РЕПУБЛИКА СЕВЕРНА МАКЕДОНИЈА
УНИВЕРЗИТЕТ "СВ. КИРИЛ И МЕТОДИЈ"
СКОПЈЕ

Примено: 16 -04- 2019			
Орг. единица:	Број:	Прилог:	Вредност:
19	545/6	1	

До интеруниверзитетска ректорска управа во

Република Северна Македонија

П Р И Ј А В А

Јас, проф. д-р Мирјана Поповска, вработена на Стоматолошкиот факултет во Скопје, УКИМ, се пријавувам по повторниот јавен повик бр. 1/2019, објавен во јавното гласило Нова Македонија од 11 април 2019 година во врска со избор на членови од Интеруниверзитетска конференција во:

1. Националниот совет за високото образование и научно-истражувачка дејност, од научно-истражувачкото поле од прво ниво според Меѓународната фракатиева класификација:

- Медицински науки и здравство , лице од редот на професорите, во работен однос на Универзитетот " Св. Кирил и Методиј " во Скопје

Во прилог на пријавата доставувам:

- Кратка биографија (CV)
- Пополнет образец на податоци

Скопје, 15.04. 2019

Проф д-р Мирјана Поповска

Кратка биографија
Формат на Европската унија

Референтен број на огласот

Лични податоци

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Работно искуство

• Датум (од - до)	јуни, 2014 год, избор во редовен професор август, 2009 год, избор во вонреден професор декември, 2006 год, избор во доцент април, 2004 год, избор во научен соработник 1992-2004 год, избор и реизбор во асистент 1989-1992 год, избор во помлад асистент 1985-1989 год, клинички лекар
• Име и адреса на работодавачот	Стоматолошки факултет, Скопје, УСКЦ " Св.Пантелејмон"
• Област на работа или сектор	Клиника за болести на устата и пародонтот
• Позиција	Редовен професор
• Главни активности и одговорности	Наставник по предмети од пародонтологија и орална медицина во I, II и III циклус доктор специјалист

Образование и обуки

• Датум (од – до)	-Доедукација по пародонтална хирургија, Љубљана, Словенија, декември 2015 год.

(1месец)
-Базичен курс по пародонтална хирургија, Белград, Србија, април 2012 год.(1 месец)
-Доедукација по орална медицина, Аристотелов Универзитет, Солун, 2004 год. март (1 месец)
-Едукативен престој по орална медицина, Аристотелов Универзитет, Солун, 2003 год. (1 месец)
-Обука за iTOP, 2011, Охрид
- Обука на Health & Laser academy Workshop Fotona with Fidelis Plus III, 2009, Софија, Бугарија
-Обука на Сектор за здравсто за едукатори и ментори, 2006, Скопје
-Курс за базични и напредни знаења од областа на имунологијата, 2004 год, Медицински факултет, Скопје

• Назив и вид на организацијата во која сте го стекнале образованието и обуката

-Доктор на стоматолошки науки, 9 мај 2000 год. Стоматолошки факултет, УКИМ, Скопје
-Специјалист по болести на устата и пародонтот, 24 април 1994 год. Стоматолошки факултет, УКИМ, Скопје
-Магистер на стоматолошки науки, 17 јуни 1991 год. Стоматолошки факултет, УКИМ, Скопје
-Доктор по стоматологија, 27 септември, 1984 год. Стоматолошки факултет, УКИМ, Скопје

• Стекната квалификација

Од 2006-
Ментор на 8 студенти на докторски студии
Ментор на 10 студенти на магистерски студии
Ментор на 5 студенти на специјализација
Ментор на 10 дипломски работи

• Професионални напредувања

2013-2017 продекан за наука, Стоматолошки факултет, Скопје
2016-2017 раководител на континуирана едукација на, Стоматолошки факултет, Скопје
2011-2015 раководител на III циклус студии-докторски студии по стоматологија
2011-2017 главен и одговорен уредник на Инфо и Vox dentarii –Стоматолошка комора
2006-2011 член на Извршен одбор на Стоматолошката комора на Македонија
2013- член на Европската асоцијација по орална медицина

Авторства на литература за наставата

Автор на 9 учебници и учебни помагала за студентите од прв циклус.
1. За стоматолошката болка (поглавје Болката во оралната патологија и пародонтологија), Стоматолошки факултет, Скопје, 1999.
2.Основи на оралната пропедевтика, Стоматолошки факултет, Скопје, 2002 (учебно помагало)
3. Диференцијална дијагноза на оралните лезии, Магнаскен, Скопје, 2004 (учебник)
4. Дијагностика на оралните лезии- практикум, Стоматолошки факултет, Скопје, 2006
5. Орална хигиена практикум, Стоматолошки факултет, Скопје, 2013
6. Орална хигиена, учебник. Стоматолошки факултет, Скопје, 2013
7. Орална медицина и патологија-практикум, Стоматолошки факултет, Скопје, 2013
8. Орална медицина и патологија, учебник, Стоматолошки факултет, Скопје, 2013
9. Клиничка пародонтологија 1, скрипта, е-издание, 2015.

Други стручни авторства

Автор на 2 книги од областа на стоматологијата:
-Дијагностички и терапевтски протоколи, Стоматолошка комора на РМ, 2010
-Стратешки план за развој на стоматологијата во периодот 2011-2021, Стоматолошка комора на РМ, 2010.

• Награди и признанија

-Плакета по повод 70 години од основање на Стоматолошкиот факултет во Софија во знак на интерфакултетска соработка, 2014 год
-Диплома по повод 50 год од основање на Стоматолошкиот факултет за посебна заложба

за работење на Стоматолошкиот факултет во Скопје, 2009

-Диплома по повод 40 год од основање на Стоматолошкиот факултет во Скопје,во знак на благодарност и придонес во работата на Стоматолошкиот факултетот,1999

-Плакета од Македонското лекарско здружение за значаен придонес во остварувањето на целите и задачите на МЛД, 1998

- Диплома од Македонското лекарско здружение за придонес и ангажман во работата на МЛД, 1995

Лични вештини и способности

Мајчин јазик: **Македонски јазик**

Други јазици

1.англиски

- Читање: Добро
- Пишување: Добро
- Говорење: Добро

2. ГРЧКИ

- Читање: Добро
- Пишување: Добро
- Говорење: Добро

3.СРПСКИ И ХРВАТСКИ

- Читање: **Одлично**
- Пишување: **Одлично**
- говорење: **Одлично**

Социјални вештини и способности

КОМУНИКАЦИСКИ
ОРГАНИЗАТОРСКИ

Организациски вештини и способности

- **Учесник.** 2017-2018 Состојбата на оралното здравје кај геријатриски пациенти
- **Учесник.** 2016-2018 билатерален проект Словенија-Македонија, финансиран од МОН, (Префабрикувани циркониумски колчиња со ретентивен коронарен облик за реставрација на ендодонтски третирани заби - Ин витро процена на третманот
- **Главен истражувач.** 2014-2015, проект финансиран од УКИМ,(Асоцијација помеѓу орална и генитална афекција со ХПВ вирусот- причини за навремено вакцинирање- ДА или НЕ?)
- **Учесник.** 2000-2003, проект финансиран од МОН (Промени во имунолошката реактивност кај млади пациенти со напреднат и фудројантен ток)

Технички вештини и способности

Оперативен систем: MS Windows,
Office апликации: MS Word, MS Excel, MS Power Point, MS Outlook

Други вештини и способности

Амбициозност
Креативност
Флексибилност
Индивидуална и тимска работа

Возачка-и дозвола-и	В -КАТЕГОРИЈА
Дополнителни податоци	Автор на повеќе од 150 научни и стручни трудови отпечатени во релевантни списанија. Активно учество како предавач на конгреси, семинари со меѓународно учество, во земјата и странство.
Прилози	-Сертификати за учество на светски и европски конгреси во последните 3 години. Europerio, Amserdam, 2018, FDI, Madrid 2017, Thessaloniki 2018 - Копии од трудовите приложени во образецот кон јавниот повик

Образец кон Повторен Јавен повик бр. 1/2019

- ***за професорите***

Име и презиме: **Поповска Мирјана**

Вработен на: **Стоматолошки факултет Скопје, УКИМ**

Научно-истражувачко поле од прво ниво според Меѓународната фраскатиева класификација:

☐ природно-математички науки;
☐ техничко-технолошки науки;
✓ **медицински науки и здравство;**
☐ земјоделски и ветеринарни науки;
☐ општествени науки ;
☐ хуманистички науки.

Податоци за најмалку 10 научни трудови*

1.назив на трудот: Rational development of nanomedicines for molecular targeting in periodontal disease. Arch Oral Biol.2018; 14;93:31-46.

(*да се наведе соодветната буква* ***а,*** *б, в, г, д, ѓ, од точката 24*)

2.назив на трудот: In vivo effects of geranyl geraniol on the development of bisphosphonate-related osteonecrosis of the jaw. Journal of cranio-maxillo-facial surgery. 2018;46(2):230-236.

(*да се наведе соодветната буква* ***а,*** *б, в, г, д, ѓ, од точката 24*)

3.назив на трудот: Human papillomavirus as a potential risk factor for oral premalignant lesions. Acta clin croat. 2017;56:369-374.

(*да се наведе соодветната буква* ***а,*** *б, в, г, д, ѓ, од точката 24*)

4.назив на трудот: Chemometricvaluation of the efficacy of lokally administered chlorhexidine in patients with periodontal disease. Saudi Pharmaceutical Journal.2017;25:1022-1031

(*да се наведе соодветната буква* ***а,*** *б, в, г, д, ѓ, од точката 24*)

5.назив на трудот: Efficacy assessment of local doxycycline treatment in periodontal patients using multivariate chromometric approach. Europian Journal of pharmaceutical sciences.2016;91:114-12.

(*да се наведе соодветната буква* ***а,*** *б, в, г, д, ѓ, од точката 24*)

6.назив на трудот: **Gene polymorphism of matrix metalloproteinase-1 in chronic periapical lesions.Dentistry. 2017;7(6):1000436.**

(*да се наведе соодветната буква* ***а,*** *б, в, г, д, ѓ, од точката 24*)

7.назив на трудот: **IL1 cluster gene polymorphisms in Macedonian patients with chronic periodontitis. Bratisl Lek Listy. 2013;114(7):380-5.**

(*да се наведе соодветната буква* ***а,*** *б, в, г, д, ѓ, од точката 24*)

8.назив на трудот: Development and validation of RP HPLC method for determination of betamethasone dipropionate in gingival crevicular fluid. Acta Pharm. 2013 Sep;63(3):419-26.

(*да се наведе соодветната буква* ***а,*** *б, в, г, д, ѓ, од точката 24*)

9.назив на трудот: Development and validation of RPB HPLC assay of chlorhexidine in gingival cervicular fluid. Arh.farm. 2014; 64:69-82.

(*да се наведе соодветната буква* ***а,*** *б, в, г, д, ѓ, од точката 24*)

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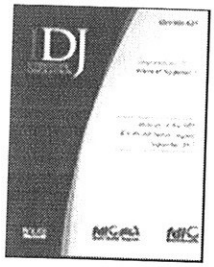

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Special Issue: Abstracts of the 105, FDI World Dental Congress, September 2017

Thursday, 31 August 2017 - Free Communication Sessions 49–72 and Poster Sessions 48–67

Thursday, 31 August 2017 - Free Communication Sessions 49–72 and Poster Sessions 48–67

- First published: 22 August 2017Full publication history
- DOI: 10.1111/idj.12340 View/save citation
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Free Communication Session 64 | 31.08.2017, 14:00–15:00 | Room A9.13 Theme: Oral Medicine

FC255

Oral Findings in Patients with Dyspeptic Disturbances

Mirjana Popovska[1], Vera Radojkova Nikolovska[1], Bruno Nikolovski[2], Lindita Zendeli-Bexheti[3], Spiro Spasovski[1], Kristina Mitic[1]

[1]Faculty of Dentistry UKIM, Faculty of Dentistry Skopje, The Former Yugoslav Republic of Macedonia, [2]Faculty of Dentistry, Skopje, The Former Yugoslav Republic of Macedonia,

[3]University Dental Clinical Center Skopje, Skopje, The Former Yugoslav Republic of Macedonia

Aim or purpose

To record oral symptoms, signs and lesions in patients with dyspeptic disturbances caused by *H. Pylori*.

Materials and methods

In total 60 patients with dyspeptic symptoms and indication for endoscopic intervention-gastroscopy were examined and divided in two groups as follows: the first group (n = 30) comprised patients with dyspeptic symptoms without *H. Pylori* and the second one (n = 30) comprised patients with dyspeptic symptoms with *H. pylori*. *H. Pylori* was detected after endoscopic examination, taken biopsy and conducted urease test (CLO test–). Oral clinical findings were registered in all participants. During endoscopic examination, few biopsy samples were taken, one of which was used for rapid urease test (RUT). The test is performed during gastroscopy by using the Pronto Dry test.

Results

In patients with dyspeptic symptoms with *H. pylori*, were registered: halitosis in 21 (35.00%), hypertrophy of tongue papillae in 16 (26.67%), burning symptoms and aphthous ulcers in 4 (6.67%) and sour taste in 4 (6.67%). The group without *H. pylori* revealed mouth burning symptoms in 2 (3.33%), aphthous ulcers in 2 (3.33%); hypertrophy of tongue papillae in 1 (1.67%) and tongue hypertrophy with sour taste in 1 (1.67%) participant. Patients with *H. pylori* had an average of 2,999 times ($B = 2,999$) higher values of IgG compared to patients with a negative diagnosis of gastric biopsy (patients without *H. pylori*), ($p < 0.001$). Used statistical method is the percentages of structure and univariate regression analysis Bx.

Conclusions

In patients with dyspeptic symptoms with H. pylori dominate symptoms and lesions of the tongue and aphthous ulcers.

Keywords

Oral findings, H. pylori, dyspeptic disturbances.

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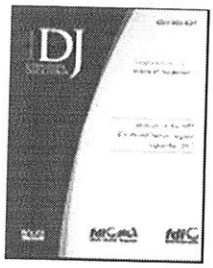

Special Issue: Abstracts of the 105, FDI World Dental Congress, September 2017

Thursday, 31 August 2017 - Free Communication Sessions 49–72 and Poster Sessions 48–67

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Free Communication Session 70 | 31.08.2017, 16:30–17:30 | Room A9.10 Theme: Periodontics

FC280

The Effects of Estrogen Hormones on Periodontal Health in Menopause

Vera Radojkova Nikolovska[1], Mirjana Popovska[1], Ana Minovska[2], Aneta Atanasovska Stojanovska[1], Bruno Nikolovski[3]

[1]Faculty of Dentistry, Skopje, The Former Yugoslav Republic of Macedonia, [2]Faculty of Medicine, Stip, The Former Yugoslav Republic of Macedonia, [3]Eterna Dent, Skopje, The Former Yugoslav Republic of Macedonia

Aim or purpose

During menopause, there are reduced estrogen levels associated with the decreased production of sex steroid hormones in women, which results in increased gingival inflammation, moderate or severe periodontitis, changes in crevicular fluid flow, microbial and pathohistological changes. Some of them may experience burning sensations, along with irritation. Aim: to establish serum and salivary levels of 17β-estradiol in women in the postmenopausal period; to determine its influence on periodontal tissue complex, followed by indices of periodontal health; by immunohistochemical analyzes to determine the presence of sex hormones 17β-estradiol in gingival tissue.

Materials and methods

30 post-menopausal women were examined clinically and laboratory examination of serum and salivary levels of 17β-estradiol were performed using the DRG Estradiol Elisa (EIA-2693) technology. Pathohistological and immunohistochemical analyzes were performed on biopsy material taken from the gingival tissue.

Results

The average values of periodontal indices demonstrated moderate form of periodontal disease with moderate to strong correlative value between indices of periodontal status, ranged from $r = 0.26$ to 0.57. Although gingival tissue is not included in the classical target tissues undergoing sex hormone action, in immunohistochemical analysis using antibodies directed to the estrogen receptors, we were able to detect nuclear and cytoplasmic positivity for estradiol, as in the epithelium and in the connective tissue of gingiva.

Conclusions

The results of hormone concentrations show potent impact they manifest on periodontal health, which suggests the role of dentists in treatment modalities in postmenopausal period in women.

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journal homepage: www.elsevier.com/locate/archoralbio

Rational development of nanomedicines for molecular targeting in periodontal disease

Nikola Geskovski[a], Simona Dimchevska Sazdovska[a], Silvana Gjosheva[a], Rumenka Petkovska[b], Mirjana Popovska[c], Liljana Anastasova[b], Kristina Mladenovska[a], Katerina Goracinova[a,d,*]

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ARTICLE INFO

Keywords:
periodontal disease
host-pathogen interactions
molecular targeted therapy
nanomedicine
nanotoxicity

ABSTRACT

Recent advances in understanding the etiology and pathogenesis of periodontal disease and polymicrobial synergy in the dysbiotic oral microbial community endorsed novel therapeutic targets and assured further improvement in periodontal disease treatment. Moreover, understanding of the events at the molecular level inspired the researchers to alleviate the stress from the disease by applying the bottom-up approach and delivering the drugs at the site of action, using nanoscale medicines. This review is focused on promising strategies for rational design of nanopaharmaceuticals for periodontal disease treatment based on novel therapeutic targets and the potential of advanced concepts for inflammation cascade targeting. Due to their size, nanomedicines are capable to interact with the elements of the immune system through cell receptor binding and to subsequently influence specific intracellular signaling pathways activation. They might also interfere with different signaling molecules continuously involved in the disease progression, in order to abolish cell activation and block the production of proinflammatory substances. Different biomacromolecules can be trafficked to the site of action using nanomedicines for gene targeting: i) decoy oligodeoxynucleotide (ODN) for suppression of NF-κB transcription activity, ii) DNA therapeutics for modulation of cell inflammatory response and iii) siRNA for cytokine production silencing. However, despite the potential of the nanotechnology for improvement of periodontal disease treatment, the translation of nano-drug delivery systems to clinical therapy is hindered by the lack of standard procedures for proper safety and efficacy profile evaluation.

1. Introduction

Periodontal disease is a complex problem with fairly unpredictable therapeutic results, often interrelated with adverse medical outcomes of several serious systemic diseases. Worldwide there is a large prevalence of periodontitis in a range between 13-54% in different countries and people of different ages are affected with this condition (Álvarez, Espinar, & Méndez, 2011; Greenberg & Glick, 2003; Hugoson & Norderyd, 2008).

The major breakthrough in the periodontal disease research was in the early 1980's when it was acknowledged that although bacteria are the primary etiological cause of this illness, the expression of bacterial pathogenic factors alone is probably not sufficient to cause periodontitis and that the basement of the pathology is of inflammatory nature (Howell & Williams, 1993; Reddy et al., 2011). Nowadays, it is known that the innate immune response generated at the periphery of sites of microbiological penetration, as a silent and physiological inflammatory response, is essentially protective in design (Sansonetti & Di Santo, 2007). However, the excessive host response, as well as the amplification of the initial inflammatory reaction (lasting approximately 21 days), might result in inadequate resolution of the inflammation which is critical to the pathogenesis of periodontitis (Bascones-Martínez et al., 2009; Di Benedetto, Gigante, Colucci, & Grano, 2013; Gierut, Perlman, & Pope, 2010). Failure of protective aspects of the host response, dysfunctional regulatory mechanisms and hyper-responsive host defense reaction in certain individuals will cause homeostatic mechanisms disruption and will result in continuous release of proinflammatory mediators (IL-1, IL-6, TNF-a, prostaglandin E2). This will lead to chronic inflammation, progression of gingival inflammation to periodontal disease, extracellular matrix destruction in the gingiva and bone resorption (Baker, 2000; Darveau, 2010; Dyke & Winkelhoff, 2013; Graves, Li, & Cochran, 2011; Noh et al., 2013). Undoubtedly, the

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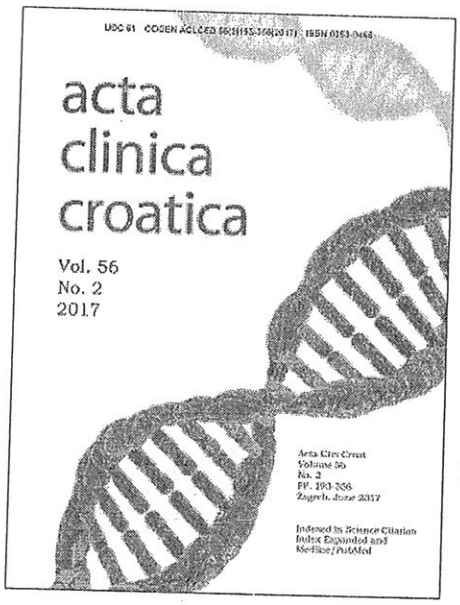

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Original Scientific Paper

HUMAN PAPILLOMAVIRUS AS A POTENTIAL RISK FACTOR FOR ORAL PREMALIGNANT LESIONS

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SUMMARY – Oral premalignant lesions (OPLs) and numerous alterations of oral mucosa remain unsolved due to their complex etiopathogenesis. Human papillomaviruses (HPVs), in particular, have been reported as the possible risk factors or cofactors. The aim of the study was to determine the association of different HPV types with oral premalignant lesions, and the potential role of smoking and alcohol use. Eighty patients (mean age ± SD, 52.45±5.56) of both genders, 19 (23.75%) male and 61 (76.25%) female, were enrolled in the study. Study group included 40 patients diagnosed with OPLs (leukoplakia, erythroplakia, actinic keratosis and lichen planus), while control group included another 40 patients with healthy oral mucosa. Genotyping of the HPV types was performed by qualitative real-time HPV typing polymerase chain reaction test. HPV DNA was detected in 30% (12/40) of study group patients and 2.5% (1/40) of control group patients. The results revealed the presence of HPV16 in 15% (6/40), HPV56 in 10% (4/40), and HPV18 in 5% (2/40) of study group cases, and HPV31 in 1 (2.5%) control group patient. The association of oral HPV positivity and smoking/alcohol use in the study group was not statistically significant ($p>0.05$). In conclusion, high-risk HPV types are associated with oral premalignant disorders. However, it remains unknown whether HPV acts as an innocent bystander or it has a role in initiating development of premalignant lesions. Smoking and alcohol use were not associated with the existing oral HPV infection.

Key words: *Mouth diseases; Papillomaviridae; Human papillomavirus 16; Polymerase chain reaction; Macedonia*

Introduction

Oral premalignant lesions (OPLs) such as leukoplakia, erythroplakia and lichen planus have been strongly associated with alcohol and tobacco use, increasing the risk of developing malignancy, although age, trauma and poor oral hygiene are pointed out as well[1-3]. In the last decades, researches emphasize the role of infective agents and of human papillomaviruses (HPV) in particular as the probable risk factors or cofactors in the etiology of these entities. The possible association of OPLs and oral squamous cell cancer with HPV, as reported by Syrjänen *et al.*[4], signifies the establishment of a new field of research. The role of HPV was additionally confirmed by verifying the presence of HPV in oropharyngeal cancers as well[5]. Regardless of different diagnostic methodology, studies pointed to the association of oral lesions and HPV infection. Previous studies report on 80% HPV positive leukoplakias[6], and another study verified HPV DNA in 17.6% of oral leukoplakic lesions and 19.7% of oral lichen planus lesions[7].

Even though it is considered that the group of oral cancers and oropharyngeal cancers are HPV associated, the role of HPV in oral cavity lesions requires further interpretation and higher level of care[8]. Signifi-

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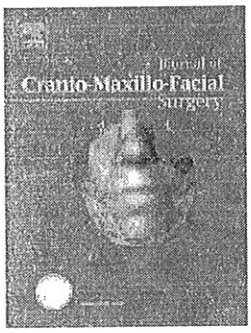

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In vivo effects of geranylgeraniol on the development of bisphosphonate-related osteonecrosis of the jaws

Filip Koneski*, Danica Popovic-Monevska, Icko Gjorgoski, Jovanka Krajoska, Mirjana Popovska [1], Ilijana Muratovska, Boris Velickovski, Gordana Petrushevska, Vladimir Popovski

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ABSTRACT

Background: Bisphosphonate-related osteonecrosis of the jaws (BRONJ) is a complication of the bisphosphonate (BP) treatment and its pathopysiology is still not fully understood. The existing preventive and treatment options require updates and more attention. Geranylgeraniol (GGOH) so far demonstrated an increased activity and viability of the cells previously treated with zoledronic acid (ZA). The aim of this study was to evaluate the in vivo effects of GGOH on the development of BRONJ.

Materials and methods: A total of 30 male Wistar rats were included in the study, divided into three groups: two experimental groups (EG1 and EG2) and a control group (CG). Rats from EG1 and EG2 were treated with 0,06 mg/kg ZA ip weekly in a duration of five weeks, while CG received saline ip. On the third week all animals underwent extraction of the lower right first molars. The rats from EG2 received a local solution of GGOH in concentration of 5 mM in the socket every day after the tooth extraction. The analyses included clinical evaluation on the wound healing and pathohistological evaluation for presence and level of osteonecrosis.

Results: EG2 showed significantly improved wound healing and tissue proliferation, when compared to EG1. EG2 significantly differed from EG1 and CG ($p<0,05$) for the presence of microscopical osteonecrosis (80% vs 22,2% vs 0%). Regarding to the number of empty lacunes without osteocytes and the level of necrosis, all groups demonstrated significant differences.

Conclusion: Geranylgeraniol in a form of local solution may be a promising option for prevention and treatment of BRONJ.

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1. Introduction

Bisphosphonate-related osteonecrosis of the jaws (BRONJ) as a complication of bisphosphonate (BP) treatment is an area of increased research interest. Although several hypotheses have been proposed (Ruggiero et al., 2014), none of them fully explain the nature and mechanism of development of the disease. However, the theory that supports the inhibition of bone resorption with mediation of osteoclastic activity is the most well researched. On the other hand, studies showed that the BPs have toxic effects on soft tissue cells, as well (Landesberg et al., 2008; Scheper et al., 2009; Walter et al., 2010; Ravosa et al., 2011; Tipton et al., 2011; Açil et al., 2012; Basso et al., 2013; Tanaka et al., 2013), indicating that the impaired wound healing and infection may play an important role in the development of BRONJ.

BRONJ has been successfully reproduced mainly in animal models, primarily rats, implementing different routes of administration, dosage of BPs and risk factors (Sonis et al., 2009; Bi et al., 2010; Aghaloo et al., 2011; Barba-Recreo et al., 2014; Jang et al., 2015; Zandi et al., 2016). Large-animal models have been introduced, as well (Allen and Burr, 2008; Allen et al., 2010; Pautke et al., 2012). Dentoalveolar trauma, i.e. tooth extraction, is one of the main factors contributing to the development of BRONJ (Ruggiero et al., 2014). A recent study showed that isolated soft tissue trauma without bone damage can also be the starting point for

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Original article

Chemometric evaluation of the efficacy of locally administered chlorhexidine in patients with periodontal disease

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ABSTRACT

The process of assessment of drug efficacy produces multivariate data which are difficult to interpret. The interpretation and extraction of relevant data requires application of chemometric algorithms for multivariate data analysis. The aim of our study was evaluation of the efficacy of local treatment with chlorhexidine (CHX) in patients suffering from periodontal disease by chemometric algorithms for multivariate data analysis. Several algorithms were used: principal component analysis (PCA), partial least squares discriminant analysis (PLS-DA) and orthogonal projection to latent structures discriminant analysis (OPLS-DA). The PCA models identified the examined variables as suitable for monitoring the periodontal disease progression at the same time revealing mutual relationship among them. The developed PLS-DA model successfully distinguished patients treated with CHX from non-treated patients. The OPLS-DA model revealed differences in the mechanism of action of the two widely applied treatments in periodontal disease, local administration of CHX and local administration of doxycycline (DOX). The approach presented in this study opens the possibility of application of chemometric algorithms for multivariate data analysis for assessment of treatment efficacy.
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1. Introduction

The process of drug efficacy assessment encompasses conduction of large controlled clinical trials where relatively homogenous group of subjects are carefully evaluated with respect to predefined clinical and laboratory parameters and closely monitored with respect to unexpected effects (Rasmussen et al., 2010; Ren et al., 2012; Cleophas and Zwinderman, 2013). The massive amounts of data generated by these trials are traditionally analyzed using univariate approach *i.e.* considering mean result versus control (Liland, 2011; Cleophas and Zwinderman, 2013).

However, the univariate approach suffers from several disadvantages such as the need for large number of samples as well as the inability to compensate for the missing data points which may require important observations to be discarded from analysis (Helmy et al., 2012).

Compared to the univariate approach, the multivariate approach that uses chemometric algorithms for data analysis represents a powerful tool for exploring large datasets derived from biological systems which contain multiple variables, missing data points or relatively small number of observations (Eriksson et al., 2006; Helmy et al., 2012). Their application provides "multicomponent insight" into treatment effects and therefore the adoption of chemometric algorithms for multivariate data analysis for assessment of treatment efficacy is highly recommendable (Durcekova et al., 2011; Mocak, 2012; Jimenez et al., 2013; Mrazova et al., 2014).

Abbreviations: GCF, gingival crevicular fluid; ALP, alkaline phosphatase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; IL-1β, interleukin -1 beta; TNF, α- tumor necrosis factor-alpha; CAL, clinical attachment loss; PD, pocket depth; GI, index of gingival inflammation; CHX, chlorhexidine; DOX, doxycycline; PCA, principal component analysis; PLS-DA, partial least square discriminant analysis; VIP, variable influence on projection; OPLS-DA, orthogonal projection to latent structures discriminant analysis.

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Efficacy assessment of local doxycycline treatment in periodontal patients using multivariate chemometric approach

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ABSTRACT

The aim of our study was application of chemometric algorithms for multivariate data analysis in efficacy assessment of the local periodontal treatment with doxycycline (DOX). Treatment efficacy was evaluated by monitoring inflammatory biomarkers in gingival crevicular fluid (GCF) samples and clinical indices before and after the local treatment as well as by determination of DOX concentration in GCF after the local treatment.
The experimental values from these determinations were submitted to several chemometric algorithms: principal component analysis (PCA), partial least square discriminant analysis (PLS-DA) and orthogonal projection to latent structures-discriminant analysis (OPLS-DA). The data structure and the mutual relations of the selected variables were thoroughly investigated by PCA. The PLS-DA model identified variables responsible for discrimination of classes of data, before and after DOX treatment. The OPLS-DA model compared the efficacy of the two commonly used medications in periodontal treatment, chlorhexidine (CHX) and DOX, at the same time providing insight in their mechanism of action. The obtained results indicate that application of multivariate chemometric algorithms can be used as a valuable approach for assessment of treatment efficacy.
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1. Introduction

The efficacy of a given pharmacological treatment is evaluated against a set of predefined variables for which sufficient evidence exists that they can provide a valid and a reliable measure of treatment's benefits. This evaluation results in generation of complex data conventionally analyzed by univariate statistical approach where a single variable is treated independently to the other variables (Rasmussen et al., 2010). Univariate approach could miss important "weak" correlations or could overestimate the importance of certain variables (Francesci et al., 2012). In contrast, application of multivariate chemometric approach for evaluation of treatment efficacy overcomes the limitations of the traditional approach, thus providing possibility of reliable exploration the complex data sets with multiple variables, missing data even with small number of observations (Helmy et al., 2012; Jimenez et al., 2013).

Multivariate chemometric approach comprises of application of versatile algorithms for multivariate data analysis which can be classified in two general categories: unsupervised and supervised. Unsupervised chemometric algorithms such as principal component analysis (PCA) or hierarchical cluster analysis (HCA) are being used for exploratory data analysis (finding patterns of similarity or outliers in complex data sets). Supervised algorithms such as partial least squares (PLS), partial least squares-discriminant analysis (PLS-DA), orthogonal projection to latent structures (OPLS) or orthogonal projection to latent structures-discriminant analysis (OPLS-DA) tempt to determine variables that can discriminate between known classes of data (for example, data before and after treatment) allowing unknown samples to be correctly classified. They require a priori knowledge of the class membership to develop the model (Ivosev et al., 2008; Cova et al., 2013; Gromski et al., 2015). All these algorithms are indispensable as they provide reliable, validated and robust tools for evaluation of treatment efficacy (Durcekova et al., 2011; Wang et al., 2012, Tomita et al., 2014).

Periodontal disease is a chronic inflammatory disorder affecting the tissues supporting the teeth. The main therapeutic approach consists of mechanical treatment of root surfaces followed by local application of antibiotics or antiseptics. Evaluation of treatment efficacy is performed

Abbreviations: DOX, doxycycline; GCF, gingival crevicular fluid; PCA, principal component analysis; PLS-DA, partial least square discriminant analysis; OPLS-DA, orthogonal partial least square-discriminant analysis; CHX, chlorhexidine; HCA, hierarchical cluster analysis; PLS, partial least squares; OPLS, orthogonal partial least squares; PD, pocket depth; CAL, clinical attachment loss; GI, index of gingival inflammation; ALP, alkaline phosphatase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; IL-1β, interleukin-1β; TNF-α, tumor necrosis factor-α; VIP, variable influence on projection.

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Research Article
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Gene Polymorphism of Matrix Metalloproteinase-1 in Chronic Periapical Lesions

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Abstract

Background/Aim: Matrix metalloproteinases (MMPs) are zinc and calcium dependent enzymes capable of degrading almost all extracellular matrix and basement membrane components. This group of proteolytic enzymes is believed to be implicated in the breakdown of extracellular matrix in normal physiological processes, as well as playing an important role in many destructive pathological oral processes, such as periodontal tissue destruction, root caries, tumor invasion, and chronic periapical inflammation (CPL). The aim of this study was to analyze polymorphism in the gene MMP-1 and their association and influence on clinical manifestation of chronic periapical lesions in order to provide new advances regarding the involvement of MMPs in various oral diseases associated with the inflammatory process.

Materials and methods: A total of 240 unrelated Macedonian subjects were included in the present study. Polymorphism -1607 1G/2G in the gene MMP-1 detected with restriction enzymes *AluI, XmnI* and polymorphism -519 A/G in the gene MMP-1 detected with restriction enzyme *KpnI* was studied in 120 patients with CPL and 120 controls without any signs of chronic or acute inflammatory process in the jaw. The amplification of the region of selected gene was made with polymerase chain reactionrestriction fragment length polymorphism (PCR-RFLP).

Results: Our results showed that there was a differences in the allele and genotype frequencies of the MMP-1 polymorphism between patients with CPL and controls ($p<0.05$). Also this study suggests that MMP-1 polymorphism -1607 1G/2G detected with restriction enzymes *AluI, XmnI* was a risk for expression of CPL (OR=18.38<4.06<OR<115.46; OR=7.73<3.1<OR<19.55) and MMP-1 polymorphism -519 A/G detected with restriction enzyme *KpnI* was a risk for expression of CPL (OR=12.11<4.64<OR<32.30).

Conclusions: Detection of this genetic polymorphism is relevant for obtaining providential treatment of patients who are at high risk of chronic periapical.

Keywords: Polymorphism; Genotype; Periapical lesions; Arteriosclerosis; Matrix metalloproteinases

Introduction

Matrix metalloproteinases (MMPs) are zinc and calcium dependent enzymes capable of degrading almost all extracellular matrix and basement membrane components [1]. This group of proteolytic enzymes believed to be implicated in the breakdown of extracellular matrix in normal physiological processes, such as embryonic development, blastocyst implantation, organ morphogenesis, nerve growth, ovulation, cervical dilatation, postpartum uterine involution, endometrial cycling, hair follicle cycling, bone remodeling, wound healing, angiogenesis, apoptosis, etc. [2].

Matrixins play a critical role in pathological processes (e.g. arthritis, cancer, cardiovascular disease, nephritis, neurological disease, breakdown of blood brain barrier, periodontal disease, skin ulceration, gastric ulcer, corneal ulceration, liver fibrosis, emphysema, fibrotic lung disease, etc. [3]. According to the important role of MMPs in inflammation [4], it has been shown that genetic variation affecting the expression of MMPs influences the susceptibility and progression of various oral diseases [5]. Matrix metalloproteinases are strongly associated with levels of inflammation and play a major role in bone remodeling and bone resorption [6].

Bone matrix is comprised mostly of mineralized fibrillar type I collagen. MMPs are capable of cleaving native, nondenatured collagens with long uninterrupted triple helices and can function as collagenases *in vivo* [7].

Expression of MMPs is low in normal cells, and these low levels allow for healthy connective tissue remodeling. In pathologic conditions, however, the level of MMPs expression increases considerably, resulting in aberrant connective tissue destruction. Expression of MMPs is regulated primarily at the transcriptional level where the promoter of the genes responds to different regulators [8]. Some functional polymorphisms have been described in the regulatory region of MMPs genes [5]. Because destructive enzymes of the MMPs family are involved in this process, allele polymorphisms of MMPs genes are interesting candidates for analyses of the influence, susceptibility and severity of chronic periapical lesions (CPLs).

Subfamily of human colagenases has three members, from which MMP-1 (fibroblast type of colgenase, colagenase-1) is one of our interest [9]. Gen of the MMP-1 is localized on chromosome 11q22 and its expression was shown in various types of healthy cells (stromal fibroblasts, macrophage, endothelial and epithelial cells), as well as in different inflammatory and carcinoma cells [10].

Level of expression of MMP-1 can be under the influence of different single nucleotide polymorphism in promontory region. Insertion or deletion of the guanine from the position -1607 can be identified in humans in promoter of the gen of MMP-1 developing two

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CLINICAL RESEARCH

IL1 cluster gene polymorphisms in macedonian patients with chronic periodontitis

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Abstract: Several studies have investigated the genetic polymorphisms for cytokines as potential genetic markers for periodontitis. The aim of this study was to determine the prevalence of *IL1* cluster genes polymorphisms and their association with chronic periodontitis in the Macedonian population. The group of 114 unrelated Macedonian subjects with chronic periodontitis and 301 periodontitis-free Macedonian subjects were studied. DNA was isolated from peripheral blood leukocytes by phenol-chloroform extraction method. Cytokine genotyping was performed by PCR-SSP. The population genetics analysis package (PyPop) was used for analysis of the cytokine data for this report. Crude odds ratio (OR) was calculated as estimates of the relative risk with 95 % confidence interval (CI). Genotype frequency of *IL1B -511/C:T* was significantly higher in patients with periodontitis than in controls (OR=2.11, 95 % CI=1.35–3.32, p=0.001). *IL1* cluster gene haplotype frequencies of *TTTCT* and *TCTTT* were associated with higher risk for periodontitis (OR=5.06, 95 % CI=1.68–15.26, p<0.0014 and OR=8.35, 95 % CI=1.67–41.69, p<0.002, respectively). No significant association of *IL1* composite genotype (*IL1 -889A:IL1B +3962*) with periodontitis in Macedonians was found. The latter association was found to be significant in genotype *IL1B -511/C:T*, haplotype *TTTCT*, and haplotype *TCTTT*, but without significant association in *IL1* composite genotype *(Tab. 5, Ref. 43)*. Full Text in PDF *www.elis.sk.*
Key words: periodontitis, SSP polymorphism, genetic, interleukine-1, Republic of Macedonia.

Periodontitis is a multifactor disease whereby both environmental and genetic factors contribute to its etiology and/or clinical severity. Cytokines are potent immunomodulating molecules that mediate the inflammation and immune response, and at the same time influence the cellular activation, differentiation, and function. There are many reports showing that a number of cytokine genes are polymorphic and that polymorphisms in gene regulatory regions correlate with the cytokine secretion (1, 2). As these polymorphisms are independently segregated, one individual may have a cytokine expression pattern quite different from that of another (3).

Until recently, the *IL1* ligand family consisted of four members: I*L1A, IL1B, IL1RA*, and *IL18*. Based on conservation of amino acid sequence, identification of gene structure and three dimensional structures, six additional members of this family have been described since. The entire new gene map of the region of chromosome 2 between the *IL1B* and *IL1RN* loci was proposed, suggesting that each of the new *IL1* family members arose from a common ancestral gene that later became duplicated (4, 5). The novel *IL1* family members have been described by several groups using their own nomenclature, thus resulting in a number of different names for the same molecule (6, 7).

The prototypic members of the *IL1* family gene cluster are the genes *IL1A* (MIM 147760), *IL1B* (MIM 147720), and *IL1RN*. *IL1A* and *IL1B* encode pro inflammatory cytokines involved in host defense against infection. The IL-1 receptor antagonist, encoded by the gene *IL1RN*, is an anti-inflammatory non-signaling molecule that competes for receptor binding with IL-1A and IL-1B (8, 9). However, hundreds of single nucleotide polymorphisms are known for each gene of the *IL1* cluster (10).

The protein encoded by *IL1R1* gene is a cytokine receptor that belongs to the interleukin 1 receptor family. This protein is a receptor for interleukin 1 alpha (IL-1A), interleukin 1 beta (IL-1B), and interleukin 1 receptor, type I (IL-1R1/IL-1RN). It is an important mediator involved in many cytokine-induced immune and inflammatory responses (11). Five cytokine polymorphisms connected with the *IL1* cluster gene on chromosome 2 were included in the cytokine polymorphism component: *IL1A −889, IL1B -511, IL1B +3962, IL1R psti 1970*, and I*L1RN mspa 11100*. Cytokines are the key factors of mediating the inflammatory process during periodontal disease. Functional polymorphisms of the *IL1* genes have been proposed to be a risk factor for periodontitis. Periodontitis is an infective disease, where chronic inflammation develops under the influence of microorganisms forming the dental plaque.

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Short communication

Development and validation of RP HPLC method for determination of betamethasone dipropionate in gingival crevicular fluid

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A simple RP HPLC method for quantification of betamethasone dipropionate (BDP) in gingival crevicular fluid (GCF) has been developed and validated. GCF represents a valuable matrix for therapeutic monitoring of drugs used in the treatment of periodontal disease. The proposed method involves single step extraction for sample preparation. The calibration curve for BDP was linear over the concentration range of 0.10–2.00 μg mL^{-1} (R^2 = 0.9971). RSD values of intra- and inter-day precision ranged 2.2–4.5 and 1.6–5.7 %, while accuracy values were higher than 96.6 and 97.0 %, respectively. The described method can be successfully applied for determination of betamethasone concentrations in GCF obtained from patients with chronic periodontitis after local treatment with BDP cream 0.5 mg g^{-1}.

Keywords: betamethasone dipropionate, gingival crevicular fluid, HPLC, periodontal disease

Periodontal disease is a chronic inflammatory disease of the oral cavity affecting the soft- and hard-supporting structures of the teeth (1, 2). Although bacterial in etiology, current findings imply that the pathogenesis of periodontitis is mediated by the host's response (3). Corticosteroids can act as host's modulation agents and represent a therapeutical approach in periodontal therapy (4–6). One of the mostly used corticosteroids in clinical practice is betamethasone dipropionate (BDP). Therapeutically, it is used in the treatment of periodontal disease by local application in the periodontal pocket, after scaling and root planing. Compared to other corticosteroids intended for local application, such as hydrocortisone or triamcinolone acetonide, BDP shows greater anti-inflammatory activity probably due to stabilization of lysosomal membranes and blocking the actions of the invasive mediators of inflammation (6, 7).

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Development and validation of RP HPLC assay of chlorhexidine in gingival crevicular fluid

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Summary

A reversed – phase HPLC method with UV detection for determination of chlorhexidine in gingival crevicular fluid (GCF) was optimized and validated, using chlorpheniramine as an internal standard. The chromatographic separation was performed on Discovery C18 HPLC column with 0.01 mol L^{-1} phosphate buffer (pH=3.0), triethylamine and acetonitrile (66:1:33, *V/V/V*), as mobile phase. Under the optimized HPLC conditions, linearity was obtained in the range of 0.5-5.0 μg mL^{-1} with LOD 0.07 μg mL^{-1} and LLOQ 0.5 μg mL^{-1}. The described method can be successfully applied for determination of chlorhexidine concentrations in GCF obtained from patients with chronic periodontal disease treated with PerioChip™.

Key words: chlorhexidine digluconate, PerioChip™, RP-HPLC, gingival crevicular fluid, periodontal disease

BOSNIAN JOURNAL

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The role of inflammation and apoptosis in cyclosporine A – induced gingival overgrowth

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ABSTRACT

Cyclosporin A(*CsA*) - induced gingival overgrowth(GO) is a current problem of tissue-specific mechanism which is still incompletely explained. The apoptotic process has been of particular interest like a new concept in the etiology of this unwanted effect.

The aim of our study was to detect the level of apoptosis, expression bcl-2 and p53, associated with the different dosis of *CsA*, in gingival stroma. A cohort of 84 kidney transplant recipients was divided into four subgroups based on average daily dose of therapeutically applied *CsA* (Neoral®), (100 mg, 125 mg, 150 mg and 175 mg). The control group consisted of 21 patients, clinically diagnosed with periodontitis, who were not subjected to any medicamentous treatment causing gingival overgrowth.

The following indexes were analyzed: plaque index (PI), index of gingival inflammation (GI) according to Loe-Silnes, and gingival overgrowth index (GOI) according to MacGaw et al. The tissue samples were subjected to a semiquantitative analysis to detect apoptotical cells and imunohistochemically stained to detect the expression of the bcl-2 and p53 proteins.

The difference in percentage of apoptotic cells between the group taking 175mg and other subgroups, as well as the control group was statistically significant ($p<0.05$). There was a significant difference in percentage of expression bcl-2 between the 175 mg group compared to the other three subgroups and the control (p 0.001). However, a statistically significant positive correlation between the medicament dose, p53, apoptosis, and bcl-2 was registered ($p<0.05$).

Inflammation plays the most important role in the induction of apoptosis and proliferation in gingival tissues.

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KEY WORDS: gingival overgrowth, cyclosporin A, gingival inflammation, apoptosis, bcl-2, p53.

INTRODUCTION

Gingival overgrowth (GO) is very often associated with the use of cyclosporine A (*CsA*) [1]. Although some studies indicate several factors as taking part in the pathogenesis of gingival overgrowth (GO), the dosage, the serum and saliva concentration of the medicament, the duration of treatment, oral hygiene and the age of each individual is of course worth emphasizing [2]. However, the genetics of each individual, the susceptibility of the gingiva including also inflammation should not be put a side as well, which can additionally render the diagnosis and prognosis of these conditions more difficult [3, 4, 5]. Some studies report that the fibroblastic gingival substrate is caused by defective collagen synthesis homeostasis and degradation, particularly of type I collagen, resulting in increased accumulation of collagen fibres, extracellular matrix and inflammation cells in gingival fibrotic tissue [6]. Other studies emphasize apoptosis as a controlling mechanism of the GO, as well as cascade of specific biochemical reactions, which go together with increased level of intracellular Ca^{2+}. A common feature of fenitoin, nifedipine and cyclosporine is the fact that they are all Ca^{2+} antagonists. The blockade of one or several steps in the cascade of the *CsA* interactions, may result in apoptotic changes and reduced caspase leading also to an increased level of growth of the gingival tissue [7, 8]. Apoptosis as a physiological death plays a vital role in the cell proliferation and differentiation. In addition, tissue homeostasis is maintained through a balance between the cell proliferation and cell death. The apoptotic cell death is considered as a possible participant in the pathogenesis of many diseases, including cancer, autoimmune illnesses and virus infections alike [9, 10, 11]. The crucial apoptotic regulation is realized through two transmembranic proteins: the deadly p53 gene

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МАКЕДОНСКА АКАДЕМИЈА НА НАУКИТЕ И УМЕТНОСТИТЕ

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ORAL FINDINGS IN END-STAGE RENAL DISEASE

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Abstract

The aim of the study was to analyse and compare the most frequent clinical oral symptoms, signs and lesions at end-stage renal disease (ESRD), before kidney transplantation (BKT) and after kidney transplantation (AKT). A total of 35 subjects with ESRD were included, 19 in group A (BKT) and 16 in group B (AKT). Oral lesions were classified according to referent clinical diagnostic criteria: Serum albumins, urea, creatinine and salivary urea, creatinine uremic acid were determined by standard biochemical spectrophotometric methods (Human, Germany). For serum albumin concentration measurement (g/L) the method of bromcresol green assay was used while serum and salivary uric acid determination (μmol/L) was performed according the uricase/PAP method. Serum creatinine concentration was measured (μmol/L) with the Jaffe kinetics method, without deproteinization. Oral signs, symptoms and lesions were higher in group A: metallic taste (O.R. = 6.61/ ± 95% CI : 1.13 < O.R. < 38.69), dry mouth (O.R. = 30/ ± 95% CI : 3.15 < O.R. < 285.71), uremic stomatitis (O.R. = 6.5/ ± 95% CI : 1.47 < O.R. < 28.80 and coated tongue (O.R. = 11.73/ ± 95% CI : 2.31 < O.R. < 59.54). On the other hand, in group B, gingival enlargement (O.R. = 59.5/ ± 95% CI : 7.41 < O.R. < 478.05) was more common. High statistically significant differences were recorded between group A and B for dry mouth and gingival enlargement ($p > 0.001$). Blood urea, creatinine and albumin levels, as well as salivary urea creatinine and uraemic acid values, were significantly higher in group A. Chances of the appearance of all symptoms, clinical signs and lesions, except gingival enlargement, were greater in group A as against group B. Some of our findings correspond with the stage of the disease and some with the use of medicaments in treatment.

Key words: End-stage renal disease, Kidney transplantation, Oral sign, Oral lesion.

Introduction

Chronic renal failure (CRF) could be defined as a progressive and irreversible glomerular filtration rate (GFR) decrease, resulting in an increase of serum creatinine and blood nitrogen-containing compounds [1, 2]. Urea levels

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T-CELL SUBPOPULATIONS IN LESIONS OF ORAL LICHEN PLANUS

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T-CELL SUBPOPULATIONS IN LESIONS OF ORAL LICHEN PLANUS

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Abstract

Aim of the study: To determine the distribution and frequency of T(CD3) cells and cell sub-populations in tissue specimens of erosive lichen planus (EOLP).

Material and Method: Tissue specimens from buccal mucosa were taken from 14 healthy individuals – control group (CG) – and 17 subjects with EF-OLP. Applying monoclonal antibodies, T(CD3) cells, T cell subpopulations, The CD4, CD8 and CD4/CD8 ratios in both groups were determined. Cells in the epithelium and lamina propria were quantitatively and qualitatively determined in both groups. Data were analysed using the Student's t-test.

Results: There were 5.95 ± 2.12% T(CD3) cells in the control group as against 9.80 ± 4.04% in the examined group ($p < 0.001$). The distribution of T(CD3) cells in the lamina propria was 25.35 ± 12.04% in the examined group compared to the control group ($p < 0.001$). There were 3.45 ± 2.05% CD4 epithelial cells in the control group and 4.00 ± 1.95% in the examined group ($p < 0.4$). There were 2.50 ± 1.8% CD8 cells in the control group and 5.80 ± 3.72% in the examined group ($p < 0.001$). The CD4/CD8 ratio was 0.51 ± 0.12% in the examined group and it was evidently reduced in comparison with the control group. An increased distribution of CD4 cells (10.30 ± 7.60%) and CD8 cells (15.05 ± 5.20%) in the lamina propria compared with the epithelium was observed in the examined group ($p < 0.001$). The CD4/CD8 ratio in the epithelium was 0.51 ± 0.12% as against the ratio of the lamina propria, which was slightly increased (0.68 ± 0.48%) with a low statistically significant difference ($p < 0.05$).

Conclusion: Differences in the distribution of T-lymphocyte subsets between the control and examined groups were found ($p < 0.001$). An increased distribution and frequency of CD4 and CD8 cells in the lamina propria was observed. These were predominantly located in the sub-basal region of the stratum papillare and rarely seen in the intra-epithelial region.

Key words: erosive lichen planus, oral lichen planus, T(CD) cells, T-cell subpopulations, CD4 lymphocytes, CD8 lymphocytes.

Introduction

Oral lichen planus (OLP) is a chronic mucosal condition that is commonly encountered in dental practice. The heterogenic clinical finding is manifested on the buccal mucosa as white plaque, papules, white striations, eryt-

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