph p/JR Dentistry/article/view/2785

- 33. Melis M. The role of physical therapy for the treatment of temporomandibular disorders. J Orthodont Sci 2013;2:113-4
- Kathuria V., Dhillon J.K., Kalra G., Low Level Laser Therapy: A Panacea for oral maladies, Laser Therapy 24.3: 215-223
- 35. Eroglu C.N., Keskin Tunc S., Effectiveness of Single Session of Low-Level Laser Therapy with a 940nm Wavelength Diode Laser on Pain, Swelling, and Trismus After Impacted Third Molar Surgery. Photomed Laser Surg. 2016 Sep;34(9):406-10.
- 36. Ayyildiz S., Emir F., Sahin C., Evaluation of Low-Level Laser Therapy in TMD Patients, Case Reports in Dentistry, vol. 2015, Article ID 424213, 6 pages, 2015.

#### **Corresponding author:**

#### Farah Curt-Mola

University of Medicine and Pharmacy of Tirgu Mures, 38 Gheorghe Marinescu street, Tirgu Mures, 540139, Romania Email: farah.curtmola@yahoo.com

Received: April 28, 2018 / Accepted: May 29, 2018

# **ORIGINAL PAPER**

# Clinical-statistical analysis of correlations between caries risk indicators and the prevalence of maxillary dental anomalies in a group of children from Tirgu Mures

Mariana Păcurar<sup>1</sup>, Eugen Bud<sup>1</sup>, Haj Alexandra<sup>2</sup>, Manuela Chibelean<sup>1</sup>, Maria Cristina Figueiredo Pollmann <sup>3</sup>

<sup>1</sup> Faculty of Dental Medicine, University of Medicine and Pharmacy of Tirgu Mures, Romania

<sup>2</sup> Psihiatric Clinical, Emergency Mures Hospital, Tirgu Mures, Romania

<sup>3</sup> Faculdade de Medicina Dentária da Universidade do Porto, Portugal

#### Abstract

Aim: The authors proposed to analyse the pattern of carious lesions in children who underwent orthodontic treatment at the Orthodontic Department of the Faculty of Dental Medicine at the University of Medicine and Pharmacy, Tirgu Mures during 2015-2017 and to determine the correlation between the pathology of carries and the prevalence of maxillary dental anomalies in these children.

Material and method. Study was a retrospective, in a group of 200 patients (91 young female and 109 young male patients), aged 6-9 years old, who underwent special treatment. We performed a caries risk assessment quantified by the DMFT/dmft scores of mixed dentition and determined a predictive factor of the occurrence of maxillary dental anomalies. We diagnosed maxillary anomalies based on study models and calculated the DAI score (Dental Aesthetic Index) characteristic to the degree of malocclusion

Results. We registered the highest percentage of vertical anomalies for deep bite malocclusion, Class II division 2 anomaly (according to Angle's classification), in a percentage of 54%, found that the DMFT/dmft score was between 0 - 11, the most frequent values being between 0 - 5. The DMFS/dmfs score was between 0 - 34, the most common score being 1, followed by values between 2 -7. A more suggestive characterization of these indices is obtained by addressing them as quantitative variables, by assessing mean and standard deviations. The DMFS/dmfs score was significantly higher in boys (10.86  $\pm$  8.902) than in girls (7.93  $\pm$  7.932), and respectively higher in rural areas (11.04  $\pm$  8.822) than in urban areas (8.02  $\pm$  8.083).

Conclusions. The presence of high DMFT/dmft index scores do not present a potential risk for the development of anomalies in the sagittal and vertical direction.

Disharmony caused by maxillary dental crowding presents direct correlations between the caries index and the severity of the anomaly.

Keywords: caries, anomalies DMFT/dmft, index DAI

#### Introduction

Although oral health has improved worldwide, oral diseases still continue to pose a major public health problem, especially within communities belonging to socially disadvantaged groups who still face increased levels of carious lesions and periodontal diseases. Currently, the distribution and severity of oral diseases vary greatly from one country to another as well as among the different areas of the same country.

There are several studies published that have attempted to establish the correlation between the indicator of dental caries in mixed dentition and the risk of maxillary dental anomalies, as well as the way in which intraarch and inter-arch modifications occur. Premature loss of temporary teeth, as a consequence of untreated dental caries, can cause severe three-dimensional disorders of the dental arches and implicitly of dental occlusion, interfering with the harmonious development of the physiological dentition.

#### Aim of research

The authors proposed to analyse the pattern of carious lesions in children who underwent orthodontic treatment at the Orthodontic Department of the Faculty of Dental Medicine at the University of Medicine and Pharmacy, Tirgu Mures during 2015-2017 and to determine the correlation between the

48

pathology of carries in the mixed dentition stage and the prevalence of maxillary dental anomalies in these children. We compared the DAI (Dental Aesthetic Index) scores, which characterizes the degree of malocclusion, with the DMFT/dmft and DMFS/dmfs

### Material and method

We conducted a retrospective study in a group of 200 patients (91 young female and 109 young male patients), aged 6-9 years old, who underwent special treatment. The inclusion criteria were: carious pathology of the temporary and permanent teeth; diagnosed maxillary dental anomalies, compliant patients, whose parents signed the informed consent.

The exclusion criteria were: noncooperative patients; patients older than nine years of dental age; patients with dental dystrophies; labial, maxillary and palatine clefts or genetic/ endocrine disorders. The processing of the collected data was performed by using SPS 22.0 for Windows, a medical statistical analysis program.

We performed a caries risk assessment quantified by the DMFT/dmft scores of mixed

dentition and determined a possible predictive factor of the occurrence of some maxillary dental anomalies. We diagnosed maxillary dental anomalies based on study models and calculated the DAI score (Dental Aesthetic Index) characteristic to the degree of malocclusion. We also established the correlations between DAI and DMFT/dmft scores respectively DAI and DMFS/dmfs scores. The modified DAI score for mixed dentition was calculated for each patient without taking into account the number of missing teeth: canine, premolars of the maxillary and mandibular arches.

### Results

Out of the 200 subjects comprised in the survey 91 (48.5%) were females with a median age of  $7.31\pm0.6$  and 109 (51.5%) were males with a median age of  $7.45\pm0.8$ ; 114 (53%) patients came from urban area and 86 (47%) from rural area.

The distribution by gender and background (urban or rural) is shown in figures 1 and 2.



Figure 1. Gender distribution

Analysing the frequency of maxillary dental anomalies we found an uneven distribution among classes of anomalies, gender and background. Thus, the most frequent sagittal anomalies were class II, division1 anomalies (40% of the cases), figure 3, and the most frequent transverse anomalies were dentalmaxillary disharmonies with crowding (secondary) (55% of the cases), figure 4.

We registered the highest percentage of vertical anomalies for deep bite malocclusion,



Figure 2. Rural-urban distribution of patients

Class II division 2 anomaly (according to Angle's classification), in a percentage of 54% (figure 5). The Chi- square test revealed statistically significant differences in the prevalence of these abnormalities. Thus, the percentage of male patients without sagittal anomalies (24.3%) was significantly higher in comparison to female patients (16.5%), and class II/2 malocclusion was more frequent in young female patients than in young male patients (32.0% versus 23.3%).



Figure 3. The frequency of sagittal malocclusions

Regarding background, the percentage of patients without anomalies (25.5%) was higher in the rural area than in the urban area (16.0%),

while class II/1 malocclusions were more frequent in patients coming from urban areas (44.3%).



Figure 4. The frequency of vertical malocclusions



Figure 5. The frequency of transverse malocclusions

We found that transverse crowding and spacing anomalies were more frequent in males

than in females (10.7% vs. 6.2%), while in females crowding anomalies were more

frequent (61.9%), and lateral balanced reverse occlusion was completely absent. Crowding anomalies were more common in patients coming from urban areas compared to rural areas (58.5% vs. 51.1%), as well as crowding and spacing (10.4% versus 6.4%), and crowding and lateral balanced reverse occlusion appeared more frequently in rural areas (21.3% vs. 13.2%).

We analyzed the frequency distribution chart of caries risk assessment and found that

the DMFT/dmft score was between 0 - 11, the most frequent values being between 0 - 5. The DMFS/dmfs score was between 0 - 34, the most common score being 1, followed by values between 2 -7. A more suggestive characterization of these indices is obtained by addressing them as quantitative variables, by assessing mean and standard deviations. From this perspective, the global DMFT/dmft score was  $3.64 \pm 2.686$  and the DMFS/dmfs score was  $9.44 \pm 8.56$ .

Graph 1. The frequency distribution of DMFT/dmft scores



The comparative study of gender indices showed a significant increase of the DMFT/dmft score in young male patients ( $3.90 \pm 2.679$ ) compared to young female patients ( $3.36 \pm 2.669$ ), as well as in rural areas ( $4.40 \pm 2.865$ ) compared to urban areas ( $2.96 \pm 2.318$ ), graph 1. Similarly, the DMFS/dmfs score was significantly higher in boys (10.86  $\pm$  8.902) than in girls (7.93  $\pm$  7.932), and respectively higher in rural areas (11.04  $\pm$  8.822) than in urban areas (8.02  $\pm$  8.083), graph 2.





The presence of class II division 1 anomaly was not influenced by the DMFT/dmft score, on the contrary, in patients with such DMFT/dmft score we observed a lower percentage of class II/1 anomalies (38.3%) compared to other patients of class II/1 anomalies scoring 40.5%. Similarly, neither the presence of class II division 2 anomaly was influenced by the DMFT/dmft score 5; on the contrary, in patients with this DMFT/dmft score, a lower percentage of Class II/2 anomalies (23.4%) were observed compared to other Class II/2 patients, with a percentage of 28.8% anomalies.





No correlation could be established between the caries risk scores and the presence of Angle Class III anomalies. The patients with DMFT/dmft score greater than 5, presented statistically significantly lower percent of class III anomalies (6.4%) compared to other lower score DMFT/dmft class III malocclusion patients (13.7%).

We observed a more complex situation regarding the variation of DMFT/dmft and DMFS/dmfs scores in case of transversal anomalies. Thus, for the DMFT/dmft indices, we found that in case of crowding of teeth, lateral balanced reverse occlusion and spacing the calculated scores were slightly lower than in patients with normal occlusion. Combined diagnoses of crowding + lateral balanced reverse occlusion showed increased DMFT/dmft score, while crowding + reverse occlusion, demonstrated a slight decrease in the DMFT/dmft score (graphs 3,4).





The frequency distribution graph (graph 5) for the study group shows that the DAI index values were between 13-60, the most frequent values being 24, 26 and 32 respectively. 42% of the patients had the DAI index values corresponding to an absent or slight

malocclusion, while 58% of patients had varying degrees of malocclusion: 24.5% presented stable malocclusion (DAI between 26-30), 16.5% sever malocclusion (DAI between 31-35), and 17.0% extremely severe malocclusion (DAI score over 36).





# Discussions

A situation of the caries risk index on the national level was reported in a study conducted by the representative of WHO (World Health Organization), Prof. Dr. P.E. Petersen in 1992, in the framework of a Tempus project comprising five of our major cities: Bucharest, Iasi, Timisoara, Cluj and Tirgu Mures. Thus, during 1986 - 1992 there was an increase in the DMFT score of 12-yearold patients from 3.1 to 4.1. (6) Subsequently a slight downward trend of the DMFT score (3.4) was recorded in 1995. In 1996, the National Oral Health Pathfinder Survey, conducted in Romania by WHO, showed that the average level of DMFT score in 12-year-old 3.1, much higher than patients was recommended for Europe (2 for children of the same age).

Attempts to demonstrate a direct link between the presence of dental caries and maxillary dental anomalies reported inconclusive results [4, 9]. Parker have found parallelism between tooth decay prevalence and mandibular overjet for mixed dentition, which proved to be statistically significant after the assessment of the risk of developing a particular malocclusion [10]. The likelihood of developing an open occlusion is twice as high in children with dental caries then in children without caries [6]. Peres reported similar results in children with a DAI index > 35 and a significantly higher caries experience compared to other children. Moreover, DAI scores have shown a significant correlation with the mean scores of the DMFT index (r = 0.368, p < 0.05). Another survey conducted in Argentina in 2016 also showed a positive correlation between the severity of malocclusions and dental caries based on the DAI index. But Axelsson [7] concluded that there was no statistically significant correlation between the DAI and DMFT index scores (although the prevalence of malocclusion and dental caries had proven to be high).

# Conclusions

1. The presence of high DMFT/dmft index scores do not present a potential risk for the

development of anomalies in the sagittal and vertical direction.

- 2. Disharmony caused by maxillary dental crowding presents direct correlations between the caries index and the severity of the anomaly, so that the premature loss of temporary teeth associated with untreated dental caries determines the drifting of antagonistic adjacent permanent teeth.
- 3. The most accurate predictor of caries activity in mixed dentition, the DMFT/dmft index, showed lower mean values in patients with dental spacing and higher in patients with dental crowding.
- 4. The combination of anomalies: disharmony caused by dental crowding and reverse occlusion, respectively by lateral reverse occlusion can be associated with higher values of the DMFT/dmft indices.
- 5. High DMFT/dmft index values influence DAI index values only in a low percentage, which cannot be considered a positive influence. Low DMFT/dmft index values have greater influence on low DAI index values.

#### **Conflict of interest:** None to declare.

#### References

- Cushing AM, Sheiham A, Meizels J. Developing socio-dental indicators -the social impact of dental disease. Community Dent Health 1996; 3: 3-17;
- Gift HG, Atchison KA, Dayton CM. Conceptualizing oral health and oral health-related quality oflife. Soc Sci Med 1997; 44: 601-609;
- Marthaller TM. Caries status in Europe and poredictions of future trends , Caries research, 1990, 24(6), 381-396
- Broder HL, Slade G, Caine R, et al. Perceived impact of oral health conditions and quality oflife among American adolescents. J Dent Res 207: 26 (8) 201-205;
- Maxim A, Bălan A, Păsăreanu M. Demographic trends of caries activity in children and teenagers, Medicina Stomatologică, 2004, 8 (1) 80-83
- Petersen PE, Hoerup N, Poomviset N, Prommajan J, Watanapa A. Oral health status and oral health behaviour of urban and rural schoolchildren in Europe . Int Dent J 2001, 51:95-102.
- Axelsson S, Soder B, Nordenram G et al. Effect of combined caries-preventive methods: a systematic review of controlled clinical trials. Acta Odontol Scand 2004; 62: 163-9.
- Dănilă I, Hanganu C, Timis T. Trends in oral health status in schoolchildren from Iasi, Romania. Oral Health and Preventive Dentistry' 2004: 2 (1): 71
- 9. Widstrom E, Eaton KA, Borutta A. Oral health care in transition in Eastern Europe. British. Dental Journal 2009; 190: 580-4
- 10. Parker MW. The significance of occlusion in restorative dentistry. Dental Clinic North. American Journal, 2013, 37 (3), 341-347

#### Corresponding author:

Manuela Chibelean

University of Medicine and Pharmacy of Tirgu Mures, 38 Gheorghe Marinescu street, Tirgu Mures, 540139, Romania Email: drmchibelean@yahoo.com

Received: April 30, 2018 / Accepted: May 29, 2018

# **ORIGINAL PAPER**

# Comparative effectiveness of alternative medication in minor aphtous stomatitis

Farah Curt-Mola<sup>1</sup>, Mircea Suciu<sup>1</sup>, Ilinca Suciu<sup>1</sup>, Anamaria Bechir<sup>2</sup>, Lelia Laurenta Mihai<sup>2</sup>, Alexandru Burcea<sup>2</sup>, Edwin Sever Bechir<sup>1</sup>

<sup>1</sup> Faculty of Dental Medicine, University of Medicine and Pharmacy of Tirgu Mureş, Romania

<sup>2</sup> Faculty of Dental Medicine, Titu Maiorescu University, Bucharest, Romania

#### Abstract

Minor aphthous stomatitis is the most common oral mucosal disease and affects almost 20% of the population. Currently, there is an increasing interest across the globe in alternative therapies that use natural products versus synthetic agents.

The objectives of the study were represented by the identification of the required time for healing, the pain intensity reduction, the recurrence of affection and the satisfaction of patients with minor aphthous stomatitis treated with Propolis tincture spray, Aloe Vera tincture, and sodium bicarbonate solution. The study was a randomized and doubleblinded clinical trial, conducted on 100 patients divided in four groups, which were diagnosed with minor aphthous stomatitis. At the beginning and during the study, patients were daily specifically questioned, examined and monitored to establish the healing stage of aphthous lesions (including erythema), the pain intensity reduction, impress regarding the taste and easiness in application of the used substances, and the apparition/existence of any adverse event. Achieved results were compared.

This study demonstrated that the therapy with Propolis tincture and Aloe Vera tincture is a rapid, low cost and easy-to-apply method, and yielded good results in treating minor AS.

Keywords: minor aphthous stomatitis, Propolis tincture, Aloe Vera tincture, Sodium bicarbonate solution, healing.

#### Introduction

Common superficial oral lesions include recurrent aphthous stomatitis, candidiasis, recurrent labial herpes, erythema migrants, hairy tongue, and lichen planus [1,2].

The recognition and the classification of oral lesions have a considerable significance in the process of diagnosis. The correct diagnosis is accomplished through the knowledge of the various lesions, a thorough history and a comprehensive clinical oral examination for the precise diagnosis in the process of differentiating between the specific conditions, management, as well as counselling [3-5]. Ulceration due to aphthous stomatitis (AS) represents the most common oral mucosal inflammatory disease, most frequently starts during the second decade of life, affects about 20% of the population and has a female predilection [6,7]. The etiology of AS is varied and is due to the perturbation of the oral ecosystem. The oral environment is unique, and is able to induce reactivity of products from the prosthetic restoration materials. The biological reactivity of dental materials in the

oral cavity can induce reactions of the oral tissues against the bacteria's adhesion, reactions to the mechanical irritation, to the direct toxic effect, and to the allergens [8]. Habitually, AS lesions begin with prodromal burning sensation, 2-48 hours before the appearance of an ulceration. AS debut is painful. It has the appearance of a rounded ulceration masked by fibrin, with erythematous margins, located especially on the nonkeratinized oral mucosa [9,10].

The described clinical types of aphthous stomatitis are:

- Minor-type (Mikulicz type) of AS, which represents 80–90% of all aphthous ulcer, usually is solitary, had 2-3 mm diameter, and heals spontaneously in two weeks;
- Major-type (Sutton type) represents about 10% of of AS, usually have 1–3 cm in size, are profound indurated, and lasts between 10 days-6 weeks, or more; about 64% of these ulcers heal with scarring;
- Herpetiform aphthae are grouped, multiple, very small ulcerative lesions (more than 100 ulcer lesions), with 1-2 mm diameter,

extremely painful, and it takes more than 15 days to completely heal; affects the keratinized oral mucosa and more than 30% of lesions heal with scarring [6,9,11].

Medical products which are not considered part of conventional care, represent the alternative medicine [12]. Currently, there is an increasing interest across the globe in alternative therapies that use natural products, as opposed to synthetic agents.

Propolis is a resinous mixture composed of mixing beeswax, saliva, sap flows, and various botanical products in the surrounding area [13-15]. For a long period, it has been used as a remedy for various types of ailments, and is thought to have anti-inflammatory, antibacterial, and anti-viral properties, because its very high levels of bioflavonoids and other bioactive compounds, which stimulate, rejuvenate the body and provide powerful support to the immune system [16,17]. Propolis tincture has a complex composition and has analgesic, antifungal, bactericidal, antiviral effects that stimulate regeneration processes [18]. ApiLand® Propolis tincture (Romania) contains 95% purified Propolis and can also be found in spray form [19].

Aloe Vera is the most effective species according to the latest medical research in the field, from about 400 existing species. Aloe Vera contains over 150 bioactive substances, with anti-inflammatory, analgesic, antiseptic and cicatrizing effects [20]. External effects of Aloe Vera Tincture are represented by their anti-inflammatory, analgesic, antiseptic and cicatrisation properties. Aloe tincture provides a special skin care and helps alleviate pain and it can be used on sprains, eczema and wounds. [21-23]. Dacia Plant® Aloe Vera Tincture 50 ml (Romania) is a hydroalcoholic solution, made by cold preparation of fresh Aloe Vera leaves [24].

Sodium bicarbonate, a white solid crystalline substance, is a salt composed of sodium ions and bicarbonate ions. Sodium bicarbonate can be administered to raise the alkalinity. It has weak disinfectant properties, and can be an effective antifungal [25-27].

The products used in this study are presented in figure 1.



Figure 1. Used products in study: A. Propolis tincture spray (ApiLand®, Romania); B. Aloe Vera Tincture (Dacia Plant®, Romania); C. Sodium bicarbonate

The aim of this study was to evaluate the healing effects of Propolis tincture, Aloe Vera tincture and sodium bicarbonate solution on minor aphthous stomatitis.

#### **Material and methods**

The study was performed according to ethical principles and good clinical practice. Subjects were invited to participate in this clinical trial and all participants signed written informed consent prior to the beginning of this study. The study was a randomized and double-blinded clinical trial.

The objectives of the study were represented by the identification of the required time for healing, the pain intensity reduction, the recurrence of affection and the satisfaction of patients with minor recurrent aphthous stomatitis treated with Propolis tincture spray (ApiLand®, Romania), Aloe Vera tincture (Dacia Plant®, Romania) and sodium bicarbonate solution.

The clinical trial was conducted in 111 patients diagnosed with minor aphthous stomatitis. During the study, 9 subjects withdrew voluntarily and 2 subjects were excluded from the study, for lack of cooperation. The study was conducted during the period of 2015-2018 at the University of Medicine and Pharmacy of Tirgu Mureş and Titu Maiorescu University of Bucharest Dental clinics. The reason for presenting of patients was the recurrence of aphthous stomatitis. The inclusion criteria of patients were as follows: an age range of 12-29 years; having at the presentation in the dental office one aphthous stomatitis lesion, measuring under 1 cm in diameter, well-demarcated, and in accessible area of the mouth, less than 48 hours' from the ulcer apparition; with at least quarterly or biannual

eruptive episodes; without other established acute or chronic diseases; systemic nonsteroidal anti-inflammatory, and immunomodulatory treatments within 1 month prior to the study.

The mean ( $\pm$ SD) of patients' age was 20.5  $\pm$  8.5 years in the included patients in the study.

Eligible patients (100) were randomized in four groups: the group of patients who benefited from Propolis spray tincture therapy (1<sup>st</sup> group, n=30, 19 female and 11 male), Aloe Vera tincture in solution therapy (2<sup>nd</sup> group, n=30, 17 female and 13 male), sodium bicarbonate solution therapy (3<sup>rd</sup> group, n=20, 12 female and 8 male) and the control group with applications in the area of aphthous stomatitis lesion of distilled water (4<sup>th</sup> group, n=20, 11 female and 9 male).

The distribution of the patients in groups, after gender and the products used, is presented in graph 1.

Graph 1. The distribution of the patients in groups, after gender and the products used



Only the head of Oral Pathology Department of Titu Maiorescu University of Bucharest knew the contents of the vials. The vials were marked only with a single digit code (1, 2, 3, and 4).

Application of substances was performed 4 daily, for 4 days, as following:

- 1<sup>st</sup> group of patients: ApiLand spray with 95% purified Propolis tincture was applied by spraying 4 times/day, by 2-3 puffs in the affected area;
- 2<sup>nd</sup> group of patients: Dacia Plant Aloe Vera tincture solution was used 4 times daily by

rinsing the oral cavity with one teaspoon of tincture diluted in 100 ml of water;

- 3<sup>rd</sup> group of patients: Sodium bicarbonate solution, was utilized by rinsing 4 times daily the oral cavity with one teaspoon of powder in 100 ml of waters;
- 4<sup>th</sup> group of patients: Distilled water, by local application with micro brush applicators.

The patients were asked to retain from eating and drinking for 30 min after application of substances. Oral hygiene of each patient was performed twice daily with Colgate Total <sup>TM</sup> toothpaste and Colgate 360° toothbrush (made available to patients by researchers), 30 minutes before the application of used substances in study. No other substances or medications were permitted during the study.

At the beginning and during the study, patients were daily specifically questioned, examined and monitored, to establish the healing stage of aphthous lesions (pain intensity and erythema), impress regarding the taste and easiness in application of the used substances, and the apparition/existence of any adverse event.

All the patients were monitored for 1 year.

First outcome was related with the assessment of efficacy of used substances in study, by evaluating the level of pain and erythema, daily for 6 days and compared to baseline. Patients classified the severity of pain by using visual analogue scale (VAS), on a 10 cm line, marked at one end with "no soreness" and the other end with "worst possible soreness". The level of erythema was evaluated on a four-point scale ranging from 0 to 3 (0 = no erythema; 1 = light red/pink; 2 = red but not dark in color; 4 = dark in color).

The second outcome was in reference with the overall assessment of the used substance on three-point description scale (poor, moderate, and good). The third outcome was to establish the recurrence rate of aphthous stomatitis in a period of 1 year.

At the end of the study, the results were unblinded.

#### **Results and discussions**

At base line, no significant differences were founded between the pain and the erythema level in all four groups.

The pain intensity reduction after the determination of VAS score is presented in table 1.

Tabla 1	Departed	nain int	oncity		to used	Vieual	Analagua	Coolo /	()/AC)
Table T.	Reported	painini	ensity a	according	lo useu	VISUAL	Allalogue	Scale (	VAS

Group	VAS	Base line	2 <sup>nd</sup> day	3 <sup>th</sup> day	4 <sup>th</sup> day	5 <sup>th</sup> day	6 <sup>th</sup> day	7 <sup>th</sup> day
	0-1	-	-	3p = 10%	5p = 16.66%	11p = 36.66%	20p = 66.66%	27p = 90%
ApiLand®	2-3	-	6p = 20%	4p = 13.33%	6p = 20%	10p = 33.33%	7p = 23.33%	3p = 10%
Propolis	4-5	4p = 13.33%	7p = 23.33%	8p = 26.66%	9p = 30%	9p = 30%	3p = 10%	-
tincture spray	6-7	11p = 36.66%	8p = 26.66%	9p = 30%	10p = 33.33%	-	-	-
(30 patients)	8-9	10p = 33.33%	7p = 23.33%	6p = 20%	-	-	-	-
	10	5p = 16.66%	2p = 6.66%	-	-	-	-	-
	0-1	-	-	1p = 3.33%	3p = 10%	10p = 33.33%	18p = 60%	25p = 83.33%
Dacia Plant®	2-3	-	4p = 13.33%	3p = 10%	5p = 16.66%	9p = 30%	8p = 26.66%	5p = 16.66%
Aloe Vera	4-5	4p = 13.33%	6p = 20%	5p = 16.66%	10p = 33.33%	11p = 36.66%	4p = 13.33%	-
tincture	6-7	11p = 36.66%	7p = 23.33%	13p = 43.33%	12p = 40%	-	-	-
(30 patients	8-9	11p = 36.66%	10p = 33.33%	8p = 26.66%	-	-	-	-
	10	4p = 13.33%	3p = 10%	-	-	-	-	-
	0-1	-	-	-	1p = 5%	5p = 25%	8p = 40%	12p = 60%
Sodium	2-3	-	2p= 10%	3p = 15%	2p = 10%	6p = 30%	6p = 30%	7p = 35%
bicarbonate	4-5	3p = 15%	4p = 20%	3p = 15%	8p = 40%	7p =35%	6p = 30%	1p = 5%
solution	6-7	7p = 35%	4p = 20%	9p = 45%	9p = 45%	2p = 10%	-	-
(20 patients)	8-9	7p = 35%	8p = 40%	5p = 25%	-	-	-	-
	10	3p = 15%	2p =10%	-	-	-	-	-
	0-1	-	-	-	-	2p = 10%	6p = 30%	9p =45%
	2-3	-	1p = 5%	1p = 5%	2p = 10%	6p = 30%	8p = 40%	9p = 45%
Distilled	4-5	3p = 15%	4p = 20%	3p = 15%	8p = 40%	11p = 55%	6p = 30%	2p = 10%
water	6-7	7p = 35%	5p = 25%	8p = 40%	8p = 40%	1p = 5%	-	-
(20 patients)	8-9	7p = 35%	7p = 35%	7p = 35%	2p = 10%	-	-	-
	10	3p = 15%	3p =15%	1p = 5%	-	-	-	-

The period of the pain reduction started with the first application of products with active substances (groups 1, 2, and 3). We founded group differences at the later visits (day 4, 5, 6, and 7), compared with the base line (at patients presentation) and at comparison

between groups. Recorded VAS scores showed that the pain intensity was the lowest in the first group of patients (who were treated with ApiLand® spray with 95% purified Propolis tincture), followed by the second group of patients (treated with Dacia Plant® Aloe Vera tincture solution) and the third group of patients (treated with Sodium bicarbonate solution). The scores in the fourth group of patients (distilled water) at all 7 sessions showed that painful intensity was the highest of the four groups surveyed. Studying the VAS scores recorded in 7 assessments, we found that there were no significant differences in VAS scores in the first and second patient groups. In the third and fourth group of patients, we found that there were differences in favor of the third group of patients.

The erythema levels in the groups is presented in table 2.

Ducatuat	Louis Loff an allowed			Level	of lesions erv	thema		
Product	Level of erythema	Base line	2 <sup>nd</sup> day	3 <sup>th</sup> day	4 <sup>th</sup> day	5 <sup>th</sup> day	6 <sup>th</sup> day	7 <sup>th</sup> day
ApiLand <sup>®</sup> Propolis tincture spray (30 patients)	No erythema	-	-	-	21p=70%	28p=93.33%	30p=100%	30p=100%
	Light red/pink	-	-	8p=26.66%	6p=20%	2p=6.66%	-	-
	Red but not dark	11p=36.663%	11p=36.663%	11p=36.66%	2p=6.66%	-	-	-
	Dark in color	19p=63.33%	19p=63.33%	11p=36.66%	1p=3.33%	-	-	-
Dacia Plant <sup>®</sup> Aloe Vera tincture	No erythema	-	-	-	19p=63.33%	27p=90%	28p=93.33%	30p=100%
	Light red/pink	-	-	7p=23.33%	7p=23.33%	2p=6.66%	2p=6.66%	-
	Red but not dark	10p=33.33%	10p=33.33%	11p=36.66%	2p=6.66%	1p=3.33%	-	-
(30 patients)	Dark in color	20p=66.66%	20p=66.66%	12p=40%	2p=6.66%	-	-	-
Sodium	No erythema	-	-	-	10p=50%	10p=50%	12p=60%	17p=85%
bicarbonate	Light red/pink	-	-	5p=25%	4p=20%	9p=45%	7p=35%	3p=15%
solution	Red but not dark	7p=35%	7p=35%	7p=35%	4=20%	1p=5%6	1p=5%	-
(20 patients)	Dark in color	13p=65%	13p=65%	8p=40%	2p=10%	-	-	-
	No erythema	-	-	-	7p=35%	8p=40%	9p=45%	16p=80%
Distilled water	Light red/pink	-	-	3p=15%	4p=20%	6p=30%	7p=35%	3p=15%
(20 patients)	Red but not dark	7p=35%	7p=35%	6p=30%	5p=25%	4p=20%	3p=15%	1p=5%
	Dark in color	13p=65%	13p=65%	11p=55%	4p=20%	2p=10%	1p=5%	-

Table 2. Level of erythema in treated and placebo groups

At base line, no significant differences were founded in groups. In all ulterior assessments, the first and second groups of patients (treated with Propolis and Aloe Vera tinctures) presented the lowest level of erythema. There were no significant differences in the level erythema in the first and second patients group. The highest erythema level was in the fourth group of patients (distilled water).

The second outcome was in reference with the overall assessment of the used substance. The distribution of scores in overall assessment of the treatment is presented in table 3. It is visible that in the "good" score, the best percentages were in the first group/Propolis (90%) and second group/Aloe Vera (86.66%), unlike the third group/Sodium Bicarbonate (50%) and fourth group/Distilled water (10%).

AS disease recurrence after 1 year of monitoring was the third outcome of this study. After one year of monitoring of the patients at every three months, is visible that the best results are in first group/Propolis tincture, with a total of 13.33% recurrences, and in second group/Aloe Vera (16.66% recurrences) in comparison with the results of fourth group/Distilled water, where appeared 75% of recurrence of AS (table 4).

Table 3. Distribution of scores in overall assessment of the treatment

Score	Group 1, ApiLand <sup>®</sup> Propolis tincture spray (30 patients)	Group 2, Dacia Plant <sup>®</sup> Aloe Vera tincture (30 patients)	Group 3, Sodium bicarbonate solution (20 patients)	Group 4, Distilled water (20 patients)
Good	27p ( = 90%)	26p ( = 86.66%)	10p ( = 50%)	2p ( = 10%)
Moderate	3p ( = 10%)	3p (= 10%)	7p ( = 35%)	8p ( = 40%)
Poor	-	1p (= 3.33%)	3p ( = 5%)	10p ( = 50%)

Product	Diseas	e recurrence after 1 v	year of monitoring/	patients	Total	
FIOduct	3 months	6 months	9 months	12 months	TOLAI	
ApiLand <sup>®</sup> Propolis tincture spray (30 patients)	-	-	2p = 6.66%	2p = 6.66%	4p = 13.33%	
Dacia Plant <sup>®</sup> Aloe Vera tincture (30 patients)	-	1p = 3.33%	2p =6.66%	2p = 10%	5p = 16.66%	
Sodium bicarbonate solution (20 patients)	-	2p = 10%	3p = 15%	3p = 15%	8p = 40%	
Distilled water (20 patients)	1p = 5%	3p = 150%	5p = 25%	6p = 30%	15p = 75%	

Table 4. Disease recurrence after 1 year of monitoring

In conformity with the followed outcomes of study, Propolis and Aloe Vera tinctures demonstrated good efficiency in the treatment of AS through alternative medication. The efficacy of both alternative medication has been proven. Healing evolution of patients in the group of ApiLand® Propolis tincture spray was better and faster than in other patient groups. In descending order, the other groups were the Aloe Vera, Sodium Bicarbonate and Distilled Water Groups. The lesions recovery of the patients with sodium bicarbonate solution in the third group of patients was slower than in patients treated with tinctures. Delayed recovery was founded in 4<sup>th</sup> group of patients/Distilled water.

Groups treated with tinctures presented lower recurrence than the other two groups of patients.

No allergic reactions or any other adverse event were detected in any of the studied groups of patients.

The use of both tinctures is an easy and inexpensive alternative therapy that greatly improves cure of the mucosa affected by minor AS.

It is essential to review the patients to assess their progress and response to any treatment instituted, and patients must be aware of the treatment's limitations. The diagnosis and treatment of oral lesions is often challenging, requiring attentive anamnesis, careful clinical examination [2,28].

Propolis tincture has antimicrobial action (bacteriostatic and bactericidal on both Gram positive bacteria and gram negative bacteria), antimycotic (against Candida albicans), antiviral (against Herpes simplex), analgesic, anti-inflammatory, anesthetic, scarring, immunostimulant, antioxidant and mucolytic

actions [29]. The mechanisms of Propolis action on diseases is not fully elucidated [17]. The immunomodulatory activity of Propolis is one of the most studied areas in conjunction with its anti-inflammatory property [30-34]. Anti-inflammatory properties and antibacterial activity of Propolis are due to the interaction between their bioactive constituents, through the interplay of flavonoids, esters and aromatic acids, while the bactericidal action results from the presence of cinnamic acid and coumarin [35-37]. Propolis contains various organic acids, minerals, vitamins (B1, B2, B6, C, E), nicotinic acid, pantothenic acid and aminoacids [38]. Propolis contains elements such as iron and zinc, which are important for the synthesis of collagen [39,40]. The antioxidant properties of Propolis have been studied by many researchers, which ascertained that their use had positive effects on oxidative status and can be used for the alleviation of oxidative stress [41-46]. The antioxidative activity deserves special interest because Propolis could be topically applied successfully to prevent and treat damaged skin [47-49].

Aloe vera contains 75 potentially active constituents: vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids and amino acids [50,51]. Aloe vera mechanisms of action are represented by its healing properties, anti-inflammatory action, effects on the immune system, antiviral and antitumor activity, and antiseptic effect [52-55]. After Babaee et al [56], the effects of Aloe Vera gel on minor AS lesions is considered curative as it decreased the healing time.

Different modalities in the management of minor AS can be used [57-59]. Several authors [60,61] consider that systemic interventions are often reserved for the patients who did not respond to topical treatments of minor AS.

After the research of El-Haddad et al [62], honey was found to be effective and safe in reducing minor aphthous ulcer pain, size, and erythema in a Saudi cohort. Babaee et al [63] constated that myrtle is beneficial in reducing the size of ulcers, the pain intensity and the level of erythema in patients with AS.

There is not enough evidence to support or refute the use of alternative treatments for the therapy of minor AS [64]. Depending upon the response to treatment, the alternative therapies could be trialled [65].

#### Conclusions

- The therapeutic effect of Propolis Tincture was faster than Aloe Vera tincture.
- Reduction of clinical symptomatology, pain degree and recurrence in minor AS lesions were observed in all patients treated with alternative natural products.
- The use of spray form is easier and more comfortable than the rinse solutions.

#### **Conflict of interest:** None to declare.

#### References

- Gonsalves WC, Chi CA, Neville BW. Common Oral Lesions: Part I. Superficial Mucosal Lesions, Am Fam Physician. 2007 Feb 15;75(4):501-6.
- 2. Siu A, Ramos DM, Landon K. Differential diagnosis and management of oral ulcers, Frontline Medical Communications, Semin Cutan Med Surg 2015, 34:171-177.
- Shulman JD, Beach MM, Rivera-Hidalgo F. The prevalence of oral mucosal lesions in U.S. adults: data from the Third National Health and Nutrition Examination Survey, 1988–1994. J Am Dent Assoc. 2004;135:1279–86.
- Santosh AB, Boyd D, Laxminarayana KK. Proposed Clinico -Pathological Classification for Oral Exophytic Lesions, J Clin Diagn Res. 2015; 9(9):ZE01-8.
- Patil S, Rao RS, Majumdar B, Jafer M, Maralingannavar M, Sukumaran A. Oral Lesions in Neonates. Int J Clin Pediatr Dent 2016;9(2):131-8.
- 6. Liang MW, Neoh CY. Oral aphthosis: management gaps and recent advances. Ann Acad Med Singapore. 2012; 41(10):463-70.
- Edgar NR, Saleh D, Miller RA. Recurrent Aphthous Stomatitis: A Review. The Journal of Clinical and Aesthetic Dermatology. 2017;10(3):26-36.

- Alnazzawi AA. Oral diseases associated with fixed prosthodontic restorations. Saudi Medical Journal. 2017;38(3):322-4.
- Mortazavi H, Safi Y, Baharvand M, Rahmani S. Diagnostic Features of Common Oral Ulcerative Lesions: An Updated Decision Tree. International Journal of Dentistry. 2016;2016:7278925.
- Lodi G, Varoni E, Robledo-Sierra J, Villa A, Jontell M. (2017) Oral Ulcerative Lesions. In: Farah C., Balasubramaniam R., McCullough M. (eds) Contemporary Oral Medicine. Springer, Cham, https://link.springer.com/referenceworkentry/10. 1007%2 F978-3-319-28100-1\_12-1#citeas
- 11. Scully C, Gorsky M, Lozada-Nur F. The diagnosis and management of recurrent aphthous stomatitis: a consensus approach. J Am Dent Assoc2003;134:200–7.
- 12. <u>http://www.europarl.europa.eu/cmsdata/135562</u> /ENVI%202017-<u>10%20WS%20CAM%20%20PE%20614.180%20(P</u> ublication).pdf
- 13. https://en.wikipedia.org/wiki/Propolis
- 14. https://draxe.com/bee-propolis/
- 15. <u>https://www.honeycolony.com/article/top-10-health-benefits-of-propolis/</u>
- 16. Wagh VD. Propolis: A Wonder Bees Product and Its Pharmacological Potentials. Advances in Pharmacological Sciences. 2013;2013:308249 doi:10.1155/2013/308249.
- Pasupuleti VR, Sammugam L, Ramesh N, Gan SH. Honey, Propolis, and Royal Jelly: A Comprehensive Review of Their Biological Actions and Health Benefits. Oxidative Medicine and Cellular Longevity. 2017;2017:1259510.
- Mot D, Tirziu E, Nichita E. Study of Bactericidal Properties of Propolis, Animal Science and Biotechnologies, 2014;47(1):256-9.
- 19. <u>https://www.apiland.ro/propolis/tinctura-de-propolis-purificat-95-spray.html</u>
- 20. Di Scala K, Vega-Gálvez A, Ah-Hen K, Nuñez-Mancilla Y, Tabilo-Munizaga G, Pérez-Won M, Giovagnoli G. Chemical and physical properties of aloe vera (Aloe barbadensis Miller) gel stored after high hydrostatic pressure processing, Food Sci. Technol, Campinas.2013;33(1): 52-9.
- 21. Egesie UG, Chima KE, Galam NZ. Anti-inflammatory and Analgesic Effects of Aqueous Extract of Aloe Vera (Aloe barbadensis) in Rats, Afr. J. Biomed. Res. 2011;209 -12.
- 22. Hajhashemi V, Ghannadi A, Heidari AH. Antiinflammatory and wound healing activities of Aloe littoralis in rats. Research in Pharmaceutical Sciences. 2012;7(2):73-8.
- 23. <u>https://www.nutritiv.ro/aloe-vera/tinctura-de-aloe-laxativ-natural-si-antiinflamator-pentru-uz-intern-sau-extern-50-ml-dacia-plant.html</u>

- 24. <u>https://comenzi.farmaciatei.ro/farmacie/afectiuni</u> <u>digestive/constipatie/tinctura de aloe 50 ml d</u> <u>acia plant-p10029693</u>
- 25. Malik Y, Goyal S. Virucidal efficacy of sodium bicarbonate on a food contact surface against feline calicivirus, a norovirus surrogate. International Journal of Food Microbiology. 2006, 109 (1–2): 160-3.
- 26. Rutala WA, Barbee SL, Aguiar NC, Sobsey MD, Weber DJ. Antimicrobial Activity of Home Disinfectants and Natural Products Against Potential Human Pathogens. Infection Control and Hospital Epidemiology. The University of Chicago Press on behalf of The Society for Healthcare Epidemiology of America. 2000;21(1):33–8.
- 27. Zamani M, Sharifi Tehrani A, Ali Abadi AA. Evaluation of antifungal activity of carbonate and bicarbonate salts alone or in combination with biocontrol agents in control of citrus green mold. Communications in agricultural and applied biological sciences. 2007;72(4):773–7.
- Minic I, Pejcic A, Kostic M, Krunic N, Mirkovic D, Igic M. Prevalence of Oral Lesions in Elderly, West Indian Med J. 2016;65(2):375-8.
- 29. <u>https://www.apiland.ro/propolis/tinctura-de-propolis-purificat-95-spray.html</u>
- Tanaka M, Okamoto Y, Fukui T, Masuzawa T. Suppression of interleukin 17 production by Brazilian propolis in mice with collagen-induced arthritis. Inflammopharmacology 2012;20(1)19-26.
- Bachiega TF, Orsatti CL, Pagliarone AC, Sforcin JM. The Effects of Propolis and its Isolated Compounds on Cytokine Production by Murine Macrophages. Phytotherapy Research 2012; doi: 10.1002/ptr.3731.
- 32. Okamoto Y, Tanaka M, Fukui T, Masuzawa T. Brazilian propolis inhibits the differentiation of Th17 cells by inhibition of interleukin-6-induced phosphorylation of signal Propolis: Alternative Medicine for the Treatment of Oral Microbial Diseases transducer and activator of transcription 3. Immunopharmacology and Immunotoxicology 2012; Feb 9. [Epub ahead of print] PMID: 22316079.
- Dimov V, Ivanovska N, Bankova V, Popov S. Immunomodulatory action of propolis: IV. Prophylactic activity against Gram-negative infections and adjuvant effect of the water-soluble derivate. Vaccine 1992;10(12) 817-23.
- 34. Nunes A, Faccioli LH, Sforcin JM. Propolis: lymphocyte proliferation and IFN-g production. Journal of Ethnopharmacology 2003;87(1) 93-7.
- 35. Chang H, Yuan W, Haizhu W, Yin X, Xuan H. Bioactive components and mechanisms of Chinese poplar propolis alleviates oxidized low-density lipoprotein-induced endothelial cells injury, BMC

Complementary and Alternative Medicine. 2018;18:142.

- 36. Santos VR. Alternative Medicine for the Treatment of Oral Microbial Diseases, Chapter 7, cdn.intechopen.com/.../InTech-Propolis\_ alternative medicin.
- 37. Saeed F, Ahmad RS, Umair Arshad M, Niaz B, Batool R, Naz R, Rasul Suleria HA. Propolis to Curb Lifestyle Related Disorders: An Overview, International Journal of Food Properties, 2015;19(2):420-437.
- 38. Ahn MR, Kunimasa K, Ohta T, Kumazawa S, Kamihira M, Kaji K, Uto Y, Hori H, Nagasawa H, Nakayama T. Suppression of tumor-induced angiogenesis by brazilian propolis: major component artepilin C inhibits in vitro tube formation and endothelial cell proliferation. Cancer Letters 2007;252(2):235-43.
- 39. Lustosa SR, Galindo AB, Nunes LCC, Randau KP, Rolim Neto PJ., Própolis: atualizações sobre a química e a farmacologia. Brazilian Journal of Pharmacognosy 2008;18:447-54.
- 40. Borrelli F, Maffia P, Pinto L, Ianaro A, Russo A, Capasso F, Ialenti A. Phytochemical compounds involved in the antiinflamatory effect of propolis extract. Fitoterapia 2002;73(suppl. 1):S53-S63.
- 41. Kocot J, Kiełczykowska M, Luchowska-Kocot D, Kurzepa J, Musik I. Antioxidant Potential of Propolis, Bee Pollen, and Royal Jelly: Possible Medical Application, Oxidative Medicine and Cellular Longevity, vol. 2018;(3):1-29.
- 42. Mujica V, Orrego R, Pérez J, Romero P, Ovalle P, Zúñiga-Hernández J, Arredondo M, Leiva E. The role of propolis in oxidative stress and lipid metabolism: a randomized controlled trial, Evidence-based Complementary and Alternative Medicine, 2017, Article ID 4272940, 11 pages, https://doi.org/10.1155/2017/4272940.
- 43. Li S, Tan H-Y, Wang N, Zang Z-J, Lao L, Wong C-W, Fenf Y. The Role of Oxidative Stress and Antioxidants in Liver Diseases, Piva T. ed., International Journal of Molecular Sciences. 2015;16(11):26087-124.
- 44. Raoa PV, Krishnana KT, Sallehb N, Gan SH. Biological and therapeutic effects of honey produced by honey bees and stingless bees: a comparative review, Brasilian Journal of Pharmacognosy, 2016;26(5):657-64.
- 45. Maciejewicz W. Isolation of flavonoid aglycones from propolis by a column chromatography method and their identification by GC-MC and TLC methods, Journal of Liquid Chromatography & Related Technologies, 2006;24(8)(8):1171-9.
- 46. Kuropatnicki AK, Szliszka E, Krol W. Historical Aspects of Propolis Research in Modern Times. Evidence-based Complementary and Alternative Medicine: eCAM. 2013;2013:9641-9.

- 47. Guo X, Chen B, Luo L, Zhang X, Dai X, Gong S. Chemical compositions and antioxidant activities of water extracts of Chinese propolis. Journal of Agricultural Food Chemistry 2011;59(23):12610-6.
- 48. Messerli SM, Ahn MR, Kunimasa K, Yanagihara M, Tatefuji T, Hashimoto K, Mautner V, Uto Y, Hori H, Kumazawa S, Kaji K, Ohta T, Maruta H. Artepillin C (ARC) in Brazilian green propolis selectively blocks oncogenic PAK1 signaling and suppresses the growth of NF tumors in mice. Phytotherapy Research 2009;23(3):423-7.
- 49. Sudina GF, Mirzoeva OK, Pushkareva MA, Korshunova GA, Sumbatyan NV, Varfolomeev SD. Caffeic acid phenethyl ester as a lipoxygenase inhibitor with antioxidant properties. FEBS 1993; 329(1-2):21-4.
- 50. Leech J. What are the benefits of aloe vera?. Medical News Today. MediLexicon, Intl., 1 Aug. 2017. Web. 19 May. 2018. https://www.medicalnewstoday.com/articles/318 591.php
- Surjushe A, Vasani R, Saple DG. Aloe Vera: A short review. Indian Journal of Dermatology. 2008;53(4):163-6.
- Zawahry ME, Hegazy MR, Helal M. Use of aloe in treating leg ulcers and dermatoses. Int J Dermatol. 1973;12(1):68-73.
- 53. Fulton JE Jr. The stimulation of postdermabrasion wound healing with stabilized aloe vera gelpolyethylene oxide dressing. J Dermatol Surg Oncol. 1990;16(5):460-7.
- 54. Schmidt JM, Greenspoon JS. Aloe vera dermal wound gel is associated with a delay in wound healing. Obstet Gynecol. 1991;78(1):115-7.
- 55. Garnick JJ, Singh B, Winkley G. Effectiveness of a medicament containing silicon dioxide, aloe, and allantoin on aphthous stomatitis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1998;86(5):550-6.
- 56. Babaee N, Zabihi E, Mohseni S, Moghadamnia AA. Evaluation of the therapeutic effects of Aloe vera gel on minor recurrent aphthous stomatitis. Dental Research Journal. 2012;9(4):381-5.

- 57. Subiksha PS. Various Remedies for Recurrent Aphthous Ulcer: A Review, /J. Pharm. Sci. & Res. 2014;6(6):251-3.
- 58. Bardellini E, Amadori F, Conti G, Majorana A. Clinical efficacy of a solution composed by sodium bicarbonate and alginate, aloe vera, propoli, chamomile, calendula and honey, in the treatment of minor recurrent aphthous stomatitis in children, Minerva Pediatr. 2016;68(6):507-9.
- 59. Sabbagh AH, Felemban MF. Therapeutic Management of Recurrent Aphthous Stomatitis: A Review of the Growing, Annals of International Medical and Dental Research, 2014;2(6):1-9.
- 60. Spivakovsky S. Inconclusive evidence on systemic treatments for recurrent aphthous stomatitis. Evid Based Dent. 2012;13(4):120.
- Brocklehurst P, Tickle M, Glenny AM, Lewis MA, Pemberton MN, Taylor J, Walsh T, Riley P, Yates JM. Systemic interventions for recurrent aphthous stomatitis (mouth ulcers). Cochrane Database Syst Rev. 2012 Sep 12; (9):CD005411, doi: 10.1002/14651858.CD005411.pub2.
- 62. El-Haddad SA, Asiri FY, Al-Qahtani HH, Al-Ghmlas AS. Efficacy of honey in comparison to topical corticosteroid for treatment of recurrent minor aphthous ulceration: a randomized, blind, controlled, parallel, double-center clinical trial. Quintessence Int. 2014 Sep;45(8):691-701.
- 63. Babaee N, Mansourian A, Momen-Heravi F, Moghadamnia AA, Momen-Beitollahi J. The efficacy of a paste containing Myrtus communis (Myrtle) in the management of recurrent aphthous stomatitis: A randomized controlled trial. Clinical Oral Investigations, 2010, 14(1):65-70.
- 64. Belenguer-Guallar I, Jiménez-Soriano Y, Claramunt-Lozano A. Treatment of recurrent aphthous stomatitis. A literature review. Journal of Clinical and Experimental Dentistry. 2014;6(2):e168-e174. doi:10.4317/jced.51401.
- 65. Talacko AA, Gordon AK, Aldred MJ. The patient with recurrent oral ulceration, Australian Dental Journal 2010;55:(1 Suppl): 14–22.

#### Corresponding author:

Ilinca Suciu

University of Medicine and Pharmacy of Tirgu Mures, 38 Gheorghe Marinescu street, Tirgu Mures, 540139, Romania Email: suciuilinca10@gmail.com

Received: May 03, 2018 / Accepted: May 29, 2018

# **ORIGINAL PAPER**

# Efficacy of periodontal debridement using an Erbium YAG laser: A scanning electron microscopic study

Alexandra Stoica<sup>1</sup>, Soos Reka<sup>2</sup>, Tudor Hănțoiu<sup>1</sup>

<sup>1</sup> Faculty of Dental Medicine, University of Medicine and Pharmacy of Tirgu Mures, Romania

<sup>2</sup> Postgraduate student, Faculty of Dental Medicine, University of Medicine and Pharmacy of Tirgu Mures, Romania

#### Abstract

The use of lasers during periodontal treatment was encouraged by their ability to remove hard-tissues, without any detrimental thermal effects on the adjacent soft tissues. Numerous studies had demonstrated its ability to ablate hard-tissues, without any detrimental thermal effects such as cracking or melting for the adjacent tissues. The aim of our paper is to compare using the images obtained on scanning electron microscopy, the in vitro effects of Er:YAG laser, sonic, ultrasonic and manual instruments on the root cement during scaling and root planning. We used extracted teeth, divided in four groups, based on the method used for scaling and root planning. The morphological alterations of the root cement were evaluated based on a specific scoring system. We observed noted unfavorable results after using Er:YAG laser, represented by craters and cracks of root cement. There was an increased amount of roughness on the radicular surface after using Er:YAg compared to manual, sonic and ultrasonic methods. Further clinical studies are needed in order to determine the final impact of laser therapy on the healing process of periodontal tissues.

Keywords: scaling and root planning, Erbium laser, root cement morphology.

#### Introduction

Current scientific research has focused on the incorporation of lasers as part of the therapy of periodontal disease. It was proved that the wavelength of different types of units might have a positive effect on both soft and hard tissues healing process consecutive periodontal treatment. Periodontal disease is a multifactorial condition characterized by a microbial etiology and also а host inflammatory component. The contribution of lasers to periodontal health is determined by their antimicrobial, debridement capacity and biostimulation effect [1-3]. The lasers were introduced in periodontology more than 50 years ago, based on the evidence that wounds heal more quickly after irradiation with lowintensity lasers, a process that might be influenced by the stimulation of growth factors. High-intensity lasers were used as part of the nonsurgical periodontal procedures, in comparison with the conventional therapy for cement and soft tissue debridement, especially in order to reduce dentinal hypersensitivity [4]. Laser light has three main characteristics: is monochromatic, directional and coherent. It can be delivered to a tissue area as continuous wave, running pulse mode or gated-pulse mode. The action of lasers on hard and soft dental tissues as well as microorganisms is influenced by the absorption of the laser by tissue chromophore as apatite minerals, water or pigmented substances found at the targeted site [5-7]. Soft tissue lasers proved to give good results in bacterial reduction and coagulation, with erbium group showing a bactericidal effect on Porphyromonas gingivalis and Aggregatibacter actinomycetem comitans. The aim of our study was to evaluate the effectiveness of an Er:YAG laser used during scaling and root planning. It will be compared with the conventional periodontal debridement methods, represented by sonic, ultrasonic and manual instruments and based on images obtained with the scanning electron microscopy, we intend to measure the in vitro effects of Er:YAG laser on the root cement.

#### **Material and methods**

We used 45 human teeth freshly extracted due to complications of dental caries or periodontal disease, which were stored in 4% formalin solution at 4°C. The study was conducted based on principles of the Declaration of Helsinki. As inclusion criteria we used the absence of caries, restorations and no history of periodontal treatment for 6 months prior to extraction.

The teeth were randomly included in one of the four groups and the debridement of the cervical area and coronal third of the root was done with different methods: Group A with ultrasonic instruments (Acteon Satelec®), Group B with sonic instruments (Sirona Siroair®, KaVo Sonicflex®), Group C with manual curettes (Gracey curettes Hu-Friedy® Chicago IL, USA) and Group D with an Erbium Yag Light Walker Laser device. The crowns were prepared for Scanning Electronic Microscopy (SEM) according to a specific protocol. The teeth were washed, dehydrated using increasing concentrations of ethyl alcohol from 70% to 100% and then dryed for 24 hours. They were mounted in copper rings with a diameter of 10 mm and fixed using a fotopolimerized composite resin. Prior to examination the dental surfaces were coated with a 30-40 nm of gold and afterwards evaluated by SEM. The cervical surface of each tooth was evaluated prior and after preparation using a microscope working at 5-10kV (JEOL 5200®, JOEL Corp. Tokyo, Japan) using different magnifications (35X, 100X, 200X, 1000X). The evaluation was carried based on the following a scoring system which measured the roughness and loss of dental hard tissue: 1smooth radicular surface with no tissue lost or



Figure 1. Specimen from group A. Debridement with ultrasonic instruments; uneven radicular surface and mild abrasion of the root cement.

traces of scaling instruments; 2-mild abrasion or uneven spots on the root surface; 3-areas with cement loss; 4-a large part of dental hard tissue is lost and there are traces of debridement instruments. The collected data were statistically analyzed with the Graph Pad Prism® 7.03 and Mann-Whitney test, a value of p <0.05 being considered statistically significant.

#### Results

Each group of teeth received surface examined by SEM received a score according to the scoring system described and the median value for each group was measured The evaluation of dental surfaces from group A, where ultrasonic instruments were used, gave a mean score of 2.31, meaning that there was a complete removal of dental calculus, localized uneven surface and mild abrasion and (figure 1) in group B we used sonic instruments and the mean score after SEM examination was 2.63. There were more pronounced morphological alterations compared with group A, we observed areas with cement loss and remnants of dental deposits (figure 2). The mean score for group C was 1.75, the lowest value recorded in our study. Most aspects were characterized by smooth appearance of the radicular cement, without traces of instruments or tissue loss (figure 3). The last group was treated with an Er:YAG laser and showed the formation of cavities on the radicular surface, with a mean score of 2.52 (figure 4).



Figure 2. Specimen from group B. The use of sonic instruments created areas with cement loss and remnants of dental deposits



Figure 3. Specimen from group C. Smooth appearance of the radicular cement, but rests of dental calculus is visible in the cervical areas.

The statistical evaluation of the scores attributed to each group showed significant differences between group A and B, but no differences between group B and D.



Figure 4. In group D the debridement was performed with an Er:YAG laser; it showed the formation of small cavities on the cement surface

Statistically significant differences we also noted between group C compared to A, B and D (Table 1).

Table 1 Mean values for	the roughness and reat comer	nt loss scores for each study group
TADIE I. IVIEAIT VAIUES IOF	the roughness and root cerner	IL IOSS SCOLES TOLEACH SLUUY BLOUP

Group	Number of specimens	Mean index value	Comparison between groups	P value
A	14	2.31	A-D	p>0.05
В	12	2.63	A-B	p<0.05*
С	12	1.75	B-C	p<0.05*
D	12	2.52	C-D	p<0.05*

\*statistically significant differences (p<0.05)

#### Discussion

During the treatment for periodontal disease, the mechanical procedures were conventionally considered of outmost importance, although a complete elimination of periodontal etiologic factors represented by microorganism and the optimal healing cannot be obtained only through this treatment option [8]. The clean, smooth radicular surface favors the healing process and the regeneration of tooth supporting tissues.

Alongside with chemotherapy and antiinflammatory drugs, phototherapy by using light-emitting diodes and lasers has been combined with other scaling and root planning procedures, for a proper debridement and decontamination; furthermore, to promote

wound healing and tissue stimulation. Most of these pathogens are gram-negative anaerobes and the immune response to these local agents and their toxins is a hyperactive inflammatory reaction [9-11]. This will destroy the epithelial attachment and connective tissue, leading in time to tooth loss. The nonsurgical treatment is represented by periodontal option debridement, aiming to remove microbial biofilm and dental calculus from supra- and subgingival dental surfaces and thus decreasing the inflammatory reactions. Previous studies regarding the use of Er:YAG laser for periodontal debridement had negative results, with the formation of small craters on the root cement [12-15]. We noticed the same aspect, probably due to insufficient water cooling.

Another explanation could be the micro explosions of vapors which increase the pressure inside dental hard tissues. We used extracted teeth, which had less water than natural teeth, a factor that has to be taken into consideration regarding the result of small cavities after laser debridement.

There were no significant differences between group D compared to group A and B, but we noticed an important difference between group A and D. In a SEM study made by Frentzen et al (2002) the amount of cement removed represented up to 22.5% in a group of teeth treated by laser, in comparison to 12.5% in a group of teeth treated by conventional methods [11]. The authors noted a larger volume of cement loss and root roughness when the periodontal debridement was done with Er:YAG laser alone, compared to manual and ultrasonic instruments. These side-effects were seen when the energy was over 50mJ/pulse, even under copious water irrigation. In a study conducted by Ratka-Kruger et al the use of Er:YAG was compared with sound debridement and no significant differences regarding clinical and microbiological parameters between the study groups were found [9]. On the contrary, Yilmaz et al observed that there were important differences in the values of clinical attachment level and reduction of pocket depth in sites treated with Er:YAG laser in addition to scaling and root planning, compared to sites treated only by conventional debridement therapy [3].

A study on extracted teeth conducted by Aoki et al [4] compared different power settings of Er:YAG lasers used during periodontal debridement and observed that removal of dental tissue was restricted to the root cement, which supports the idea of using this instrument during clinical procedures. The total removal of cement in the coronal third of the root could lead the invasion of the underlying dentin by oral microorganisms, with consecutive hypersensitivity or irreversible dental pulp inflammation. Many studies observed that the use of both hand curettes and ultrasonic instrumentation could completely remove the necrotic cement and proper decontamination of allow the periodontal pockets. In ultrasonic scalers, the

tip of the instrument has an elliptical motion being unlikely to remove the calculus uniformly. The defects produced by hand instruments depend on the applied force that can be adjusted by the specialist [14-17]. Compared with the conventional debridement techniques, the Er:YAG laser is one of the most versatile instruments and can be effectively used in periodontal therapy or maintenance phase. The complete mechanical debridement of the periodontal pockets cannot be achieved with conventional instruments; lasers can improve the removal of calculus, granulation tissue and lining epithelium, offering better local healing conditions. The use of laser systems in combination with conventional debridement therapy could be a better future solution for periodontal therapy.

#### Conclusions

Even though the favorable results obtained after periodontal treatment promote the use of lasers, we consider that further studies are necessary in order to determine in which moment of the therapy these methods are best suitable and appropriate. Despite the use of copious water cooling, we noted unfavorable results on the root cement after using Er:YAG laser as craters and cracks induced by heat. There was a greater amount of roughness on the root surface after Er:YAG was used for scaling and root planning compared to manual, sonic and ultrasonic methods.

# **Conflict of interest:** None to declare.

#### References

- 1. Eberhart J, Ehlers H, Falk W, Acil Y, Albert HK, Jepsen S. Efficacy of subgingival calculus removal with Er:YAG laser compared to mechanical debridement. An in situ study. J Clin Periodontol. 2003;30:511-8.
- 2. Ishikawa I, Aoki A, Takasaki AA. Clinical application of erbium:YAG laser in periodontology. J Int Acad Periodontol. 2008;10:22-30.
- 3. Yilmaz S. Er:YAG laser versus systemic metronidazole as an adjunct to non-surgical periodontal therapy: a clinical and microbiological study. Photomedicine and Laser Surgert. 2012;30:325-30.
- 4. Aoki A, Ando Y, Watanabe H, Ishikawa J. In vitro studies on laser scaling of subgingival calculus with

an erbium:YAG laser. J Periodontol. 1994;65:1097-1106.

- Sculean A, Schwarz F, Berakdar M, Romanos GE, Arweiler NB, Becker J. Periodontal treatment with an Er:YAG laser compared to ultrasonic instrumentation. A pilot study. J Periodontol. 2004;75:966-73.
- Aoki A, Mizutani K, Schwartz F, Sculean A et al. Periodontal and peri-implant wound healing following laser therapy. Periodontol. 2000. 2015;68:217-69.
- Solomon SM, Stoleru S, Agop Forna D, Tampu D, Mârțu Stefanache MA, Ursarescu IG, Mârțu S. The quantitative and qualitative assessment of dental substance loss as consequence of root planning by three different techniques. Mater Plast. 2016;53(2):304-7.
- Kellesarian SV, Molignaggi VR, Majoka AH, Al-Kheraif AA, Kellesarian TV, Romanos G, Joved F. Effects of laser-assissted scaling and root planning on the expression of pro-inflammatory cytokines in the gingival crevicular fluids of patients with chronic periodontitis: A systematic review. Photodiagnosis and Photodynamic Therapy. 2017;18:63-77.
- Ratka-Kruger P, Mahl D, Deimling D, Monting JS, Jachmann J, Al-Machot E. Er:YAG laser treatment in supportive periodontal therapy. J Clin Periodontol. 2012;39:483-9.
- 10. Minovska A, Popovska M, Radojkova-Nikolovska V, Cvetanovska Stojceva D, Poposcu E, Forna Agop D.

Study Regarding the Use of Er:YAG Laser for Initial Treatment of Periodontal Disease. Rev.Chim. 2015;66(7):1052-6.

- 11. Frentzen M, Braun A, Aniol D. Er:YAG laser scaling of diseased root surfaces. J of Periodontol. 2002;73:524-30.
- Gupta S, Sawhney A, Jain G, Dhar S, Gupta B, Singh R, Kumar SS, Pathak TS. An evaluation of diode laser as an adjunct to scaling and root planning in the nonsurgical treatment of chronic periodontitis: A clinic-microbiological study. Dent Med Res. 2016;4:44-9.
- 13. Goldstep F, Freedman G. Diode lasers for periodontal treatment: The story so far. J Oral Health. 2009;4:45-6.
- 14. Kawashima H, Sato S, Kishida M, Ito K. A comparison of root surfaces using two ultrasonic scalers. J Periodontal Res. 2007;42:90-5.
- 15. Gokhale SR, Padhye AM, Byakod G, Jain SA, Padbictari V, Shivaswamy S. A comparative evaluation of the efficacy of diode laser as an adjunct to mechanical debridement in periodontal flap surgery: A clinical and microbiological study. Photomed Laser Surg. 2012;30:598-603.
- 16. Petersilka GJ, Flemmig TF. Periodontal debridement with sonic and ultrasonic scalers. Quintessenz J. 2004;4:353-62.
- 17. Goldstep F, Freedman G. Diode lasers for periodontal treatment: The story continues. Aus Dent. 2012;44:56-8.

#### **Corresponding author:**

Alexandra Stoica

University of Medicine and Pharmacy of Tirgu Mures, 38 Gheorghe Marinescu street, Tirgu Mures, 540139, Romania Email: alexandramihaelastoica@yahoo.com

Received: April 30, 2018 / Accepted: May 29, 2018

# **ORIGINAL PAPER**

# The influence of cervical finish line and type of cement on microleakage

Adriana Elena Crăciun<sup>1</sup>, Roxana Vodă<sup>2</sup>, Janosi Kinga<sup>3</sup>, Cerghizan Diana<sup>3</sup>

<sup>1</sup> Tirgu Mureș Emergency Clinical County Hospital

<sup>2</sup> Private practice

<sup>3</sup> Faculty of Dental Medicine, University of Medicine and Pharmacy of Tirgu Mures, Romania

#### Abstract

The appropriate marginal fit of the fixed dentures is required in all the cases, but the appearance of marginal deficiencies is inevitable at the tooth-restoration interface. Besides the improvement of the technological processes, different cements with adequate sealing capacity had been developed in order to minimalize the marginal discrepancies. The most important features of an ideal cement are biocompatibility, sealing capability and caries prevention. Microbial infiltration may be the most critical factor influencing the long-term success of a fixed prosthetic restoration. The aim of this study was to measure the rate of microleakage between tooth and restoration according to the type of finish line and luting agent. Sixty healthy premolars, extracted for orthodontic reason were prepared with chamfer and knife-edge finish line. Full metal crowns were manufactured in a dental laboratory. The luting of dental restorations was done with glass ionomer, zinc phosphate and dual-cured glass fiber reinforced resin. In order to monitor the marginal infiltration rate, methylene blue (1%) was used. The result showed that dual-cured glass fiber reinforced resin has the highest sealing capacity preventing microleakage.

Keywords: microleakage, luting agent, finish line

#### Introduction

The fixed dentures are commonly used in the daily practice to restore and preserve the hard dental tissues. The appropriate marginal fit of these restorations is required in all the cases, but the appearance of marginal deficiencies is inevitable at the toothrestoration interface. The different luting agents used at the cementation of the fixed restorations pretended to seal the gap at the restoration margins and avoid the infiltration of the fluids from the oral cavity followed by microbial invasion into the dental structures. [1]

The inappropriate use of these luting agents in vital teeth results inflammation and necrosis of the pulp, which affects the longevity of the restorations. [1, 2] The microleakage is detected by clinical signs of the chronic dental hypersensitivity and color changes of the abutment at the restoration margins. [3 The water-based cements with a high degree of solubility in the oral cavity, used in the past, served only to "fill" the space between the restoration and the abutment. The twocomponent, powder-liquid systems, were traditionally used to fill the gaps between the tooth and restoration. However, due to their high solubility in the oral fluids, the sealing capacity of these cements depends on the precision of the marginal fit. [4] Numerous studies demonstrated that 100-500  $\mu$ m is the acceptable gap at the tooth-restoration interface regarding the protection against microleakage. [5-7]

Besides the improvement of the technological processes, different cements with adequate sealing capacity had been developed in order to minimalize the marginal discrepancies. The glass ionomer cements are effective, due to their ability to continuously release fluoride ions and also the resin cements through their ability to establish chemical bonds with dental tissues. [4, 8]

The most important features of an ideal cement are biocompatibility, sealing capability and caries prevention. Microbial infiltration may be the most critical factor influencing the long-term success of a fixed prosthetic restoration. [3]

The aim of this study was to measure the rate of microleakage between tooth and restoration according to the type of finish line and luting agent.

#### Material and method

For this study were used sixty healthy premolars, extracted for orthodontic reason.

Prior to tooth preparation, the teeth were immersed in artificial saliva for ninety days. After preparation, the teeth were separated into two groups: thirty teeth with knife edge finish line and another thirty with chamfer finish line. Full metal crowns were manufactured in a dental laboratory. In order to monitor the marginal infiltration rate, methylene blue (1%) was used. To avoid the infiltration of the root surface with methylene blue spacing varnish was applied before crown cementation. For cementation were selected three materials, frequently used in daily practice: glass ionomer, zinc phosphate, and dual-cured glass fiber reinforced resin. Six groups resulted. The cementation was performed in accordance with the manufacturers' indications. For cementation with dual-cured resin were applied tribochemical technic which involves microblasting with silica AlO<sub>3</sub> followed by silanization. After five days the teeth were embedded in transparent autopolymerizing acrylic resin. Each tooth was vertically sectioned mesiodistally with a water-cooled diamond disc. After sections 12 teeth were

compromised so in the final, we achieved six samples with eight teeth each.

All the pieces obtained were photographed with Canon Sx40 HS IS - 12 MPx, optical zoom 35x. All photos were taken at the same ambient light intensity at the same distance using a tripod, and they were placed in the same position. For all photos, the camera was set with the macro option.

In order to evaluate the resistance of the cement to the liquids of the oral cavity, irrespective to the marginal adaptation of the restorations, all the specimens were included in this study, even those with dehiscences bigger than 0.05 mm between the restoration and the tooth.

To measure the infiltration rate, the Digimizer Image Analysis Software® was used. For this purpose, a ruler was used to calibrate the unit of measure (pixels/mm) during shooting. Measurements were made on both halves of the pieces taking into account the highest values obtained. Each measurement was performed three times using their arithmetic mean (Figure 1).



Figure 1. The Digimizer Image Analysis Software®

Statistical analysis: The GraphPad InStat® and NCSS Dowson Edition® software were used. The statistical significance was set at p<0,05. The mean (M) and standard deviation (SD/±) were calculated. The used test was Mann-Whitney.

#### Results

The value obtained after measurements are represented in Table 1.

Table 1. The degree of infiltra	ation (mm)
---------------------------------	------------

Cementing material				
		Glass ionomer	Dual-cured glass fiber reinforced resin	Zinc phosphate
	Knife	2,1887	1,4742	2,9915
		2,1046	1,1678	2,3657
		2,1976	1,005	2,6155
		2,2653	1,2098	2,7896
	edge	2,1807	1,4035	3,0005
line		2,1246	1,1773	2,3743
hsh		2,1771	1,3705	2,7153
of fir		2,1633	1,2098	2,8842
Type of finish line	M	2,173	1,252	2,717
Ţ	(SD) Chamfer	(±0.052)	(±0.152)	(±0.251)
	Chamler	0,2742	-	0,718
		0,2052	0	0,6792
		0,3742	0	0,5473
		0,2652	0	0,62
		0,2742	0,1024	0,5176
		0,2052	0,0987	0,5792
		0,3742	0,2093	0,7042
		0,2652	0	0,7324
	М	0,280 (±0,07)	0,051 (±0,078)	0,637 (±0,082)

As is showed in Table 2 was found a statistical difference between teeth with knife edge finish line based on the cement used for fixation.

Table 2. Difference between teeth with knife edge finish line based on the cement used for fixation.

	p-value
Glass ionomer vs. Dual-cured glass fiber reinforced resin	0,0015
Glass ionomer vs. Zinc phosphate	0,0003
Dual-cured glass fiber reinforced resin vs. Zinc phosphate	0.0009

Statistical difference was also obtained in case of teeth with chamfer finish line (table 3).

Tablel 3. Difference between teeth with chamfer finish line based on the cement used for fixation

	p-value	
Glass ionomer vs. Dual-cured	0,0026	
glass fiber reinforced resin	-,-520	
Glass ionomer vs. Zinc	0,0014	
phosphate		
Dual-cured glass fiber reinforced	0.0008	
resin vs. Zinc phosphate		

The results obtained comparing the degree of infiltration according to the type of finish line and cement used for fixation is represented in Table 4.

Table 4. Degree of infiltration according to the type of finish line

Finish line/Cementing material	p-value
Knife edge vs. Chamfer/Glass ionomer	0,0021
Knife edge vs. Chamfer/Dual- cured glass fiber reinforced resin	0,0008
Knife edge vs. Chamfer/Zinc phosphate	0.0002

#### Discussion

In our study, we have shown that dualcured glass fiber reinforced resin has the highest sealing capacity preventing microfiltration.

Studies have shown that resin-modified cement exhibit adhesion to the tooth, so it provides a superior sealing capacity relative to conventional cement (e.g., zinc phosphate cement). [1,4,9,10] Numerous studies have assessed the sealing capacity of different types of cement in different types of restorations, on different types of teeth prepared with different convergence angles. [11]

Similar results were also obtained in the 2011 year in a study in which was assessed the influence of marginal adaptation and the type of cement used in all ceramic systems on microleakage. In this study, a self-adhesive composite and glass ionomer cement was used as a luting material. The results showed that composite cement showed lower levels of microleakage. [7]

In the study by Reza Eftekhar Ashtiani et al., in which four types of cementing materials have been tested, zinc phosphate cement has been shown to have the lowest resistance in a wet environment, favoring marginal microleakage, as it was demonstrated in our study. [8]

Similar to our results, in a study comparing the degree of infiltration correlated with the type of restoration and the cement used in the fixation, it was demonstrated that, regardless of the type of restoration, all ceramic or metalceramic, the adhesive cementation showed the lowest degree of infiltration compared to zinc phosphate and glass ionomer cement [9]. Another study that used noble alloy crown restoration has shown that the best marginal provides self-adhesive sealing cement compared to glass ionomer and dual composite cement, although no statistically significant differences have been found. [10]

In the in-vivo study, where local changes induced by zinc phosphate and self-adhesive cement were observed in the batch of patients over 38 months, no significant differences were found at the level of the observed parameters (bleeding gingival index, plate index, pulp vitality, etc.). [11]

In a study that considered as parameters the retention, the finish line and the sealing effect of the luting material for all metallic restorations, it was demonstrated that the shoulder and shoulder with bevel provide higher retention than the chamfer, but the finish line and luting material did not affect marginal sealing. [12]

In our study, we have shown that there are significant differences between the marginal preparation, the cement used and the degree of infiltration. Boftino et al. demonstrated that the best adaptation at the cervical level was obtained in the case of a chamfer finishing line compared to the 135<sup>o</sup> angle and rounded shoulder. From the point of view of the influence on the marginal adaptation of the best cement was the zinc phosphate cement followed by the glass ionomer and the resin-based cement. [13]

# Conclusions

- 1. Microleakage is directly influenced by the type of cementing material used.
- 2. Large-scale use of glass ionomer cement for fixation of the dental crown with metallic infrastructure can result in microleakage by solubilizing it in saliva.

3. Most practitioners only use composite cement only in case of cementation of the all-ceramic crown, but it has been shown that they perform a good marginal sealing when are used to cement crown with metallic infrastructure.

#### **Conflict of interest:** None to declare.

#### References

- 1. Qualtrough AJE, Satterthwaite JD, Morrow LA, et al. Principles of operative dentistry, Ed. Blackwell Publishing, 2005, 107-122.
- Rastogi A, Kamble V. Comparative analysis of the clinical techniques used in evaluation of marginal accuracy of cast restoration using stereomicroscopy as gold standard. J Adv Prosthodont 2011;3:69-75.
- 3. Forna N, Popșor S, Mercuț V. Protetică dentară Vol.1, Ed. Univers Enciclopedic, București, 2011, 555-589.
- 4. Jacobsen P, Adams R, Addy M, et al. Restorative Dentistry an Integrated Approach 2-nd edition, Ed. Blackwell Publishing Ltd, 2008, 160-166.
- Shillingburg HT, Hobo S, Whitsett LD, et al. Fundamentals of fixed prosthodontics 3-rd edition, Ed. Quintessence Publishing 131-135.
- Molnar Varlam CS, Szekely MG, Mucenic SG. Materiale dentare, Ed. University Press, 2011 64-72, 89-90.
- 7. Yüksel E, Zaimoğlu A. Influence of marginal fit and cement types on microleakage of all-ceramic crown systems. Braz Oral Res. 2011;25(3):261-6.
- 8. Ashtiani RE, Farzaneh B, Azarsina M, Aghdashi F, Dehghani N, Afshari A, Mahshid M. Microleakage of Four Dental Cements in Metal Ceramic Restorations With Open Margins. Iran Red Crescent Med J. 2015;17(11): e19611.
- 9. Albert FE, El-Mowafy OM. Marginal adaptation and microleakage of Procera AllCeram crowns with four cements. Int J Prosthodont. 2004;17(5):529-35.
- Hooshmand T, Mohajerfar M, Keshvad A, Motahhary P. Microleakage and marginal gap of adhesive cements for noble alloy full cast crowns. Oper Dent. 2011;36(3):258-65.
- 11. Behr M, Rosentritt M, Wimmer J, Lang R, Kolbeck C, Bürgers R, Handel G . Self-adhesive resin cement versus zinc phosphate luting material: a prospective clinical trial begun 2003. Dent Mater. 2009;25(5):601-4.
- Piemjai M. Effect of Seating Force, Margin Design, and Cement on Marginal Seal and Retention of Complete Metal Crowns. Intl J Prosthod. 2001;14(5):412-6.
13. Boftino MA, Valandro LF, Buso L, Özcan, M. The influence of cervical finish line, internal relief, and

cement type on the cervical adaptation of metal crowns. Quintessence IntL . 2007;38(7):425-32.

#### **Corresponding author:**

#### Janosi Kinga

University of Medicine and Pharmacy of Tirgu Mures, 38 Gheorghe Marinescu street, Tirgu Mures, 540139, Romania Email: janosi.kinga@umftgm.ro

Received: April 30, 2018 / Accepted: May 29, 2018

# **ORIGINAL PAPER**

# Possibilities in alleviation of dentin sensitivity in vital abutments

Anamaria Bechir<sup>1</sup>, Violeta Hancu<sup>1</sup>, Gabriela Ciavoi<sup>2</sup>, Doina Lucia Ghergic<sup>1</sup>, Valentin Pribac<sup>3</sup>,

Cherana Gioga<sup>1</sup>, Claudia Florina Andreescu<sup>1</sup>, Farah Curt-Mola<sup>3</sup>

<sup>1</sup> Faculty of Dental Medicine, Titu Maiorescu University of Bucharest, Romania

<sup>2</sup> Faculty of Dental Medicine, University of Medicine and Pharmacy of Tirgu Mures, Romania

<sup>3</sup> Faculty of Medicine and Pharmacy, University of Oradea, Romania

#### Abstract

The preparation of vital abutments, in absence of an adequate management of their vitality, may impose their pulp extirpation.

The aim of this clinical study was to evaluate the alleviation of dentin sensitivity (DS) in vital abutments after the application of desensitizing biomaterials on the exposed dentin surfaces.

The randomized controlled clinical trial included 93 patients (312 vital abutments), divided in three groups. The vital abutments of the first group (30 patients, 102 vital abutments) were protected in-office with Gluma® Desensitizer (Kulzer). The second group of 31 patients (105 vital abutments) used at-home Sensodyne® Advanced Repair & Protect with Novamin™ toothpaste and Sensodyne® Mouthwash for Sensitive Teeth (GlaxoSmithKline). For the alleviation of the dentin sensitivity in the third group (32 patients, 105 abutments), both in-office and at-home desensitizing substances were used, as an associated method. The trial evaluated the DS of vital abutments on the visual-analogue scale (VAS), with range from 0 to 10, in 8 sessions, under cold thermal agent, after the use of desensitizing agents.

The results of the study revealed that DS decreased in all three groups, but the highest rate of desensitization was found in the vital abutments of the third patients group.

The benefits of all desensitizing agents used were confirmed.

**Keywords:** vital abutments, desensitizing agents, desensitization.

#### Introduction

After the preparation of vital abutments, by opening the dentinal tubules the apparition of different degrees of dentin sensibility (DS) can be induced.

Preparation of the teeth for full crowns can induce drying of the dentin, pulpal inflammation or even burn lesions after the reduction of the odontoblastic layer. Clinical researches demonstrated that the preparation of vital teeth for full coverage fixed prosthetic restorations can determine sharp, transient pain as a result of DS [1].

The hydrodynamic theory of dentin hypersensitivity (DHS) suggests that external stimuli determine movements in the fluid of dentin tubules, which induce nociceptive transduction in adjacent pulpal nerve fibers [2-4]. Dentinal tubules contain the odontoblastic processes, which may extend from the pulp to the dentino-enamel junction. The odontoblastic processes are the extensions of odontoblasts and they are surrounded by dentinal fluid inside the dentin tubules. The dentinal fluid is an ultrafiltrate of blood from the dental pulp and represents the

communication between the dental pulp through the odontoblastic layer and the outer regions of the dentin [5,6].

DS is characterized by a short and sharp pain, with a rapid onset. DS occurs after the removal of the protective smear layer, which determines the opening of dentinal tubules and the exposure of the odontoblastic processes to chemical, thermal, tactile or osmotic stimuli [6,7,8]. Great variations were observed in the prevalence of DS, which varies from 4% to 57% [9,11].

Sealing the dentinal tubules represents a current method in decreasing DS [11]. The therapeutic approach of closing the dentinal tubules, in order to impede the fluid shifts from the dentinal tubules, is represented by the application of chemical and mechanical methods in dentin desensitization. Significant advancement in the understanding and in treatment of DH, have been developed, respectively in the use of various methods and desensitizing agents [8,12].

Gluma® Desensitizer is used in-office, for dentin desensitizing [13]. Its formula contains of 5% <u>glutaraldehyde</u> and 35% HEMA (hydroxyethyl methacrylate) in purified water [14]. Its effect is obtained by the precipitation of plasma proteins, which determine the reduction of dentinal permeability, the occlusion of the peripheral dentinal tubules and the inhibition of the flow of fluid from the dentinal tubules. It is indicated in cases of pain in thermal, osmotic or tactile stimuli [15]. Indications of Gluma® Desensitizer are related with the reduction/elimination of pain in exposed cervical areas of teeth crowns that not require restoration and do the reduction/elimination of dentin sensitivity after the preparation of teeth for fixed prosthetic restorations [16].

At-home desensitizing agents include toothpastes or mouthwashes, which act by occluding the dentinal tubules or by blocking the neural transmission [6]. Sensodyne® toothpaste uses one of the two main ingredients for treating DS: potassium nitrate and stannous fluoride. Potassium nitrate acts by numbing the pain by soothing the prolongations of pulp nerves. Stannous fluoride acts by closing the open dentinal tubules by forming a protective barrier and heaving remineralization properties. Both methods are effective ways to treat sensitivity, and Sensodyne® features a range of toothpastes using each ingredient [17]. Sensodyne® Repair and Protect toothpaste (GlaxoSmithKline), contains stannous fluoride and is used for decreasing occasional DS in sensitive teeth exposed to hot or cold substances. Sensodyne® Repair and Protect advanced Novamin<sup>TM</sup> Toothpaste with calcium formula (GlaxoSmithKline), is different from other Sensodyne® toothpastes with its desensitizing technology, acts as a reparative layer over the exposed dentine and on the natural crystals of the teeth structure, and contains Sodium Monofluorophosphate 1.08% w/w (1450 ppm fluoride) [18,19]. Sensodyne® Oral Care for Sensitive Teeth Mouthwash (GlaxoSmithKline), contains potassium chloride which prevents pain due to sensitive teeth [20].

Visual analogue scale (VAS) is a measurement instrument for epidemiologic studies and clinical researches, and measures the intensity /frequency of different symptomatology in mature populations. The VAS for pain survey is a single-item scale which studies the pain intensity and is comprised between "no pain" (score of 0) and "pain as bad as it could be" (score of 10) [21-23].

The purpose of the clinical study was to evaluate the alleviation of dentin sensitivity (DS) in vital abutments after the application of desensitizing agents on the exposed dentin surfaces. The null hypothesis of study was that the effectiveness of used desensitizing agents would not be different in reducing DS.

## Materials and methods

The clinical trial was accomplished according to the good practice and the ethical principles. The participating dentists followed trainings in order to assure consistency of clinical examination, diagnosis and treatments. The clinical trial was conducted during the period of 2015-2017, in the Dental Clinics of Dental Medicine Faculties.

The patients were selected after a detailed anamnesis, were informed about the research requirements, and were attended only by those that entered voluntarily in the research program. The selection of the patients was performed after the completion of all dental, periodontal and proprosthetic treatments.

The inclusion criteria in this clinical trial were represented by following patients: healthy adults demonstrating good general health with no history of chronic illness; age range of 36vears; different classes of partial 55 edentations, which necessitate restoration by bridges, but without acute or chronic dental or/and periodontal sensitivity/pain; capability willingness to effectuate in-office and desensitization; brushing teeth at least 2 times a day for 5 minutes and cleaning the oral cavity with desensitizing agents used in the study; established DS diagnosis after the abutments preparation.

The exclusion criteria were represented by the patients: which received odontal or/and periodontal treatments within the period of the trial; bridge abutments with extended dental hard tissue lesions; participants with antiinflammatory treatment due to medical problems; adverse effects/intolerances/ allergic reactions at the used desensitizing agents; acute or chronic, general or dental diseases (e.g. gastritis, digestive ulcer, gastrointestinal haemorrhages, liver- and renal disturbances, etc.) in personal history; use of a desensitizing agent in the 3 months prior to the study; being pregnant or nursing.

The selected patients signed the written informed consent prior to the beginning of the research. Out of 99 eligible patients, the number of patients participating in the study until the end of the research was 93. The 6 dropout patients were not included in the final results. The mean ( $\pm$ SD) of selected patients' age was 45.5  $\pm$  9.5 years. We noticed that the prevalence of females in the analysed batches was 60.21% (56 females of 93 participants) and of male patients was 39.78% (37 males of 93 participants).

This randomized controlled clinical trial compared the effectiveness of Gluma® Desensitizer, Sensodyne® Repair and Protect Toothpaste with advanced Novamin<sup>TM</sup> calcium formula and Sensodyne® Oral Care for Sensitive Teeth Mouthwash in DS reduction.

The clinical protocol used for all the selected patients consisted by the sanitation of the oral cavity, preparation of the vital teeth for mixed metal-ceramic restorations in proper conditions (grinding by cooling with water, with proper rotary diamond instruments, without excessive pressure, etc.), application of desensitization agents, impression, training the patient to ensure proper oral hygiene and the list with indicated beverages. The in-office method for desensitization involved gentle cleaning of vital abutments, rinsing with water, isolation and gentle drying of vital abutments, application of Gluma® desensitizing agent on the vital abutments strictly on the area to be protected by using pellets or brushes, it's maintaining for 30-60 seconds, rinsing. For the use at-home of desensitizing agents, we gave the patients Sensodyne® toothpaste, tooth brush and mouthwash, and the written instructions regarding their at-home use. The determinations of DS intensity in vital

abutments were realized by the patient's response to air-blast stimuli, applied with the air syringe of the dental unit, for 3 s, at a distance of 2mm from the cervical area of labial/buccal surfaces. The temperature was of 22°C. The neighbouring teeth were protected with dental gauze and/or the operator's hand. Patients were then asked about the level of sensitivity they experienced.

The selected patients were randomized by the lottery method in three batches:

- The first batch (G) of 102 vital abutments (30 patients, 19 females and 11 males), were in-office protected with Gluma® Desensitizer (Kulzer), 5 daily applications; the first application was realized after the preparation of vital abutment and the impression, and the last application before the insertion of final prosthetic restoration on the abutments.
- The second batch (S) of 105 vital abutments (31 patients, 19 females and 12 males) were at-home protected with Sensodyne® Advanced Repair & Protect with Novamin<sup>TM</sup> toothpaste and Sensodyne® for Sensitive Mouthwash Teeth (GlaxoSmithKline), performed twice a day, in the morning and evening, for 5 days.
- The third batch (G+M) of 105 vital abutments (32 patients, 18 females and 14 males) benefited by the associated in-office with Gluma<sup>®</sup> Desensitizer (5 applications, effectuated daily), and at-home protection, with Sensodyne<sup>®</sup> Advanced Repair & Protect with Novamin<sup>™</sup> toothpaste and Sensodyne<sup>®</sup> Mouthwash for Sensitive Teeth (performed twice a day, in the morning and evening, for 5 days).

The patients were monitored during the period of 2012-2018 in the Dental Clinics of the Dental Medicine Faculties.

The distribution of the patients in batches, by the used desensitising agents and gender is depicted in graph 1.



Graph 1. Distribution of patients in batches, by used desensitizing agents and gender

The duration of the clinical trials assessing the efficacy of the desensitizing agents was developed in 8 sessions, for 3 months: first assessment of patients (baseline) was effectuated after the preparation of vital abutments and the impression; 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup>, and 5<sup>th</sup> assessments, before the application of Gluma® desensitizer; 6<sup>th</sup> assessment before the insertion of the bridges on the vital abutments (the 7<sup>th</sup> day after the baseline); 7<sup>th</sup> assessment 2 weeks later;  $8^{th}$  assessment 3 months after the baseline. The trial evaluated on the visualanalogue scale (VAS), with range 0–10. The reference points used in our study were: VAS 0-1 = no pain; VAS 2-3 = mild pain; VAS 4-5 = moderate pain; VAS 6-7 = severe pain; VAS 8-9 = very severe pain; VAS 10 = the most intense pain possible. The VAS scale used in this study is presented in figure 1.



## Results

The intensity of DS determined after the application of desensitizing agents is summarized in table 1.

The values highlight the fact that the reported DS in the vital abutments decreased as following:

- In the Ist batch (G) of in-office desensitization, in the first assessment the maximum "severe pain" (VAS = 10) was reported in 4 vital abutments (= 3.92%), in the 5th assessment and in the 8th assessment, the minimum "no pain", VAS = 0-1, was found in 42 (= 41.17%), respectively in 92 vital abutments (= 90.19%).
- In the IInd batch (S) of at-home desensitization, in the first assessment the maximum "severe pain" (VAS = 10) was reported in 5 vital abutments (= 4.76%), in the 5th assessment and in the 8th assessment, the minimum "no pain", VAS = 0-1, was found in 30 (= 28.57%), respectively 80 vital abutments (= 76.19%).
- In the IIIrd batch (G+S) of in-office and athome desensitization, in the first assessment the maximum "severe pain" (VAS = 10) was reported in 5 vital abutments (= 4.76%), in the 5th assessment and in the 8th assessment, the minimum "no pain", VAS = 0-1, was found in 49 (= 46.66%), respectively 101 vital abutments (= 96.19%).

• In the 7th, and 8th assessments, vital abutments of all 3 batches presented a visible decreasement of DS, due to the

protection offered by the cemented restorations on their surface.

Batch	I <sup>st</sup> Batch Gluma <b>®</b>						II <sup>nd</sup> Batch Sensodyne <b>®</b> (S)						III <sup>rd</sup> Batch G+S					
	Desensitizer (G) 30 patients,						31 patients, 105 vital						32 patients, 105 vital					
	102 vital abutments						abutments						abutments					
VAS	0-	2-	4-	6-	8-	10	0-	2-	4-	6-	8-	10	0-1	2-	4-	6-	8-	10
	1	3	5	7	9		1	3	5	7	9			3	5	7	9	
1 Ass	-	-	42	48	8	4	-	-	44	48	8	5	-	6	61	35	3	5
2 Ass	2	18	42	35	3	4	1	13	39	41	7	4	6	32	32	30	2	3
3 Ass	6	34	42	15	2	3	2	24	36	35	4	4	19	42	29	11	2	2
4 Ass	35	37	20	6	2	2	21	26	31	21	2	4	42	42	15	4	1	1
												F						
5 Ass	42	36	16	4	2	2	30	33	23	13	2	4	49	41	11	2	1	1
						F						F						
6 Ass	62	28	6	3	1	2	49	33	11	7	1	4	71	27	4	1	1	1
						F						F						F
7 Ass	81	21	-	-	-	2	68	24	9	-	-	4	92	12	-	-	-	1
						F						F						F
8 Ass	92	8	-	-	-	2	80	21	-	-	-	4	101	3	-	-	-	1
						F						F						F

Table 1. Reported DS according to used Visual Analogue Scale (VAS)

\*Ass = assessment

We emphasize the fact that after the 5<sup>th</sup> assessment, the fixed prosthetic restorations were cemented temporarily on the vital abutments. According to the quantified responses on the VAS scale, the insertion and cementation of restorations determined the reduction of the painful intensity in the investigated vital abutments.

We also underline that VAS values were the lowest in the patients of the III<sup>rd</sup> batch (G+S), thus patients who received associated in-office and at-home desensitization, followed by VAS values of the I<sup>st</sup> batch of patients (G), which benefited only by in-office desensitization. VAS values in the II<sup>nd</sup> batch (S) with only athome desensitization, were higher than in the other two batches. The yellowish color of the boxes in table 1 indicate the maximum number of vital abutments, and the pink color of the boxes emphasizes the number of vital abutments which have required endodontic treatment.

The rate of failures in the batches (graph 2) was as following:

- In the I<sup>st</sup> batch (Gluma<sup>®</sup>, G) = 1.96%, and
  2 vital abutments of 102 required vital extirpation.
- In the II<sup>nd</sup> batch (Sensodyne®, S) = 3.80%, and 4 vital abutments of 105 have imposed their vital extirpation.
- In the III<sup>rd</sup> batch (G+S) = 0.95%, and only 1 vital abutment of 105 needed endodontic treatment.



Graph 2. Rate of failures in batches of vital abutments

The results of the study revealed that DS decreased in all three groups, but the highest rate of desensitization was in the vital abutments of the third patients group, with in-office and at-home desensitization.

We recorded no side effects in the use of desensitizing agents.

## Discussion

Maintaining vitality of the pulp has the purpose to keep and treat the functionality of dental pulp tissues [24]. The treatment of dentinal wounds in vital abutments is different versus the resulting wound of a cavity preparation, because the varnishes and the liners used in cavities are covered and protected by the temporary or permanent fillings. The same materials, used for the protection of vital abutments, are dissolved by the oral fluid, and they will prejudice the quality of permanent cementation of fixed prosthetic restoration.

In their researches, Jackson et al [25], show that 5.7% of 603 analysed vital abutments required root canal therapy after the prosthetic restorations were cemented.

Goodacre et al [26] identified the incidence of complications associated with single crowns and fixed prosthetic restorations and the need for endodontic treatment appeared to be situated between in 3%-11%, by the type of prosthetic restoration used to restore the functionality of oro-facial system. Favourable conditions for the healing of the pulp tissues after oral exposure demand a free of bacteria environment, absence of severe haemodynamic changes and absence of severe inflammatory cell infiltration. The degree of the defence reaction is in interdependence with the healing answer of the dental pulp tissues or with the extension of pulp inflammation [27].

Requirements of actual biomedical researches are to find new possibilities in recovering the dentin-pulp complex. Regenerative treatment in mild dentin lesions is applied to stimulate the constitution of peritubular dentin, to have effect in biosynthetis activity of odontoblasts, and to provide their survival [28].

Schüpbach et al [29], demonstrated that the glutaraldehyde of Gluma® desensitizer can intrinsically obturate the dentinal tubules by the genesis of deposition , which may counteract the hydrodynamic mechanism of dentin sensitivity.

The literature underlines that Gluma® Desensitizer components react with the albumin serum of the dentinal liquid, precipitate the protein, and that induces polymerization of HEMA. Gluma® Desensitizer has proven to penetrate the exposed dentinal tubules up to 200µ depth, which induces the restructuration of collapsed collagenous fibbers, the apparition of multiple layers of protein septas, the hermetic sealing of dentinal tubules, and through that, acts as a microbial barrier, and inhibit bacterial growth (figure 2) [30-33].



Figure 2. SEM of Gluma Desensitizer action: A. Gluma<sup>®</sup>-induced septa in dentinal tubuli; B. SEM magneification of a single Gluma<sup>®</sup>-induced speptum in dentinal tube [34]

Sensodyne<sup>®</sup> repair and protect toothpaste which contains Novamin<sup>TM</sup> desensitising and concentrated calcium which is activated in contact with saliva, helps in repairing the exposed dentine by building protective mineral layers over the sensitive areas [22].

The researches of Wang et al [35], respectively Zhong et al [36] demonstrated that

the use of new Novamin bioglass-containing Sensodyne toothpaste decrease the permeability and seal the dentinal tubules after teeth brushing.

In order to prevent the stimulation of the area with DS, patients have the tendency to avoid cleaning those teeth, particular drinks and food of their nourishment [37,38]. This attitude induces a vicious circle, which, unfortunately, often has an unpleasant end, represented by the loss of vitality of those teeth / vital abutments, and thus the failure of the therapy for maintaining the pulp organ vitality.

For a valuable management of DS condition, dentists should be open not only in DS detection, but also in the necessity of pertinent and correct diagnosis, for elimination of confounding factors from other oro-facial pain conditions [41].

Currently there are a lot of biomaterials for in-office or/and at-home use in reducing the DS, but none of the products represent the "gold standard" in the long term therapy of pulp vitality maintenance [39,40].

## Conclusion

- The benefits of the desensitizing agents used in the study was confirmed.
- The least invasive and cost effective therapy in the maintenance of pulp tissue vitality is represented by the use of desensitizing agents, both in-office and at-home.
- Controlled clinical trials and multicenter studies are necessary for implementation athome use of the desensitizing agents in their daily utilization.

## **Conflict of interest:** None to declare.

#### References

- 1. Yadav K, Sofat A, Gambhir RS, Galhotra V. Dentin hypersensitivity following tooth preparation: A clinical study in the spectrum of gender. Journal of Natural Science, Biology, and Medicine. 2014;5(1):21-24.
- 2. Brännström M: A hydrodynamic mechanism in the transmission of pain-produced stimuli through the dentine; in Anderson DJ (ed): Sensory mechanisms in dentine. New York: Pergamon Press; 1963, P. 73-79
- 3. Brännström M: The sensitivity of dentine. Oral Surg Oral Med Oral Pathol. 1966;21:517-526
- 4. Gysi A. An attempt to explain the sensitiveness of dentin. Br J Dent Sci. 1900;43:865-868

- 5. Orchardson R, Cadden SW. An update on the physiology of the dentine-pulp complex. Dent Update. 2001;28(4):200-6, 208-9.
- Miglani S, Aggarwal V, Ahuja B. Dentin hypersensitivity: Recent trends in management. J Conservative Dent. 2010;13(4):218-224.
- 7. Addy M., Dowell P., Dentine hypersensitivity--a review. Clinical and in vitro evaluation of treatment agents. J Clin Periodontol. 1983;10(4):351-63.
- 8. Davari A, Ataei E, Assarzadeh H. Dentin Hypersensitivity: Etiology, Diagnosis and Treatment; A Literature Review. J Dent. 2013;14(3):136-145.
- 9. Splieth CH, Tachou A. Epidemiology of dentin hypersensitivity. Clin Oral Investig. 2013;17(Suppl 1):S3-8.
- 10. Rees JS, Addy M. A cross-sectional study of dentine hypersensitivity. J Clin Periodontol. 2002;29:997–1003
- 11. Cartwright RB. Dentinal hypersensitivity: a narrative review. Comm Dent Health. 2014; 31(1):15-20.
- Parolia A, Kundabala M, Mohan M. Management of dentinal hypersensitivity: a review. J Calif Dent Assoc 2011;39:167–179
- 13. <u>https://www.dentistryiq.com/articles/2011/09/herae</u> <u>us-gluma-desensitizer.html</u>
- 14. <u>http://kulzercn.com/media/webmedia\_local/china/h</u> <u>kcn/sm/dentistry\_1/Sci-Info\_Desensitizing.pdf</u>
- 15. <u>https://www.kulzerus.com/media/webmedia local/d</u> <u>ownloads new/gluma 5/gluma desensitizer 2/GBA</u> <u>Gluma Desensitizer INT.pdf</u>
- 16. <u>https://www.kulzer.gr/media/webmedia\_local/downl</u> oads\_new/gluma\_5/gluma\_desensitizer\_2/GLUMA\_ Desensitizer\_Sellsheet\_GB.pdf
- 17. <u>https://us.sensodyne.com/why-sensodyne/how-does-sensodyne-work/</u>
- 18. <u>https://us.sensodyne.com/products/repair-and-protect-toothpaste/</u>
- 19. <u>http://www.expresschemist.co.uk/sensodyne-repair-and-protect-75ml.html</u>
- 20. <u>https://www.amazon.com/Sensodyne-Mouthwash-</u> <u>Sensitive-Teeth-European/dp/B009GA40UG</u>
- 21. Hawker GA, Mian S, Kendzerska T, French M., Measures of Adult Pain. Arth Care & Res. 2011;63(S11):S240 –S252.
- 22. McCormack HM, Horne DJ, Sheather S. Clinical applications of visual analogue scales: a critical review. Psychol Med 1988;18:1007–19
- 23. Jensen MP, Karoly P, Braver S. The measurement of clinical pain intensity: a comparison of six methods. Pain 1986;27:117–26
- 24. Ghoddusi J, Forghani M, Parisay I. New Approaches in Vital Pulp Therapy in Permanent Teeth, Iranian Endodontic Journal. 2014;9(1):15-22.
- 25. Jackson CR, Skidmore AE, Rice RT. Pulpal evaluation of teeth restored with fixed prostheses, J. Prosth. Dent. 1992;67(3):323-5.
- 26. Goodacre CJ, Bernal G, Rungcharassaeng K, Kan JZK. Clinical Complications in Fixed Prosthodontics, J. Prosth. Dent. 2003;90(1): 31-41.

- Farges J-C, Alliot-Licht B, Renard E, et al. Dental Pulp Defence and Repair Mechanisms in Dental Caries. Mediators of Inflammation. 2015; 2015: 230251. doi:10.1155/2015/230251
- 28. Cooper P.R., Holder M.J., Smith A.J., Inflammation and regeneration in the dentin-pulp complex: a double-edged sword. J Endod. 2014;40(4 Suppl):S46-51.
- 29. Schüpbach P, Lutz F, Finger W, Closing of dentinal tubules by Gluma desensitizer. Eur J Oral Sci. 1997;105(5):414-21
- 30. Ishihata H, Finger Wj, Kanehira M, et al. In vitro dentin permeability after application of Gluma® desensitizer as aqueous solution or aqueous fumed silica dispersion. J Appl Oral Sci. 2011;19(2):147-153.
- Yilmaz NA, Ertas E, Orucoğlu H. Evaluation of Five Different Desensitizers: A Comparative Dentin Permeability and SEM Investigation In Vitro. The Open Dent J. 2017;11:15-33.
- 32. Kim SY, Kim EJ, Kim DS, et al. The evaluation of dentinal tubule occlusion by desensitizing agents: a real-time measurement of dentinal fluid flow rate and scanning electron microscopy. Oper Dent. 2013;38(4):419-28.
- 33. <u>https://www.kulzer.com/en/int/dentist/products\_from\_a\_to\_z/gluma\_2/gluma\_desensitizer.aspx</u>

- 34. <u>https://www.kulzer.com/en/int/dentist/products\_from\_a\_to\_z/gluma\_2/gluma\_desensitizer.aspx</u>
- 35. Wang Z, Sa Y, Sauro S, et al. Effect of desensitising toothpastes on dentinal tubule occlusion: a dentine permeability measurement and SEM in vitro study.J Dent. 2010;38(5):400-10.
- 36. Zhong Y, Liu J, Li X, et al. Effect of a novel bioactive glass-ceramic on dentinal tubule occlusion: an in vitro study. Aust Dent J. 2015;60(1):96-103.
- 37. Bissada NF. Symptomatology and clinical features of hypersensitive teeth. Arch Oral Biol1994;39:31S–32S
- 38. Chen CL, Parolia A, Pau A, et al. Comparative evaluation of the effectiveness of desensitizing agents in dentine tubule occlusion using scanning electron microscopy. Aust Dent J. 2015;60(1):65-72.
- 39. Gillam D.G., Current diagnosis of dentin hypersensitivity in the dental office: an overview. Clin Oral Investig. 2013;(17)( Suppl 1):S21-9.
- 40. Talioti E, Hill R, Gillam DG. The Efficacy of Selected Desensitizing OTC Products: A Systematic Review. ISRN Dentistry, vol. 2014, Article ID 865761, 14 pages, 2014. https://doi.org/10.1155/2014/865761

#### Corresponding author:

Valentin Pribac

University of Medicine and Pharmacy of Tirgu Mures, 38 Gheorghe Marinescu street, Tirgu Mures, 540139, Romania Email: valentin.pribac@gmail.com

Received: April 26, 2018 / Accepted: May 25, 2018

# **CASE REPORT**

# Prosthodontic rehabilitation of a patient with osteoporosis and bisphosphonates treatment

Ciprian-Emanuel Rusu<sup>1</sup>, Serfözö Norbert Erich<sup>1</sup>, Andrei Petruț<sup>1</sup>, Carmen Biriș<sup>1</sup>, Claudiu Horga<sup>1</sup> Faculty of Dental Medicine, University of Medicine and Pharmacy of Tirgu Mures, Romania

## Abstract

The oral rehabilitation of a patient with osteoporosis and bisphosphonates treatment represents a challenge involving the terapeutical decisions of the dental practitioner, due to the high risk of osteonecrosis, which occurs in surgical procedures like dental implants and bone graft substitutes. The main direction in these cases includes minimal invasive dental solutions like fixed and removable dental prostheses, which achieve aesthetic and masticatory function. **Keywords:** osteoporosis, bisphosphonates, oral rehabilitation.

## Introduction

Teeth are fundamental to the quality of life throughout the human existence [1]. An association between tooth loss and osteoporosis has been reported in the literature. Women with osteoporosis are three times more likely to experience tooth loss than those who do not have the disease [2,3].

Osteoporosis as described by World Health Organization (WHO) is a progressive systemic skeletal disease characterised by low bone mass and micro architectural deterioration of the bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. The main treatment of osteoporosis involves the use of Bisphosphonates (BPs) to improve bone density and new bone growth. BPs act on macrophages in the blood reducing their life span and causing morphological alterations and changes in differentiation of monocytes into macrophages. This reduces the body's ability to defend against pathogens [4].

The action mechanism of BP is based on the inhibition of the farnesyl diphosphate synthase enzyme (FPPS), which in turn stimulates isoprenylation of small guanosine-5'-triphosphatases (GTPases), which signals proteins that activate and regulate changes in osteoclast morphology [5].

There have been studies with a low level of specificity and many of them with a small number of clinical cases or a poorly defined control group that cannot suggest a direct link between BPs and implant failure. Therefore, the BPs effect on implant ostointegration is not well established [6].

Subclinical hypothyroidism (SCH) is defined by the presence of serum free thyroxine levels (FT4) and triiodothyronine (FT3), within reference limits, in the presence of thyroid stimulating hormone (TSH) levels [7]. There is evidence to suggest that subclinical hypothyroidism is also linked to dyslipidemia and osteoporosis [8]. It is diagnosed based on symptoms and clinical signs associated with low thyroid stimulating hormone (TSH) levels [9]. There are studies that confirm the association of low levels of TSH with bone demineralization and alteration of trabecular bone structure. [10,11].

Patients with SCH can present with anxiety, irritability, poor concentration, slow information processing, and poor learning in comparison to healthy subjects [12].

Psychiatric illnesses such as anxiety, bipolar disorder or depression, as well as the medication associated with these diseases can reduce salivary secretion <u>to</u> the appearance of xerostomia [13].

In these clinical situations, associated with poor economic and social conditions, conventional prosthetic treatment is often preferred and can include crowns, bridges, inlays, onlays, veneers or conventional dentures or overdentures.

## **Case Report**

A 62-year-old female patient, with poor social condition, came to the Integrated Centre

of Dental Medicine, University of Medicine and Pharmacy of Tirgu Mureş with worn out upper jaw fixed bridges on a metal framework with acrylic veneers and a class II/1 Kennedy edentation treated partially with a fixed bridge in the lower jaw. Her general medical history bipolar schizophrenic disorders showed diagnosed 23 vears ago, diagnosed osteoporosis, hyperlipidemia and nodular goiter in the left lobe, associated with a suspected diagnosis of hypothyroidism. The patient was treated with BPs for osteoporosis and completed the treatment one month before checking in for dental treatment. In addition, the patient is prescribed antipsychotic 900mg/dav. (valpronic medication acid risperidone 4mg/day, venlafaxine 225mg/day and alprazolam 0.5 mg/day)and antihyperlipidemic drugs (atorvastatin 20mg/day and fenofibrate 145mg/day). Blood tests confirm hyperlipidemia (cholesterol 280 mg/LDL cholesterol 195 mg/dl, triglyceride 242 mg/dl in serum) and a subclinical hypothyroidism diagnosis is susggested (anti-TSO 1.1 IU/ml, cortisol 11.1µg/dl, FT40, 86 ng/dl). The ultrasonographic examination of the thyroid revealed the presence of a welldefined 10.3/11.1 mm node in the left lobe. Thyroid biopsy showed a smear with atypia of undetermined significance. CT scanning in the conical fascicle (CBCT) showed moderate bone demineralization and a tender bone in the mandible was acceptable from a dimensional point of view.

After the clinical (figure 1A and 1B) and radiological examination (figure 2), the remaining teeth had multiple carious lesions. In the upper jaw, the teeth were previously treated with multiple single crown restorations and a fixed bridge. In the lower jaw the patient had a fixed bridge extended from 4.3 to 4.7. All prosthetic elements had a metal base framework with acrylic veneers.

The initial orthopantomography shows the presence of multiple carious lesions involving several teeth on the arch, periodontal disease, incorrect endodontic obturations and bone resorption. Initial impressions were taken with hydrocolloids. irreversible The oral rehabilitation was started with the buildup of the frontal area with nanohybrid composite fillings. Root canal retreatment of 1.6, 2.5, 1.4, 2.4 was performed with a rotatory system using ProTaper<sup>®</sup> Gold and the root canals were then obturated with AdSeal® sealer and guttapercha points condensed laterally.

The old fillings have been removed and they were replaced with nanohybrid composite fillings (figure 3 A, B).



Figure 1. A- Initial clinical appearance; B-details



Figure 2. Initial orthopantomography



Figure 3. A-appearance of the teeth after cavity preparation; B- aesthetic composite restorations in the front

The following treatment option was suggested and discussed with the patient during the following visits:

- Removal of all fixed dental prosthetics in the upper jaw, treatment of the carious lesions and replacement with the following (figure 4):
- fixed dental bridge from 1.4 to 1.7 with a metallic framework with ceramic veneers,
- single crown restorations from 2.4 to 2.7 with the same materials as previously mentioned,
- aesthetic composite restorations in the frontal teeth.



Figure 4. Final status on the maxilla

Removal of the fixed dental bridge in the lower jaw and replacement with a removable partial denture (RPDs) specially fixed on OT-CAP® systems united by a rigid Dolder bar (figures 5-8). For better stability a clasp on 3.3 was advised. We advised OT-CAP® systems on the teeth 4.3 and 4.7 and a clasp on 3.3 resulting from the skeletal prosthesis. For the lower jaw a removable partial denture was made for better stability and a metal clasp was added on the 3.3 for extra reinforcement. The fixed prosthetic elements were adhesively attached to the prepared tooth surfaces with glass ionommer cement.

All the decisions have been made to enhance aesthetics and functionality in the maxillar and mandibular jaw.



Figure 5. intraoral view of the OT-CAP® system



Figure 7. Intraoral View of the finished prosthetic rehabilitation in the lower jaw

## Discussion

The use of dental implants is becoming more common in modern dentistry, but fear of surgery is at elevated levels [14]. Therefore, the possibility of inserting dental implants into the mandible was evaluated in terms of the patient's psychiatric and dismetabolic diseases. The diagnosis of osteoporosis and BPs treatment has also been taken into account. For these reasons and in agreement with the patient, conventional prosthetic treatment was considered, although the satisfaction of RPDs wearers is low due to alteration of oral functions, pains and injuries in the tissues [15].

A 10-year longitudinal study which was carried out on 27 patients treated with RPDs showed that no significant deterioration of the periodontal status of the remaining teeth. In addition, there was a low increase in the frequency of decayed and filled tooth surfaces [16].

Another study showing the success rate of clasp retained removable partial dentures determined that this type of rehabilitation has a 36,6% success rate, 23,8% partial success rate



Figure 6. Jaw relation recording



Figure 8. Final result of the oral rehabilitation

and 39,6% were casted as failures on a 10-year retrospection. This study was carried out on 72 patients [17].

The terapeutical decision of removable partial dentures was motivated by a number of case report studies showing bisphosphonate related osteonecrosis of the jaw when performing dental implants. It was reported that the incidence rate of Bisphosphonate Related Osteonecrosis of the Jaw (BRONJ) in patients taking bisphosphonates who had intraoral surgery was seven times higher than that of those who did not have surgery [18-20].

The treatment objectives for patients with an established diagnosis of BRONJ are to alleviate pain, eliminate inflammation in soft and hard tissues, and minimize the progression of bone necrosis, that also leads to removal of the dental implants [21,22].

A number of studies have recently reported that the incidence of BRONJ decreased after discontinuation of oral BPs therapy [23-25].

Following the growth of the aging population patients diagnosed with osteoporosis, further studies need to be carried out to elucidate the subject on the most successful treatment option regarding these patients [26].

### Conclusion

The treatment of anxious patients with RPDs enhances mastication, functionality and it represents a good therapeutical decision in patients diagnosed with osteoporosis because of the surgical limitations associated with its treatment. The use of ball attachment systems in drug-induced xerostomia and subclinical hypothyroidism increases the maintenance and stability of prostheses. An RPD also provides important support for the facial structures such as the lips, maintaining a more youthful appearance. When a patient is faced with both general and dental conditions, it is important to provide not only long-term oral healthcare, but to also help the patient by causing the least amount of psychological trauma.

## **Conflict of interest:** None to declare.

### References

- Sogur E, Önem E, Kalfa M, et al. Oral health and oral quality of life in inactive patients with familial Mediterranean fever without amyloidosis. Clin. Exp. Rheumatol. 2013;31(3 supl.77):15-9.
- 2. Erdogan O, Incki KK, Benlidayi ME, et al. Dental and radiographic findings as predictors of osteoporosis in postmenopausal women. Geriatr Gerontol Int. 2009;9(2):155-64.
- Gur A. Nas K. The relation between tooth loss and bone mass in postmenopausal osteoporotic women in Turkey: a multicenter study. J Bone Miner Metab. 2003;21(1):43-7.
- Patntirapong S, Poolgesorn M. Alteration of macrophage viability, differentiation, and function by bisphosphonates. Oral Dis. 2018 Jun 5. doi: 10.1111/odi.12908. [Epub ahead of print]
- Goes P, Melo IM, Dutra CS, et al. Effect of alendronate on bone-specific alkaline phosphatase on periodontal bone loss in rats. Arch Oral Biol. 2012;57(11):1537-44.
- Chrcanovic BR, Albrektsson T, Wennerberg A. Bisphosphonates and dental implants: A metaanalysis. Quintessence Int. 2016;47(4):329-42
- Tagami T, Kimura H, Ohtani S, et al. Multi-center study on the prevalence of hypothyroidism in patients with hypercholesterolemia. Endocr J. 2011;58(6):449-57
- 8. Surks MI, Ortiz EO, Daniels GH, et al. Subclinical thyroid disease: scientific review and guidelines for

diagnosis and management. JAMA. 2004;291:228-238.

- Eriksen EF. Normal and pathological remodeling of human trabecular bone: three dimensional reconstruction of the remodeling sequence in normals and in metabolic bone disease. Endocr Rev. 1986; 7(4):379–408. [PubMed: 3536460]
- Marwaha RK, Garg MK, Tandon N, et al. Thyroid function and bone mineral density among Indian subjects. Indian J Endocrinol Metab. 2012; 16(4):575–579. [PubMed: 22837919]
- González-Rodríguez LA, Felici-Giovanini ME, Haddock L. Thyroid dysfunction in an adult female population: A population-based study of Latin American Vertebral Osteoporosis Study (LAVOS) -Puerto Rico site. P R Health Sci J. 2013 Jun;32(2):57-62.
- 12. Bathla M, Singh M, Relan P. Prevalence of anxiety and depressive symptoms among patients with hypothyroidism. Indian J Endocrinol Metab. 2016 Jul-Aug;20(4):468-74.
- Veerabhadrappa SK, Chandrappa PR, Patil S, et al. Evaluation of Xerostomia in Different Psychological Disorders: An Observational Study. J Clin Diagn Res. 2016 Sep;10(9):ZC24-ZC27.
- 14. Lalabonova CK. Impact Of Dental Anxiety On The Decision To Have Implant Treatment. Folia Med (Plovdiv). 2015 Apr-Jun;57(2):116-21.
- 15. Arslan A, Orhan K, Canpolat C, et al. Impact of xerostomia on oral complaints in a group of elderly Turkish removable denture wearers. Arch Gerontol Geriatr. 2009 Sep-Oct;49(2):263-7.
- Bergman B, Hugoson A, Olsson C-O. Caries, periodontal and prosthetic findings in patients with removable partial dentures: A ten-year longitudinal study. J Prosthet Dent. 1982;48(5):506-14.
- 17. Wagner B, Kern M. Clinical evaluation of removable partial dentures 10 years after insertion: success rates, hygienic problems, and technical failures. Clin Oral Investig. 2000;4:74-80.
- Shin EY, Kwon YH, Herr Y, et al. Implant failure associated with oral bisphosphonate-related osteonecrosis of the jaw. J Periodontal Implant Sci. 2010;40(2):90-5.
- 19. Zandi M, Dehghan A, Mohammadi-Mofrad A, et al. Short-term perioperative teriparatide therapy for the prevention of medication-related osteonecrosis of the jaw: A randomized, controlled preclinical study in rats. J Cranio Maxill Surg. 2016;45(2):275-80.
- 20. Ömür D, Ekim OO, Özgür I, Sinan A. The effect of the duration of intravenous zolendronate medication on the success of non-surgical endodontic therapy: A retrospective study. BMC Oral Health, 2016;16:2-6.

- 21. McGowan K, Ivanovski S, Acton C. Osteonecrosis of the jaws: A 14-year retrospective survey of hospital admissions. Aust Dent J. 2018;63(2):202-7.
- 22. Ripamonti Cl, Maniezzo M, Campa T, et al. Decreased occurrence of osteonecrosis of the jaw after implementation of dental preventive measures in solid tumour patients with bone metastases treated with bisphosphonates: the experience of the National Cancer Institute of Milan. Ann Oncol. 2009;20(1):137-45.
- 23. Dimopoulos MA, Kastritis E, Bamia C, et al. Reduction of osteonecrosis of the jaw (ONJ) after implementation of preventive measures in patients with multiple myeloma treated with zoledronic acid. Ann Oncol. 2009;20(1):117-20.

- 24. Jeffcoat MK. Safety of oral bisphosphonates: controlled studies on alveolar bone. Int. J. Oral Maxillofac Implants. 2006;21(3):349-53.
- 25. McGowan K. Insufficient Evidence to Compare the Efficacy of Treatments for Medication-Related Osteonecrosis of the Jaws. J Evid Based Dent Pract. 2017;18(1):70-2.
- 26. Advisory Task Force on Bisphosphonate-Related Ostenonecrosis of the Jaws, American Association of Oral and Maxillofacial Surgeons. American Association of Oral and Maxillofacial Surgeons position paper on bisphosphonate-related osteonecrosis of the jaws. J Oral Maxillofac Surg. 2007;65(3):369–76.

#### Corresponding author:

Carmen Biriș

University of Medicine and Pharmacy of Tirgu Mures, 38 Gheorghe Marinescu street, Tirgu Mures, 540139, Romania Email: biriscarmen74@yahoo.com

Received: April 25, 2018 / Accepted: May 27, 2018

## **STATEMENT OF ETHICS**

All research studies involving human subjects must have received approval of the appropriate institutional ethics committee and informed consent must be obtained from all the patients participating in the studies, prior to manuscript submission.

In cases where the institutional ethics review committee ruled that approval from them was not required or that the need for informed consent was unnecessary, a statement from the committee to this end should be forwarded to the Editor with the manuscript.

#### Human and animal rights

Studies involving experimental research on animals or humans must conform to the guiding principles of the Declaration of Helsinki. In order to respect a patient's right to privacy, identifying information such as patients' names, images, initials of hospital numbers should not be included in any published material (tables, figures, text), unless the information is essential for scientific content. In these cases written permission must be obtained from the patient, and should be submitted to the editorial office at the time of manuscript submission. In the case of animal experiments, both national and the institutional guidelines pertaining to the experimental use of laboratory animals should be rigidly followed.

Conflict of interest (Declaration of Interests)

# **INSTRUCTIONS FOR AUTHORS**

Acta Stomatologica Marisiensis Journal is an international journal dedicated to publishing high quality peer-reviewed articles pertaining to dental medicine. The themes covered by the journal include all the fields of dentistry, within a broad spectrum of disciplines and therapeutic areas, including, but not restricted to oral health, prosthetic dentistry, endodontics, paedodontics, orthodontics, oromaxillo-facial surgery, implantology, dental materials, digital dentistry, nanotechnology and materials or medial engeneering.

All manuscripts submitted to ASMJ must be original, high quality and conform to the "Uniform Requirements for Manuscript Submitted to Biomedical Journals" published in Annals of Internal Medicine (1997;126:36-47).

Authors should not submit the same manuscript simultaneously to more than one journal, in the same or different language.

#### Authorship

All individuals listed as authors should qualify for authorship and should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. The manuscript should contain a statement fully disclosing any conflict of interest related to the manuscript. If there are no conflicts of interest, this should be stated as "none declared". Material and financial support should also be acknowledged. Scientific misconduct

Scientific misconduct includes data fabrication, falsification, plagiarism, redundant publication, ghost authorship or other fraudulent research practices. In order to prevent plagiarism issues, all manuscripts sent to the journal will be screened using antiplagiarism software. Where there is a suspicion of scientific misconduct, the Editor will act in conformity with the principles stated in the COPE guidelines and if the fraudulent practice is confirmed the manuscript will be rejected outright and without the Editor entering into any further correspondence. Clinical trials

In case of manuscripts presenting clinical trials, the clinical trial should be registered in a public trials registry at or before the time of first patient enrollment, as a condition for consideration for publication. Trials should be preferably registered in ClinicalTrials.gov, but any registry that is a primary register of the WHO International Clinical Trials Registry Platform (ICTRP) is acceptable, in accordance with the guidelines of the International Committee of Medical Journal Editors.

Authors included in the manuscript should meet all of the following conditions as stated in the ICMJE (International Committee of Medical Journals Editors) guidelines:

Substantial contributions to the conception and design of the work, acquisition, analysis or interpretation of data;

Drafting the article or revising it critically, for important intellectual content;

Final approval of the version to be published.

Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Any other contributors, who do not qualify for authorship, should be acknowledged in an acknowledgment section. For further information about authorship, please refer to the ICMJE guidelines.

Studies involving experimental research on animals or humans must conform to the guiding principles of the Declaration of Helsinki. In case of research involving human subjects, the manuscript must contain a statement within the "Material and Methods" section indicating that the study protocol has been approved by the author(s) institutional ethical committee and that all study participants have given informed consent to participate, or that the ethical committee has waived the need for informed consent. In order to respect patient confidentiality and the right to privacy, identifying information such as patient's names, images, hospital or hospital record details, should not be included in any published material unless the information is essential for the scientific content. If so, written permission must be obtained from the patient, and this permission should be submitted to the editorial office prior to publication.

In case of manuscripts reporting clinical trials, these should be registered in a public trials registry at or before the time of first patient enrolment, as a condition for consideration for publication. Trials should preferably be registered in ClinicalTrials.gov, but in accordance with the guidelines of the International Committee of Medical Journal Editors any primary register of the WHO International Clinical Trials Registry Platform (ICTRP) is acceptable.

The journal does not have article processing charges nor article submission charges.

All manuscripts should be submitted via email to the email address asmj@umftgm.ro

The submission should include the following attachments:

Cover letter and Declaration of interests

License to publish

Manuscript

Figures

Tables

Appendices

1. Cover letter and Declaration of interests

All manuscripts should be submitted together with a cover letter attached as a separate file, stating that:

- the manuscript is original
- no portion of the manuscript is under consideration for publication in any other journal or has been previously published, except as an abstract of fewer than 400 words.
- all authors have read and approved the manuscript and accept responsibility for the full content.
- Authors must state all possible conflicts of interest relating to the manuscript (Declaration of interests form), or, if there are none, this should be stated as "none declared".

The cover letter should be signed by all of the authors of the paper and submitted by the corresponding author with the manuscript to the editorial office.

The cover letter may include a list of potential reviewers or persons which the author(s) do not wish

as reviewers. A brief statement of reasons of suitability/non-suitability should be given.

2. License to publish

A license to publish statement should be signed by all of the authors. The standard format of this document is available at www.asmj.ro

3. Manuscript

The manuscripts, including all tables and references, must be prepared in Word format. The text should be typed double-spaced with no indent, using "Times New Roman" font size 12.

Please arrange the contents of your manuscript in the following order:

I. Essential title page information

Title. Concise and informative. Titles are often used in information-retrieval systems. Avoid abbreviations and formulae where possible.

Author names and affiliations. Where the family name may be ambiguous (e.g., a double name), please indicate this clearly. Present the authors' affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lower-case superscript letter immediately after the author's name and in front of the appropriate address. Provide the full postal address of each affiliation, including the country name and, if available, the e-mail address of each author.

Corresponding author. Clearly indicate who will handle correspondence at all stages of refereeing and publication, also post-publication. Ensure that phone numbers (with country and area code) are provided in addition to the e-mail address and the complete postal address. Contact details must be kept up to date by the corresponding author.

Please also provide information on grants, contracts and any other form of financial support received in connection with the reported study.

II. Abstract – an abstract of no more than 300 words should accompany manuscripts relating to original research, case presentations and review articles. This should be structured using the following headings: Introduction, Aim of the study, Material and Methods, Results, Conclusions. Detailed instructions on abstract preparation according to each manuscript type are given below.

III. Key words – up to 10 keywords should be supplied by the author(s).

IV. Full text – should be formatted in Microsoft Word, double-spaced, single columned. Use headings and subheadings in all the sections. Original research articles should not exceed 5.000 words including references, tables, table legends and figure legends, and should be divided into the following sections: a. Introduction

This must be presented in a structured format, covering the following subjects, although actual subheadings should not be included:

- succinct statements of the issue in question;
- the essence of existing knowledge and understanding pertinent to the issue (reference);
- the aims and objectives of the research being reported relating the research to dentistry, where not obvious.
- b. Materials and methods:
- describe the procedures and analytical techniques.
- only cite references to published methods.
- include at least general composition details and batch numbers for all materials.
- identify names and sources of all commercial products e.g.Voltarol<sup>®</sup> Emulgel<sup>®</sup> Gel (Company, Town, Country).
- specify statistical significance test methods.
- c. Results
- refer to appropriate tables and figures.
- refrain from subjective comments.
- make no reference to previous literature.
- report statistical findings.
- d. Discussion
- explain and interpret data.
- state implications of the results, relate to composition.
- indicate limitations of findings.
- relate to other relevant research.
- e. Conclusion
- must NOT repeat Results or Discussion
- must concisely state inference, significance, or consequences

When preparing your manuscript, consider the following rules:

Define abbreviations that are not standard the first time they appear in the text, followed by the abbreviation in brackets.. Such abbreviations that are unavoidable in the Abstract must be defined at their first mention there. Ensure consistency of abbreviations throughout the article

All references, tables and figures should be cited in numerical order.

Language editing will be available during the editorial process, however authors whose native language is not English are strongly advised to seek appropriate grammatical assistance when preparing the manuscript. Poorly written manuscripts will be returned for improvement before commencing the editorial process.

V. Acknowledgments – please indicate any source of funding including grants, contracts or any other form of financial support relating to the study.

VI. References – Number the references in the order in which they are first cited in the text. References should be indicated as full-size Arabic numerals in square brackets placed before punctuation marks.

VII. Reference style – List all authors if six or less; otherwise list first three and add "et al". Please

abbreviate titles of periodicals according to Index Medicus, or spelled out in full if not listed in Index Medicus. Use the following formats, paying close attention to the use of punctuation i.e.colon (:), semicolon (;), coma (,) and full-stops (.).

For journal articles: Kim J, Fitzgerald JG, Sanders AK, Hofman HG. Long term survival following implantation of drug eluting stents. J Am Coll Cardiol. 2002;42:652-8.

For articles-in-press: Hendricks-Ferguson VL, Sawin KJ, et al. Novice Nurses' Experiences with Palliative and End-of-Life Communication. J Pediatr Oncol Nurs. 2015. doi: 1043454214555196. [Epub ahead of print] For a chapter in a book: La Rovere MT, Schwartz PJ: Baroreflex sensitivity. In Opie, L: Drugs for the Heart, Sixth Edition. Philadelphia: WB Saunders. 2006, pp.67-93.

For a Book: Eisen HN. Immunology: an introduction to molecular and cellular principles of the immune response. 5thed. New York: Harper&Row; 1974. P.406.

VIII. Acknowledgements – collate acknowledgements in a separate section at the end of the article before the references and do not, therefore, include them on the title page, as a footnote to the title or otherwise. List here those individuals who provided help during the research (e.g., providing language help, writing assistance or proof reading the article, etc.).

IX. Units – follow internationally accepted rules and conventions: use the international system of units (SI). If other units are mentioned, please give their equivalent in SI.

4. Figures

Figures should be prepared separately and sent as additional files, in TIF or JPG format, or compressed into one ZIP file. The figures should be prepared at the standard resolution of 300 dpi. All abbreviations used in a figure should be explained in the figure legend. Figure legends should be concise but explicit, enabling a clear understanding of the illustration. Figures and figure legends should be numbered in Arabic numerals in the order of appearance in the text and should not be imbedded within the text. Colour figures are preferred. Where a figure(s) is reproduced or adapted from another source, the author must first seek permission from both the author and publisher of the original material. Written evidence of permission for reproduction in both print and electronic formats for worldwide distribution must be forwarded with the manuscript and state "Reproduced with permission from..." or "Adapted with permission from ... ".

5. Tables

These must be self-explanatory and should not duplicate the text. Tables should be numbered in Arabic numerals in the order of mention in the text and should not be imbedded within the text. Instead, each table should be typed on a separate page at the end of the manuscript. All the abbreviations used in the table should be typed as footnotes immediately below the table. Tables should be created with Word's Insert Table function in order to be editable. Do not submit tables as image files.

#### 6. Appendices

If there is more than one appendix, they should be identified as A, B, etc. Formulae and equations in appendices should be given separate numbering: Eq. (A.1), Eq. (A.2), etc.; in a subsequent appendix, Eq. (B.1) and so on. Similarly for tables and figures: Table A.1; Fig. A.1, etc.

Acta Stomatologica Marisiensis Journal also publishes the following types of papers:

Reviews

The journal publishes comprehensive review papers on actual topics of interest related to dental medicine. Review articles should include a brief nonstructured abstract of no more than 250 words and the text should be limited to 5.000 words including, tables and figures, excluding references. In extraordinary situations or relevant and extensive topics, the Editor-in-Chief may decide to accept papers with a higher number of words, a maximum of 400 words for the abstract and 6.500 for the text, including tables and figures, excluding the references. Review articles can be submitted by invitation or unsolicited. In both cases, full consideration will be given to articles providing a substantial contribution to a better understanding of a pathophysiological or clinical aspect in a field related to dental medicine.

Case reports and case series

Case reports should be limited to presentation of a single particular and uncommon case, or uncommon presentation of a disease. Case series include description of a series of a maximum of 10 cases with common particularities. The abstract should be limited to 250 words, being divided into introduction, case presentation/presentation of case series and conclusions. The full manuscript should not exceed 2.500 words including references, figures and tables, being divided into sections headed Introduction, Case presentation/presentation of case series, Discussions, Conclusions. In manuscripts pertaining to case presentation or case series, the number of authors should be limited to four and the number of references to thirty and the number of figures to 8. Original papers

Definitive reports on a full study, describing original preclinical or clinical study (which is not a case presentation or a case series report) research of high scientific level and timeliness. A concise abstract of no more 250 words is required. The abstract should briefly state the purpose of the research, the main results and major conclusions. An abstract is often presented separate from the article, so it must be able to stand alone. The manuscript should be written clearly and concisely. The authors are responsible for providing the correct nomenclature, which must be consistent and unambiguous. The text should be arranged in the following order: Introduction, Materials and Methods, Results, Discussion and Conclusions.

The length of the manuscript should be limited to 3.500 words (including references, tables and figures).

Letter to editor

A letter to the editor may refer to an article recently published by the journal, commenting on the article in a constructive professional manner the content of which, in the opinion of the author(s) would add the current status of knowledge in the field. If accepted, the letter will be sent to the authors of the original article who will have the opportunity to respond and to have their response published in the same journal issue as the letter to the editor. The letters should be limited to 500 words, 5 references and 3 authors. No abstract is required.

#### Editorial

Editorials should be limited to 2000 words (including references) and should be related to an article published in the current number or to a specific topic that is current and of high interest to the readers.

State-of-the-art papers

The journal publishes state-of-the-art articles that aim to provide an update on the current status of areas of high interest dental medical specialities. The principal/main aim of such articles is to offer the specialist and other practitioners a source of continuing education and forum for discussion. A state-of-the-art article should have a full text limited to 4.000 words, in addition to a 200 word unstructured abstract. Sections of the article should be divided using headings relevant to each particular case.

#### Complaints

In cases where the authors wish to file a complaint, please contact the editorial office:

Acta Stomatologica Marisiensis Journal

University of Medicine and Pharmacy Tirgu Mures

Gheorghe Marinescu street no.38, Tirgu Mures, 540139, ROMANIA

#### Phone: +40-265-21 55 51, fax +40-265-21 04 07 Email: asmj@umftgm.ro

Please describe the reason for complaining and specify the address for correspondence. Where the complaint is related to the editorial process, related to a manuscript, please include the name of the manuscript and the date the manuscript was submitted. The Editor in Chief, together with the editorial office will analyze the complaint and will answer in maximum three working days. Acta Stomatologica Marisiensis