



УНИВЕРЗИТЕТ У БЕОГРАДУ

Адреса: Студентски трг 1, 11000 Београд, Република Србија
Тел.: 011 3207400; Факс: 011 2638818; E-mail: officebu@rect.bg.ac.rs

**ВЕЋЕ НАУЧНИХ ОБЛАСТИ
МЕДИЦИНСКИХ НАУКА**
Тел. 3207-432; 3207-430

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На основу члана 47. став 5. тачка. 3. Статута Универзитета у Београду ("Гласник Универзитета у Београду", број 162/11- пречишћени текст, 167/12, 172/13 и 178/14) и чл. 14. – 21. Правилника о већима научних области на Универзитету у Београду ("Гласник Универзитета у Београду", број 134/07, 150/09, 158/11, 164/11 и 165/11), а на захтев Стоматолошког факултета, број: 1192/1 од 19.6.2014. године, Веће научних области медицинских наука, на седници одржаној 8.7.2014. године, донело је

ОДЛУКУ

ДАЈЕ СЕ сагласност на предлог теме докторске дисертације:

Кандидат:
др Драгана Ракашевић

Назив теме: „Процена ефикасности фотодинамске терапије код периимплантитиса“.

Председник Већа

Проф. др Весна Спасојевић-Калимановска



Доставити:

- Факултету,
- секретару Већа,
- архиви Универзитета

УНИВЕРЗИТЕТ У БЕОГРАДУ
СТОМАТОЛОШКИ ФАКУЛТЕТ
СЕКРЕТАРИЈАТ

ПРИМЉЕНО: 14-07-2014

Орг. јед.	Број	Прилог	Вредност
03	1192/1		



Univerzitet u Beogradu
STOMATOLOŠKI FAKULTET

Dr Subotića 8, tel: 2685-288, e-mail: biblioteka@stomf.bg.ac.rs
Centralna biblioteka



P O T V R D A

U Centralnoj biblioteci Stomatološkog fakulteta urađena je kategorizacija objavljenih radova DRAGANE RAKAŠEVIĆ, indeksiranih u Web of Science bazi.

Na osnovu Pravilnika o postupku i načinu vrednovanja, i kvantitativnom iskazivanju naučnoistraživačkih rezultata istraživača ("Službeni glasnik RS", br. 24/16) utvrđeno je da je Dragana Rakašević publikovala rad u časopisu sa impakt faktorom (*Journal Citation Reports* lista).

Dragana Rakašević, Zoran Lazić, Bojan Rakonjac, Ivan Soldatović, Saša Janković, Marko Magić, Zoran Aleksić. Efficiency of photodynamic therapy in the treatment of peri-implantitis – A three-month randomized controlled clinical trial. SRPSKI ARHIV ZA CELOKUPNO LEKARSTVO (2016), 144(9-10):478-484. (Kategorija M23)

Bibliotekar

Centralne biblioteke

Jelena Jaćimović



U Beogradu, 3.11.2016. godine

**NAUČNOM VEĆU STOMATOLOŠKOG FAKULTETA
UNIVERZITETA U BEOGRADU**

PREDMET

Izveštaj komisije za ocenu i odbranu doktorske disertacije kandidata dr Dragane Rakašević

Na sednici Nastavnog Nučnog veća Stomatološkog fakulteta u Beogradu, održanog 28.02.2017. godine, broj 3/10, imenovana je komisija za ocenu završene doktorske disertacije pod naslovom:

„ Procena efikasnosti fotodinamske terapije kod periimplantitisa“

kandidata **dr Dragane Rakašević**, zaposlenog u zvanju naučni saradnik na projektu Ministarstva prosvete i nauke republike Srbije. Mentor doktorske disertacije je Prof. Dr Zoran Aleksić.

Komisija za ocenu završene doktorske disertacije imenovana je u sastavu:

1. Profesor Dr Saša Janković, Stomatološki fakultet, Univerzitet u Beogradu
2. Profesor Dr Božidar Dimitrijević, Stomatološki fakultet, Univerzitet u Beogradu
3. Profesor Dr Zoran Lazić, Vojno Medicinska Akademija, Beograd
4. Docent Dr Jelena Roganović, Stomatološki fakultet, Univerzitet u Beogradu

Na osnovu analize priložene doktorske disertacije, komisija za ocenu završene doktorske disertacije jednoglasno podnosi Naučnom veću Stomatološkog fakulteta sledeći

IZVEŠTAJ

BIBLIOGRAFSKI PODACI O KANDIDATU

Dragana Rakašević rođena je 17.10.1987. godine u Sremskoj Mitrovici. Svoje osnovno, gimnazijsko i srednje-mužičko obrazovanje završila je u Sremskoj Mitrovici, 2006. godine, sa prosečnom ocenom 5.00. Stomatološki fakultet, Univerziteta u Beogradu upisala je 2006. godine. Tokom osnovnih studija prezentovala je 2 naučna rada. Nagrađena je 2010. godina za najbolji naučno-istraživački rad na biomedicinskom studentskom kongresu sa internacionalnim učešćem.

Takođe, 2011. proglašena je za najboljeg studenta V godine, Stomatološkog fakulteta u Beogradu. Diplomirala je u oktobru, 2011.godine sa prosečnom ocenom 8.78. Pripravnički staž obavila je na klinikama Stomatološkog fakulteta Univerziteta u Beogradu, a stručni ispit položila je 2012. godine. Doktorske studije iz oblasti Parodontologije upisala je 2011. godine. Naučno-istraživački rad u okviru svoje doktorske disertacije objavila je pod mentorstvom Prof. dr Zorana Aleksića. Položila je sve ispite predviđene planom i programom akademskih doktorskih studija sa prosečnom ocenom 9,94 (devet i devedeset četiri/100). Upisala je 2015. godine, specijalizaciju iz oblasti Parodontologija i Oralna Medicina na Stomatološkom fakultetu, Univerziteta u Beogradu. Saradnik je na projektu Ministarstva Prosvete i nauke republike Srbije (#41008: „Interakcija etiopatogenetskih mehanizama parodontopatije i peri-implantitisa sa sistemskim bolestima današnjice“, rukovodilac Prof. dr Vojislav Leković). Autor i koautor je na sedam radova saopštenih na domaćim i međunarodnim kongresima i naučnim skupovima, predavač po pozivu i učesnik u brojnim nacionalnim i međunarodnim kongresima i skupovima. Svoje znanje svakodnevno usavršava čitajući stručnu literaturu i posećujući brojne inostrane workshop-ove i kongrese. Od 2013. godine član je Udruženja parodontologa Srbije i Evropske federacije parodontologa.

Objavljeni radovi i izvodi u zbornicima međunarodnih i domaćih skupova:

- Rakasevic D., Layic Z, Rakonjac B, Soldatovic I, Jankovic S, Magic M., Aleksic Z *Efficiency of photodynamic therapy in the treatment of peri-implantitis - A three-month randomized controlled clinical trial (Article)*. SRPSKI ARHIV ZA CELOKUPNO LEKARSTVO, (2016), vol. 144 br. 9-10, str. 478-484 (M23).
- Rakasevic D, Lazic Z, Nikolic Jakoba N, Jankovic S, Roganovic J., Djukic Lj., Aleksic Z. *Impact of photodynamic therapy on clinical and immunological parameters in the treatment of peri-implantitis after a period of three months*. Simpozijum oralnih hirurga i oralnih implantologa Srbije. Beograd, Serbia 25rd-26rd of November 2016.
- Markovic D, Rakasevic D, Trisic D. *Application of High-Power Diode Laser and Photodynamic Therapy in Endodontic Treatment- Review of Literature*. *Balk J Dent Med*, 2015, 19:71-74
- Rakasevic D, Lazic Z, Rakonjac B, Nikolic Jakoba N, Aleksic Y. *Efficiency of photodynamic therapy in the treatment of peri-implantitis. A randomized controlled trial*. 8th Conference of the European Federation of Periodontology. Journal of Clinical Periodontology, 42(Suppl S17): p.441. London, United Kingdom, June 2015.
- Milinkovic I, Rakasevic D, Aleksic Z, Jankovic S. *Clinical application of collagen tissue matrix and enamel matrix derivate in the treatment of multiple gingival recessions. A randomise controlled clinical trial*. 8th Conference of the European Federation of

Periodontology. Journal of Clinical Periodontology, 42(Suppl S17): p.238. London, United Kingdom, June 2015.

- Rakasevic D, Rakonjac B, Lazic Z, Aleksic Z. *Efficiency of photodynamic therapy in the treatment of peri-implantitis. A randomised controlled trial*. Oral presentation at 20th Congress of the Balkan Stomatological Society. Bucharest, 23rd-26rd of April 2015.
- Rakasevic D. Evaluation of photodynamic therapy in the treatment of peri-implantitis. Oral presentation as a lecture by invitation in BREDENT days, Belgrade, March 2015.
- Rakasevic D, Peric T, Belca I, Tadic N, Markovic D. *Influence of soft drink in initiation and progression of enamel carious lesion: AFM study*. Poster presentation at 19th Congress of the Balkan Stomatological Society. Belgrade, April 2014.

PREGLED DOKTORSKE DISERTACIJE

Nastavno-naučno veće Stomatološkog fakulteta, Univerziteta u Beogradu je na drugoj redovnoj sednici održanoj 25.02.2014. godine usvojilo pozitivan izveštaj stručne komisije za ocenu predloga teme, pod mentorstvom prof. dr Zorana Aleksića.

A) Prikaz sadržaja doktorske disertacije

Doktorska disertacija dr Dragane Rakašević napisana je na ukupno 120 strana i podeljena je na sledeća poglavlja: uvod, hipoteza i ciljevi rada, materijal i metode, rezultati, diskusija, zaključci i literatura. U disertaciji se nalazi ukupno 10 tabela, 9 grafikona i 28 slika. Doktorska disertacija sadrži Sažetak na srpskom i engleskom jeziku, Zahvalnost, Biografiju kandidata i Podatke o komisiji.

U **uvodu** je definisano šta su peri-implantna oboljenja i data je precizna definicija i podela ovih oboljenja sa prevalencom zastupljenosti ove bolesti. Navedena je najsavremenija klasifikacija peri-implantitisa, etiopatogeneza nastanka ovog oboljenja kao i potencijalni faktori rizika koji dovode do pojave, nastanka i progresije peri-implantitisa. Poseban akcenat u etiologiji nastanka peri-implantitisa prikazan je kroz imunološki odgovor organizma na ovo oboljenje. Prikazana je klinička slika i metode uz pomoć kojih mogu da se dijagnostikuju peri-implantitisi. Detaljno su objašnjeni svi terapijski postupci koji se mogu primenjivati u terapiji peri-implantitisa. Poseban akcenat i pažnja data je na metodama dekontaminacije implantne površine tokom hirurške procedure. Na adekvatan način je u potpunosti opisana razlika između svih do sada primenjenih metoda dekontaminacije implantne površine i date su prednosti i nedostaci do sada primenjivanih metoda.

Laserska terapija i primena fotodinamske terapije spominju se kao savremenije metode terapije peri-implantitisa sa potencijalnom mogućnosti efikasne dekontaminacije same implantne površine. U doktorskoj disertaciji detaljno su opisani principi rada lasera, podela lasera i njihove međusobne razlike kao i njihova upotreba u stomatologiji. Poseban akcenat stavlja se na fotodinamsku terapiju, koja je opisana kao novo neinvazivno pomoćno terapijsko sredstvo sa širokom primenom u stomatologiji i medicini. Pozivajući se na savremenu literaturu pokazan je način delovanja i mehanizam fotodinamske terapije, kao i primena i uticaj ove metode u savremenoj parodontološkoj i implantološkoj terapiji. U dosadašnjoj naučnoj i stručnoj literaturi postoji malo radova koji se bave uticajem fotodinamske terapije na imunološke i mikrobiološke parametrima nakon hirurške terapije peri-implantitisa. **Hipoteza** ove disertacije polazi od pretpostavke da primenom fotodinamske terapije kao neinvazivne terapijske metoda može da dođe do poboljšanja u kliničkim, imunološkim i mikrobiološkim parametrima, nakon hirurške terapije. Primenom ove pomoćne terapije može se postići značajno smanjenje nivoa pro-inflamatorinih citokina koji pospešuju i održavaju zapaljenski odgovor tkiva i indirektno učestvuju u koštanoj resorpciji, u odnosu na primenu standardnih metoda. Na ovaj način omogućava se poboljšanje kliničkih parametara.

Ciljevi rada su precizno definisani.

U poglavlju **materijal i metode** je navedeno da se radi o randomizovanom kliničkom istraživanju, koje je izvođeno u dve Kliničke institucije: Klinika za parodontologiju, Stomatološki fakultet Univerzitet u Beogradu i Klinika za Implantologiju, Vojno-Medicinska Akademija. Obrazloženi su kriterijumi za uključanje u studiju, kao i kriterijumi za isključenje iz studije. Svi pacijenti su dali pisani pristanak pre uključanja u studiju. Opisani su klinički parametri koji su bili praćeni. Detaljno su opisani postupci i metode za imunološku i mikrobiološku analizu. Precizno i jasno objašnjen je terapijski postupak koji je bio podeljen u više faza. Peri-implantitisi bili su podeljeni u dve grupe na osnovu metode dekontaminacije implantne površine, tokom hirurške procedure. Obrazložen je period praćenja. Klinički, mikrobiološki i imunološki parametri posebno su obrađeni i analizirani pomoću savremenog ANOVA statističkog programa. Međusobno je upoređena povezanost kliničkih i imunoloških parametara. Pearsonov koeficijent korelacije korišćen je da bi se pokazalo postojanje povezanosti između kliničkih parametara i interleukina i između samih interleukina pre i nakon terapije. Ova studija je sprovedena u skladu sa Helsinškom deklaracijom, a odobrena je i od strane Etičkog komiteta, Stomatološkog fakulteta, Univerziteta u Beogradu. Svi pacijenti su dali pisani pristanak pre uključanja u studiju.

U poglavlju **rezultati** detaljno su opisani i jasno predstavljeni svi dobijeni rezultati.

Diskusija je napisana jasno i pregledno, uz prikaz podataka drugih istraživanja sa uporednim pregledom dobijenih rezultata doktorske disertacije.

Zaključci sažeto prikazuju najvažnije nalaze koji su proistekli iz rezultata rada.

Korišćena **literatura** sadrži spisak od 178 referenci.

B) Kratak opis postignutih rezultata

Ukupno je bilo tretirano 52 peri-implantitisa kod pacijenata približno iste starosne dobi, bez statistički značajne razlike u distribuciji godina i pola između ispitivanih grupa. Nisu bili zabeleženi neželjeni efekti i komplikacije nakon hirurške procedure i tokom perioda praćenja. Kod trećine ispitanika (35%) dijagnostikovana je ranije lečena parodontopatija. Rezultati istraživanja pokazali su pozitivan uticaj makrodizajna i mikrodizajna implantne površine na pojavu peri-implantitisa. Peri-implantitisi najčešće su bili zastupljeni kod implantata sa paralelnim zidom (59.6%), dok je najučestalija pojava ovog oboljenja bila zabeležena kod implantata sa TiU površinom (53.85%) i cementiranim fiksni rad (62%). Lokalizacija peri-implantitisa bila je učestalija u molarnoj regiji mandibule (63%). Rezultati istraživanja nisu pokazali povezanost uticaja lokalizacije peri-implantitisa sa kliničkim, mikrobiološkim i imunološkim parametrima ($p > 0.05$). Pokazano je da u obe tretirane grupe dolazi do statistički značajnog smanjenja dubine peri-implantnog džepa (DPDŽ) i povećanja nivoa pripojnog epitela (NPE), 3 meseca nakon terapije, u odnosu na zabeležene početne vrednosti ($p < 0.0001$). Nije postojala statistički značajna razlika u primeni terapijskih modaliteta u DPDŽ i NPE između ispitivanih grupa u periodu praćenja. Prikazano je da primenom FDT u eksperimentalnoj grupi, dolazi do statistički značajnog smanjenja krvarenja na provokaciju u odnosu na zabeležene početne vrednosti, kao i u poređenju sa vrednostima dobijenih u kontrolnoj grupi ($p = 0.002$). Primenom obe terapijske metode dekontaminacije implantne površine omogućava se smanjenje pro-inflamatornih citokina IL-17A, IL-6, IL-21 i IL-1 β , poređenih sa koncentracijama detektovanih pre početka terapije. Nivo koncentracije IL-17A, IL-6 i IL-1 β statistički se značajno razlikovao 3 meseca nakon primene fotodinamske terapije u odnosu na primenu standardne terapijske metode ($p < 0.001$). Nije zabeleženo prisustvo IL-22 i IL-23, kako pre tako i nakon primenjene terapije. U rezultatima istraživanja prikazana je pozitivna korelacija između ispitivanih interleukina pre i tri meseca nakon terapije. Pokazano je da pre terapije postoji statistički značajna povezanost između IL-21 i IL-17A ($p = 0.003$), dok je tri meseca nakon terapije pozitivna korelacija i statistički značajna razlika postojala između IL-17 i IL-1 β ($p = 0.005$); IL-17 i IL-6 ($p = 0.02$). Iz periimplantnog džepa i sa implantne površine bili su izolovani striktno i fakultativno anaerobni mikroorganizmi: *Porphyromonas gingivalis*, *Prevotella spp.*, *Peptostreptococcus spp.*, *Fusobacterium nucleatum*, *Actinomyces spp.*, *Veillonella*, *Streptococcus spp.*. Nije zabeležena statistički značajna razlika u distribuciji ovih anaeroba pre terapije ($p > 0.05$). Nakon primenjene obe metode dekontaminacije implantne površine došlo je do statistički značajnog smanjenja i eliminacije anaerobnih mikroorganizama.

C) Uporedna analiza doktorske disertacije sa rezultatima iz literature

Peri-implantitis je multikauzalno oboljenje, čiji glavni uzročnici, parodontopatogeni i neadekvatni imuni odgovor organizma, dovode do promena u peri-implantnom tkivu praćeno koštanom resorpcijom, inflamacijom mekog tkiva i krvarenje na provokaciju. Pokazano je da

progresijom bolesti i pogoršavanjem kliničkih parametara dolazi do produkcije citokina: IL-1 β , IL-6, IL-12 i IL-21, aktivacije osteoklasta i regurgitacije limfocita. Aktivirani pro-inflamatorni citokini povećavaju destrukciju tkiva i aktiviraju rezidualne ćelije koje dodatno povećaju destruktivni odgovor organizma (Mootha, Malaiappan et al. 2016). Ranije su rađene brojne studije preseka koje su detektovale koncentracije pro-inflamatornih interleukina i prikazivale njihov uticaj u nastanku i progresiji peri-implantitisa. Prisutnost IL-17 detektovanog iz periimplantnog cervikalnog fluida kod peri-implantitisa dokazano je više puta (Severino, Beghini et al. 2016). Polazeći od ranije poznatih činjenica i uzroka nastanka i progresije peri-implantitisa, otvara se potreba za adekvatnom metodom dezinfekcije i dekontaminacije implantne površine i periimplantnog prostora. Nedostatak standardnih protokola za dekontaminaciju implantne površine tokom hirurške terapije peri-implantitisa sa ciljem postizanja stabilnih i predvidljivih rezultata, utiču na potrebu ispitivanja značaja i uloge neinvazivnih metoda kao što je fotodinamska terapija. Prethodne studije koristile su razne metode dekontaminacije kao što je primena sistemski ili lokalnih antibiotika koje su dovodile najčešće do rezistencije mikroorganizama ili alergijske reakcije i neželjenog dejstva (Heitz-Mayfield and Mombelli 2014). U istraživanju autor primenjuje fotodinamsku terapiju kao metodu za dekontaminaciju implantne površine sa ciljem smanjenjem inflamatornog odgovora domaćina i omogućavanja kasnije reparacije periimplantnog tkiva. Do danas se nijedna studija još uvek nije bavila uticajem fotodinamske terapije na kliničke i imunološke parametre nakon hirurške terapije peri-implantitisa. Mali broj studija bavio se metodama dekontaminacije i njegovim uticajem na kliničke i mikrobiološke (de Waal, Raghoobar et al. 2013, de Waal, Raghoobar et al. 2014). U ranijoj studiji pokazano je da primenom diodnog lasera i fotodinamske terapije dolazi do statističkog značajnog smanjenja IL1- β i IL-17 u poređenju sa samo kauzalnom (nehirurškom) terapijom (Teymouri, Farhad et al. 2016). Rezultati doktorske disertacije nisu pokazali statistički značajno smanjenje pro-inflamatornih interleukina nakon nehirurške terapije. Ranije rađene studije dokazale su da nehirurška terapija peri-implantitisa nema značajan uticaj u postizanju stabilnih i predvidljivih rezultata (Schwarz, Hegewald et al. 2013). Rezultati doktorske disertacije potvrdili su ovu činjenicu jer su pokazali da nakon primene hirurške terapije praćene adekvatnom metodom dekontaminacije dolazi do statistički značajnog smanjenja koncentracije pro-inflamatornih interleukina. Primenom fotodinamske terapije pokazana je mogućnost potpune eliminacije parodontopatogena sa implantnih površina dovodeći do poboljšanja kliničkih parametara. Na ovaj način pokazana je i potvrđena je superiornost i veća efikasnost hirurške terapije u odnosu na nehiruršku terapiju (Schwarz, Sahm et al. 2011, Schwarz, John et al. 2014).

D) Objavljeni radovi koji čine deo doktorske disertacije

Rakasevic D., Lazic Z, Rakonjac B, Soldatovic I, Jankovic S, Magic M., Aleksic Z *Efficiency of photodynamic therapy in the treatment of peri-implantitis - A three-month randomized controlled clinical trial (Article)*. SRPSKI ARHIV ZA CELOKUPNO LEKARSTVO, (2016), vol. 144 br. 9-10, str. 478-484

E) Zaključak (obrazloženje naučnog doprinosa)

Doktorska disertacija „ **Procena efikasnosti fotodinamske terapije kod periimplantitisa**“ dr Dragane Rakašević, kao prvi ovakav rad u našoj populaciji predstavlja originalni naučni doprinos o primeni fotodinamske terapije u terapiji peri-implantitisa. Sagledavajući aktuelnu problematiku, uz jasno zadate ciljeve, savremenu metodologiju, adekvatnu statističku obradu naših podataka, došli smo do zaključaka da primenom fotodinamske terapije može se postići adekvatna dekontaminacija implantne površine, smanjujući nivo koncentracije pro-inflamatornih interleukina, eliminišući parodontopatogene i poboljšavajući kliničke parameter. Na ovaj način pokrenuli smo pitanje za potrebom daljih istraživanja i daljeg praćenja postignutih rezultata. Istraživanje je pokazalo da fotodinamska terapija može biti korisna pomoćna metoda u terapiji peri-implantitisa i da kao takva može više da se upotrebljava u budućnosti.

KONAČNA OCENA DOKTORSKE DISERTACIJE

Ova doktorska disertacija je urađena prema svim principima naučnog istraživanja. Ciljevi su bili precizno definisani, naučni pristup je bio originalan i pažljivo izabran, a metodologija rada je bila savremena. Rezultati su pregledno i sistematično prikazani i diskutovani, a iz njih su izvedeni odgovarajući zaključci. Rezultati prikazani u ovoj disertaciji predstavljaju dobru osnovu za buduća istraživanja koja će primenom navedenih metoda ispitivati uspeh fotodinamske terapije u lečenju raznih drugih oboljenja. Doktorska disertacija ispunjava sve kriterijume propisane Zakonom o Univerzitetu i statutima Univerziteta i Stomatološkog fakulteta u Beogradu

Na osnovu svega navedenog, imajući u vidu dosadašnji naučni rad kandidata, komisija predlaže Naučnom veću Stomatološkog fakulteta, Univerziteta u Beogradu da prihvati doktorsku disertaciju dr Dragane Rakašević i odobri njenu javnu odbranu radi sticanja akademske titule doktora medicinskih nauka.

U Beogradu, 15.03.2017.

Članovi Komisije:

Prof. Dr Saša Janković

Prof. Dr Božidar Dimitrijević

Prof. Dr Zoran Lazić

Doc. Dr Jelena Roganović

Efficiency of photodynamic therapy in the treatment of peri-implantitis – A three-month randomized controlled clinical trial

Dragana Rakašević¹, Zoran Lazić², Bojan Rakonjac³, Ivan Soldatović⁴, Saša Janković¹, Marko Magić⁵, Zoran Aleksić¹

¹University of Belgrade, Faculty of Dental Medicine, Department of Periodontology, Belgrade, Serbia;

²Medical Military Academy, Department of Oral Implantology, Belgrade, Serbia;

³Medical Military Academy, Institute of Microbiology, Belgrade, Serbia;

⁴University of Belgrade, School of Medicine, Institute of Medical Statistics and Informatics, Belgrade, Serbia;

⁵University of Belgrade, Faculty of Dental Medicine, Department of Oral Surgery, Belgrade, Serbia

SUMMARY

Introduction Peri-implantitis is an inflammatory lesion of peri-implant tissues. Eradication of the causative bacteria and decontamination of the implant surface is essential in achieving predictable and stable clinical results. Photodynamic therapy (PDT) is non-invasive adjuvant therapeutic method to surgery in the treatment of bacterial infection.

Objective The aim of this study was to evaluate early clinical and microbiological outcomes of peri-implantitis after surgical therapy with adjuvant PDT.

Methods Fifty-two diagnosed peri-implantitis sites were divided into two groups. PDT was used for decontamination of implant surface in the study group; in the control group, chlorhexidine gel (CHX) followed by saline irrigation was applied. Several clinical parameters were recorded before the treatment (baseline values) and three months after surgical treatment. Samples for microbiological identification were collected before therapy, during the surgical therapy (before and after decontamination of implant surface), and three months thereafter, and analyzed with identification systems using biochemical analysis.

Results The use of PDT resulted in significant decrease of bleeding on probing in comparison to CHX ($p < 0.001$). It showed significant decontamination of implant surfaces with complete elimination of anaerobic bacteria immediately after surgical procedure and three months later.

Conclusion The results indicate that PDT can be used as an adjuvant therapy to surgery for decontamination of implant surface and surrounding peri-implant tissues within the treatment of peri-implantitis.

Keywords: peri-implantitis; decontamination; photodynamic therapy

INTRODUCTION

Peri-implantitis has been defined as an inflammatory process that affects the supporting marginal bone around an implant in function and results in bone resorption [1, 2]. It has been shown that the biofilm formed around osseointegrated implant has an important role in initiation and progression of peri-implant diseases [3, 4]. Most common microorganisms that are related to peri-implantitis are anaerobic bacteria, such as *Prevotella intermedia*, *Porphyromonas gingivalis*, *Aggregatibacter actinomycetemcomitans*, *Bacteroides forsythia*, *Treponema denticola*, *Prevotella nigrescens*, *Peptostreptococcus* spp., *Fusobacterium nucleatum*. Some authors suggested that *Staphylococcus aureus* and *Candida albicans* may be connected with initiation of peri-implantitis [3, 5]. Excessive mechanical stress, residual cement, poor plaque control could be among risk factors in the onset and development of peri-implantitis [2].

Peri-implantitis is a complex disease; therefore, the therapy continues to be a challenge. Surgical therapy of peri-implantitis has been suggested to be superior to non-surgical ther-

apy [6]. Decontamination of implant surface is one of the most important and difficult steps because of the screw-shaped design and roughness where microorganism and their products are incorporated. Many methods have been suggested, such as mechanical (dental curettes, ultrasonic scalers, air-powder abrasive), physical and/or chemical methods (citric acid, chlorhexidine, EDTA), usually combined with local or systematic antibiotics [7–12]. No single protocol has been suggested for solving this problem.

Photodynamic therapy (PDT) can be a new alternative approach for decontamination of implant surfaces combined with mechanical debridement during surgical therapy. It is a non-invasive therapeutic treatment of various infections caused by bacteria, fungi and viruses [13]. PDT has been defined as an oxygen-dependent reaction that occurs by action of low-energy single-frequency light (diode laser) and activation of the photoactive materials (photosensitizer). The photosensitizer is administered onto exposed tissue. It binds and dyes cells. Upon irradiation with light of specific wavelength of laser, photosensitizer undergoes a transition from a low energy ground state to

Correspondence to:

Dragana RAKAŠEVIĆ
Faculty of Dental Medicine
University of Belgrade
Dr Subotića 4, 11000 Belgrade
Serbia
dr.rakasevic@gmail.com

an excited singlet state. Subsequently, it may decay back to its ground state, transition high-energy triplet state, which can react with biomolecules such as endogenous oxygen to produce very reactive products, like singlet oxygen. Singlet oxygen has cytotoxic effect through damage of cell membrane and cell wall. Using this therapy, the target bacteria can be destroyed without adverse effect on the implant surface and surrounding peri-implant tissue [14, 15].

Some articles showed that using chlorhexidine (CHX) as adjunctive chemical agent to decontamination, reduced inflammation and microorganisms on the implant surface. Bioadhesive gels with higher concentrations of CHX have shown greater effectiveness in various clinical situations [16, 17]. However, ideal treatment for peri-implantitis is not defined yet. There are no clinical trials showing effects of PDT during surgical therapy of peri-implantitis.

OBJECTIVE

The aim of this study was to compare early clinical and microbiological effects of the adjuvant use of PDT to surgical treatment of peri-implantitis, comparing the effects of decontamination of the implant surface to those when 1% CHX gel was used.

METHODS

Patients were selected from two dental clinics: Department of Periodontology, University of Belgrade, and Department of Implantology, Military Medical Academy, from January 2014 to February 2015. The research protocol was submitted to and approved by the Ethical Committee, University of Belgrade, Serbia (number 36/28). The study was carried out in accordance with the ethical principles of the World Medical Association Declaration of Helsinki. Before the procedure, all participants were informed about the study and signed a written consent. All participants had to meet the following inclusion criteria: age >18 years, no periodontal or peri-implant treatment three months prior to the study, presence of minimum one implant in function, early or moderate type of peri-implantitis classified by Froum and Rosen [18]. Exclusion criteria were the following: uncontrolled medical conditions, use of systemic antibiotics in the previous three months, use of anti-inflammatory drugs in the previous six months, pregnancy and lactation, therapy of peri-implantitis in the last three months previously.

Measurements and recording of clinical parameters

The measurements were done and recorded before any treatment. All measurements were made at the following six sites of the implant with signs of peri-implantitis: mesiobuccal, mid-buccal, distobuccal, mesio-oral, mid-oral, disto-oral by one examiner (DR), using a graduated probe (PCPUNC 15, Hu Friedy, Chicago, IL, USA). The applied probing force was standardized force of 0.25 N. The im-

plant shoulder was used as landmark for calculation of mucosal recession and clinical attachment level. The following clinical parameters were registered:

- Peri-implant probing depth (PPD) – measured in millimeters from the mucosal margin to the bottom of the peri-implant pocket;
- Clinical attachment level (CAL) – measured in millimeters from the implant shoulder to the bottom of the peri-implant pocket;
- Mucosal recession (MR) – calculated as the difference between the CAL and PPD;
- Bleeding on probing (BOP) – evaluated as being **present** if bleeding was evident within 30 seconds after probing, or **absent**, if no bleeding was observed;
- Suppuration (SUP) – present or absent.

Clinical parameters were measured and recorded before (baseline values) and three months after therapy. All clinical examinations were performed after removal of the abutments attached to the implants. Fifteen days after therapy the provisional restoration was performed on the treated implants.

Microbiological samples and analysis

The first samples for microbiological analysis were taken before any measurements from the deepest peri-implant pockets. After the removal of subgingival plaque, sample sites were isolated with cotton rolls and gently air dried to avoid contamination with saliva. Fine sterile paper points were inserted into the peri-implant pocket until mild resistance and left in place for 30 seconds. The paper points were immediately transferred to the substrate used as multipurpose transport system (ESWAB LQ Amies, COPAN Diagnostics Inc., Murrieta, CA, USA).

The second and third samples were taken separately during the surgical therapy from the implant surfaces. After opening the flap and removing granulation tissue, the second sample was obtained from the implant surface by a transport swab. The swab was immediately transferred to the substrate used as multipurpose transport system (ESWAB LQ Amies, COPAN Diagnostics Inc.). After decontamination using chemical/PDT therapy, the third swab was taken from the implant surface applying the aforementioned procedure.

The samples were inoculated by standard procedures for the diagnosis of anaerobic bacteria. Each sample was inoculated on two blood agars (Columbia agar). One blood agar was incubated at 36.5°C for the diagnosis of aerobic pathogens; the other was incubated at the same temperature in a container for anaerobic diagnostics. Anaerobic conditions in the container were provided by generation bags for anaerobic conditions GENbox anaer (bioMérieux, Marcy l'Etoile, France). Cultivated and isolated anaerobic strains underwent identification process. Identification of isolated strains was reaffirmed by automatic systems of two different manufacturers: BBL Crystal ID Kit for anaerobes (Becton Dickinson, Sparks Glencoe, MD, USA), and VITEK 2 ID ANC (bioMérieux, Marcy l'Etoile, France).

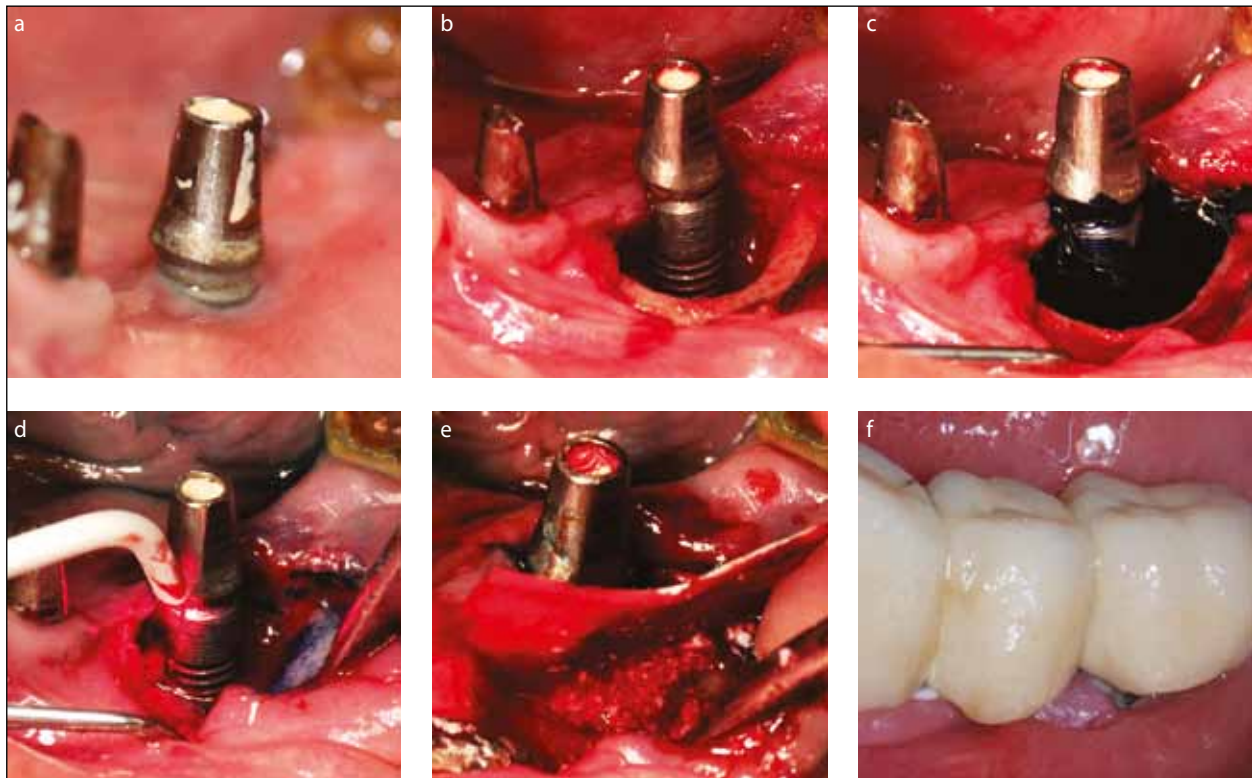


Figure 1. Surgery procedure using PDT for decontamination implant surface: a) peri-implantitis around the implant in function; b) peri-implant defect; c) application of photosensitizer (HELBO® Blue); d) activation of photosensitizer by using diode laser; e) application of bovine bone graft and resorbable membrane; f) result three months after the treatment

Treatment procedure

After clinical parameters were recorded and samples were taken, all the patients underwent a single episode of non-surgical therapy. It implied mechanical method for debridement of implants and remaining dentition in order to reduce signs of inflammation. Instructions for oral hygiene were proposed during the same visit.

Surgical treatment

During the surgical procedure, all the patients were randomly divided into two groups: the study group (PDT group) and the control group (CHX group). Similar methodology procedure was described in a study by De Waal et al. [17].

Surgical treatment of peri-implantitis was performed by one experienced oral surgeon (ZL) two weeks after non-surgical therapy (in accordance with Schwarz et al. [19]). Mucoperiosteal buccal and lingual incisions were made with surgical blade No. 15 under local anesthesia (2% lidocaine with epinephrine, 1:100,000). Flaps were designed to permit optimal access to the peri-implant bone defect for granulation tissue removal and decontamination of the implant surface. Full thickness mucoperiosteal flaps were elevated buccally and lingually. Removal of granulation tissue and mechanical implant surface cleaning were done using graphite curettes (Straumann® Dental Implant System; Straumann AG, Basel, Switzerland).

Decontamination of implant surfaces

In the study group, after careful removal of granulation tissue and mechanical debridement of implant surface, decontamination of implant surfaces and peri-implant tissues was performed using PDT (HELBO, Photodynamic Systems GmbH, Wels, Austria). Photosensitizer, phenothiazine chloride (HELBO® Blue Photosensitizer, bredent medical GmbH & Co. KG), was applied onto implant surface, bone and peri-implant soft tissue, for 3 minutes. Irrigation of photosensitizer was performed with saline, according to instructions of the manufacturer. Implant surface and the surrounding tissue were exposed to the laser light by means of fibers (HELBO® TheraLite Laser HELBO® 2D Spot Probe; Bredent medical GmbH & Co. KG) for 30 seconds/spot, which operates on wave length of 660 nm and irradiance of 100 mW (Figure 1a–f).

In the control group, after removal of granulation tissue, 1% gel of chlorhexidine (Chlorhexamed® – Direkt; GlaxoSmithKline, GmbH & Co. KG, München, Germany) was put on implant surface. One minute after exposing implant surface with CHX, it was irrigated for 1 minute by saline.

Bone augmentation and bio-resorbable membrane were applied in peri-implant defects using artificial bone of bovine origin (Bio-Oss and Bio-Gide; Geistlich Pharma, Wolhusen, Switzerland). The mucoperiosteal flaps were repositioned and sutured [17, 19].

All the patients from both groups were prescribed antibiotics over a five-day period (amoxicillin caps. 500 mg,

Table 1. Demographic and clinical description of the study population

Characteristics		Study group	Control group	p-value
Number of subjects		21 (52.5%)	19 (47.5%)	
Gender	Male	12 (57.14%)	12 (63.15%)	0.703
Mean age (years) (mean $\pm$ SD)		57.59	60.00	0.408
Mean time (years) after implant placement (mean $\pm$ SD)		7.68 $\pm$ 3.76	6.21 $\pm$ 3.064	0.236
Subjects with a history of treated periodontitis; n (%)		8 (29.6%)	10 (40%)	0.432
Localization of implants, n (%)	Maxilla	8 (29.6%)	6 (24)	0.647
	Mandible	19 (70.4%)	19 (76%)	
Type of restoration, n (%)	Cement retained fixed partial denture	13 (46.4%)	19 (79.2%)	0.010 ^a
	Screw retained fixed partial denture	6 (21.4%)	2 (8.3%)	
	Cement retained single crown	4 (14.3%)	3 (12.5%)	
	Overdenture on implants	5 (17.9%)	0 (0)	

^aSignificant statistical difference in type of prosthetic restoration among the groups at baseline by Pearson's χ^2 test ($p < 0.01$)

SD – standard deviation

No significant differences were observed among the groups at baseline by Pearson's χ^2 or Independent Samples Test (T-test).

Table 2. Mean pocket probing depth (PPD) $\pm$ SD, mean clinical attachment level (CAL) $\pm$ SD, mean number of marginal recession (%), mean bleeding on probing (BOP) – positive sites (%) at each implant at baseline and three months later

Parameter	Baseline		3 months	
	PDT	CHX	PDT	CHX
Peri-implant PPD (mm)	5.74 $\pm$ 1.55 ^a	4.48 $\pm$ 1.08 ^b	3.26 $\pm$ 0.79 ^a	2.86 $\pm$ 0.755 ^b
CAL (mm)	5.32 $\pm$ 1.36 ^a	4.63 $\pm$ 1.28 ^b	3.35 $\pm$ 1.67 ^a	3.16 $\pm$ 1.25 ^b
BOP	28 (100%)	24 (100%)	5 (17.9%) ^c	12 (50%) ^c

^aSignificant statistical difference measured before and three months after PDT by T-test ($p < 0.001$);

^bSignificant statistical difference measured before and three months after CHX by T-test ($p < 0.001$);

^cSignificant statistical difference between the groups by Pearson's χ^2 test ($p < 0.001$)

CHL – chlorhexidine gel

three per day). It was recommended that patients don't use mouthwash during the postoperative period.

Followed up period

Three months after therapy samples for microbiological analysis were taken from the reduced peri-implant pockets in the same way described above. In addition, measurements of clinical parameters were recorded as well.

Statistical analysis

Data are presented as mean $\pm$ standard deviation or n (%) depending on data type. Chi-squared test, Mann-Whitney U-test, and Student's t-test were used to assess the differences between the groups. Cochran's Q-test and Wilcoxon signed-rank test were used to assess significant differences within the groups. All analyses were performed in SPSS Statistics for Windows 20.0 (IBM Corp., Armonk, NY, USA). All p-values less than 0.05 were considered statistically significant.

RESULTS

There were 52 peri-implantitis sites diagnosed in 40 systemically healthy patients, which were treated and re-examined in a three-month period. Demography and clinical description of the study population are shown in Table 1. No adverse events and side effects were reported during and after therapy.

Clinical parameters and outcomes

From a total of 52 treated peri-implantitis sites, 12 peri-implantitis sites belonged to the category of moderate, and 31 to the category of early peri-implantitis, classified by Froum and Rosen [18]. The rest of peri-implantitis instances had depths of ≥ 5 mm in only one peri-implant pocket, as one of the inclusion criteria.

The mean value and standard deviation of PPD and CAL are shown in Table 2. Both groups showed statistically significant reduction of peri-implant pockets ($p < 0.001$). It has been shown that the greater (but not statistically significant) reduction of PPD was in the study group compared to the controls ($p = 0.07$). The results of our study showed that there was no statistically significant difference in CAL between the two tested groups three months after the therapy ($p = 0.883$). Also, there were no statistically significant differences in marginal recession.

In the study group, there was a statistically significant reduction of BOP at all six points compared with the control group three months after the therapy ($p < 0.001$). Changes in percentage of BOP are shown in Table 2. PDT has shown statistically significant reduction of suppuration compared to CHX treatment ($p < 0.002$).

Microbiological outcomes

All cultivated anaerobic microorganisms which were isolated from deepest peri-implant pockets and implant surfaces are shown in Table 3. It was shown that some of these bacteria were isolated only from implant surfaces.

Table 3. Number (n) of culture-positive implants at baseline and culture-negative after decontamination of selected anaerobes; mean number (%) of total anaerobic bacteria load on culture-positive implants; before any treatment (T_{pre}); before decontamination – during surgical therapy (S_{pre}); after decontamination – during surgical therapy (S_{post}); three months later (T_{post})

Anaerobes	Experimental group (PDT, n = 27)				Control group (1% CHX gel, n = 25)			
	T_{pre}	S_{pre}	S_{post}	T_{post}	T_{pre}	S_{pre}	S_{post}	T_{post}
<i>Porphyromonas gingivalis</i>	4 (14.3)	8 (28.6)	0 (0)	0 (0) [†]	4 (16.7)	2 (8.3)	0 (0)	0 (0)
<i>Prevotella intermedia</i>	5 (17.9)	6 (21.4)	0 (0)	0 (0) [†]	1 (4.2)	3 (12.5)	0 (0)	0 (0)
<i>Peptostreptococcus</i> spp.	5 (17.9) [*]	3 (10.7)	0 (0)	0 (0) [†]	0 (0)	5 (20.8)	0 (0)	0 (0) [†]
<i>Fusobacterium nucleatum</i>	1 (3.6)	4 (14.3)	0 (0)	0 (0) [†]	2 (8.3)	5 (20.8)	0 (0)	0 (0) [†]
<i>Peptostreptococcus asaccharolyticus</i>	4 (14.3)	1 (3.6)	0 (0)	0 (0) [†]	2 (8.3)	0 (0)	0 (0)	0 (0)
<i>Actinomyces naeslundii</i>	2 (7.1)	8 (28.6)	0 (0)	3 (10.7) [†]	4 (16.7)	6 (25)	0 (0)	2 (8.3)
<i>Veillonella</i> spp.	9 (32.1)	9 (32.1)	2 (7.1) [*]	2 (7.1) [†]	3 (12.7)	9 (37.5)	7 (29.2) [*]	3 (12.5) [†]
<i>Staphylococcus aureus</i>	0 (0)	3 (10.7)	0 (0)	0 (0) [†]	0 (0)	5 (20.8)	0 (0)	0 (0) [†]
<i>Staphylococcus saccharolyticus</i>	0 (0)	2 (7.1)	0 (0)	0 (0)	0 (0)	2 (8.3)	0 (0)	0 (0)
<i>Actinomyces meyeri</i>	0 (0)	4 (14.3)	0 (0)	0 (0) [†]	2 (8.3)	0 (0)	0 (0)	0 (0)
<i>Actinomyces odontolyticus</i>	1 (3.6)	0 (0)	0 (0)	3 (10.7)	4 (16.7)	0 (0)	0 (0)	4 (16.7) [†]

N = 52;

^{*} Statistically significant change from baseline to three months after therapy, as well as before and after decontamination of implant surface between the two groups according to Pearson's χ^2 test, $p < 0.05$;

[†] Statistically significant change from baseline to three months after therapy, as well as before and after decontamination of implant surface during surgical procedure within the two tested groups according to Cochran's Q-test, $p < 0.05$

Candida spp. was also isolated from the deepest peri-implant pockets.

The results showed that the amount of anaerobic microorganisms was significantly reduced and in most cases eliminated, after using both anti-infection therapeutic methods during surgery therapy as well as three months after the therapy procedure. It showed significant reduction of anaerobic microorganisms in the study group in comparison with the control group, immediately after decontamination of the implant surface and also three months after (*Veillonella* spp., $p < 0.010$; *Staphylococcus aureus*, $p < 0.002$; *Peptostreptococcus* spp., $p < 0.002$; *Peptostreptococcus asaccharolyticus*, $p < 0.035$; *Actinomyces naeslundii*, $p < 0.014$; *Prevotella intermedia*, $p < 0.011$; *Porphyromonas gingivalis*, $p < 0.001$; *Actinomyces meyeri*, $p < 0.007$). Three months after therapy, *Actinomyces naeslundii* was only isolated in peri-implant pockets in the control group.

The results of the study show that using chlorhexidine leads to significant reduction of *Actinomyces odontolyticus* ($p < 0.046$), *Fusobacterium nucleatum* ($p = 0.23$) compared with using photodynamic therapy. The presence of *Aggregatibacter actinomycetemcomitans*, *Tannerella forsythia*, and *Treponema denticola* was not identified.

DISCUSSION

The short-term results of the present study show that both examined methods for debridement and decontamination of implant surfaces during surgical therapy (PDT and 1% chlorhexidine gel), significantly improve clinical and microbiological outcomes.

In the current literature, most attention is given to systemic and/or local use of antibiotics or implantoplasty for the decontamination of implant surfaces during surgical procedures [3, 10, 20]. However, these methods showed side effects, as well as bacterial resistance to some drugs

and allergic reactions during and after their consumption [10]. It has been recorded that implantoplasty leads to marginal recession, which is disadvantageous in terms of function and aesthetics [2, 20].

Some authors consider PDT to be less harmful and effective solution for the decontamination of the implant surface [13, 14]. This therapy was widely used in non-surgical therapy of peri-implantitis [15, 21, 22]. It has been suggested that using only photodynamic therapy several times may lead to total recovery [22]. Schwarz et al. [6] suggested that surgical therapy of peri-implantitis has been superior to non-surgical therapy. The explanation lies in the open access and controlled removal of granulation tissue and decontamination of the exposed implant surfaces.

The results of the present study show that there are statistically significant changes in peri-implant probing depth and clinical attachment level measured at baseline and three months after therapy. The depth of peri-implant pockets in both tested groups was reduced approximately 2 mm. Higher reduction of peri-implant pocket depth was in the study group, but without statistical significance. This could be explained by larger baseline levels of peri-implant pockets depth recorded in the study group. It seems that PDT can promote re-osseointegration more rapidly than CHX, without side effects on the bone. The results show significant reduction of BOP and suppuration three months after using PDT. It is known that BOP is one of the most essential and important signs of peri-implantitis; therefore, the use of PDT can achieve elimination of BOP and promote better healing. In the study by De Waal et al. [17], similar methodology was used, but they didn't achieve the significant difference in clinical parameters using two concentration of chlorhexidine solutions (0.12% and 2%) in the examined follow-up periods. These results differ from ours due to improvements of clinical parameters in our study. In the study by Heitz-Mayfield et al. [10], after surgical debridement and implant surface decontamination following by saline irrigation, systemic amoxicillin

and metronidazole were prescribed. Although clinical results of their study were similar to ours, using adjunctive PDT could be efficient, as it leads to lower consumption of antibiotics and antiseptics, without side effects.

Cultivation of anaerobic microorganisms showed the presence of various anaerobes isolated from peri-implant pocket before any treatment, as well as on implant surface before decontamination. Most of these bacteria belonged to the pathogenic microorganisms from red and orange complex described by Socransky et al. [23]. In our study, bacteria of yellow, purple, and green complex were also found, which is assumed to be the first phase of colonization of implant surface. This can also represent a possible bridge for the adherence of bacteria from orange and red complexes in a later phase of colonization and maturation of dental biofilm. The results also showed the presence of *Staphylococcus aureus*. It was mentioned that it can be one of the possible pathogenic microorganisms that promote initiation and progression of peri-implantitis. This bacteria was isolated only from the implant surface, so it can be assumed that this can be a very virulent strain, which can enable the progression of peri-implantitis [24]. The presence of *Candida albicans* could be due to inappropriate oral hygiene. Therefore, *Candida* couldn't have had an influence on initiation of peri-implantitis, as mentioned in some early papers [2].

In both examined groups, statistically significant reduction of anaerobic microorganisms from the peri-implant pockets was evident in the follow-up period and also from implant surface immediately after decontamination. The results show that application of PDT significantly reduced the amount of bacteria, especially those from the red and orange complex. De Waal et al. [17] achieved reduction of microorganisms from implant surface between groups during a surgical procedure, but results were not as statistically significant as in our study. Our study showed significant reduction of microorganisms after using both anti-infection therapeutic methods of decontamination during surgical therapy. *In vitro* study of Marotti et al. [14] showed significant reduction of anaerobic microorganisms after application of PDT and 0.12% solution of chlorhexidine on anodized implants, which are results similar to ours. Another study showed that using PDT with toluidine blue as a dye can reduce but not eliminate pathogenic micro-

organisms from implant surfaces (*Prevotella intermedia*, *Porphyromonas gingivalis*) [15]. Presence of these bacteria is one of the most important factors in peri-implantitis progression. In contrast, our study has shown elimination of these bacteria. The reason for these differences could be the composition of photosensitizer. Phenothiazine chloride might have greater ability to bind different microorganisms compared to toluidine blue.

In the control group, chlorhexidine gel was chosen for decontamination because of its widely spread use as an antiseptic in different therapeutic procedures. It might be capable of adhering to implant surface. The results show statistically significant reduction of *Fusobacterium nucleatum* and *Actinomyces odontolyticus* after using 1% of CHX in adhesive gel, which can be explained by high concentration and viscosity of CHX in the gel. Although earlier studies described that CHX has a bactericidal effect on microorganisms regardless of the concentration [17], it seems that CHX cannot remove dental biofilm, which can lead to renewed adherence of microorganism and reappearance of inflammation. Similarly, in the control group, the results of the present study showed the reduction of BOP, as one of the signs of inflammation, of only 50%, which confirmed the earlier assumption.

CONCLUSION

Even with limitations of the present study, such as short observation period, it can be concluded that photodynamic therapy achieves significant reduction of microorganisms from implant surface and peri-implant tissue when compared with chlorhexidine application, without adverse and side effects on implants and surrounding tissue. Therefore, PDT could be suggested as a new strategy for decontamination of implant surface during surgical treatment of peri-implantitis.

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Процена ефикасности фотодинамске терапије у терапији периимплантитиса после три месеца: рандомизирана контролисана клиничка студија

Драгана Ракашевић¹, Зоран Лазић², Бојан Ракоњац³, Иван Солдатовић⁴, Саша Јанковић¹, Марко Магић⁵, Зоран Алексић¹

¹Универзитет у Београду, Стоматолошки факултет, Клиника за пародонтологију и оралну медицину, Београд, Србија;

²Војномедицинска академија, Клиника за оралну имплантологију, Београд, Србија;

³Војномедицинска академија, Институт за микробиологију, Београд, Србија;

⁴Универзитет у Београду, Медицински факултет, Институт за медицинску статистику и информатику, Београд, Србија;

⁵Универзитет у Београду, Стоматолошки факултет, Клиника за оралну хирургију, Београд, Србија

КРАТАК САДРЖАЈ

Увод Периимплантитис је инфламаторни процес који захвата мека ткива и потпорну кост око осеоинтегрисаног имплантата. Елиминација патогених микроорганизама и деконтаминација имплантне површине представља најбитнији корак у постизању стабилних клиничких резултата. Фотодинамска терапија (ФДТ) представља додатни неинвазивни метод у терапији бактеријских инфекција.

Циљ рада Циљ рада била је процена клиничких и микробиолошких параметара након хируршке терапије периимплантитиса уз додатну примену ФДТ.

Методе рада Сва дијагностикована места периимплантитиса ($n = 52$) била су подељена у две групе: у студијској групи, за деконтаминацију имплантне површине током хируршке процедуре коришћена је ФДТ; у контролној групи, за деконтаминацију имплантне површине коришћен је хлорхексидин у гелу (СНХ). Клинички параметри праћени су пре терапијске процедуре и три месеца после терапије.

Узорци за микробиолошку анализу узимани су пре и три месеца после терапије, као и током хируршке процедуре, пре и после деконтаминације имплантне површине. За идентификацију изолованих анаероба коришћен је систем који ради по принципу биохемијске анализе изолованих микробиолошких сојева.

Резултати Резултати студије су показали да применом ФДТ долази до знатне редукције крварења на провокацију у поређењу са применом СНХ ($p < 0,001$). Примена ФДТ, као помоћног терапијског средства, омогућава потпуну елиминацију анаеробних бактерија са имплантне површине.

Закључак Резултати показују да ФДТ може да се користи као помоћно терапијско средство за деконтаминацију имплантне површине и периимплантног ткива у оквиру терапије периимплантитиса.

Кључне речи: периимплантитис; деконтаминација; фотодинамска терапија

Na osnovu člana 49. Statuta Stomatološkog fakulteta Univerziteta u Beogradu, Nastavno naučno veće Stomatološkog fakulteta, na IV redovnoj sednici u školskoj 2016/17. godini, održanoj 25.04.2017. godine, donelo je sledeću

O D L U K U

Usvaja se pozitivan izveštaj Komisije za ocenu završene doktorske disertacije **dr Dragane Rakašević**, pod nazivom „PROCENA EFIKASNOSTI FOTODINAMSKE TERAPIJE KOD PERIIMPLANTITISA“.

Imenovani/a će javno braniti doktorsku disertaciju, ukoliko dobije pozitivno mišljenje Veća naučnih oblasti medicinskih nauka Univerziteta u Beogradu, pred komisijom u sastavu:

1. prof. dr Saša Janković
2. prof. dr Božidar Dimitrijevića
3. prof. dr Zoran Lazić, Vojnomedicinska akademija u Beogradu
4. doc. dr Jelena Roganović

O b r a z l o ž e n j e

Veće naučnih oblasti medicinskih nauka, na sednici od 08.07.2014. godine, dalo je saglasnost na predlog teme doktorske disertacije dr Dragane Rakašević, pod nazivom „PROCENA EFIKASNOSTI FOTODINAMSKE TERAPIJE KOD PERIIMPLANTITISA“.

Imenovani/a je u časopisu Srpski arhiv za celikupno lekarstvo, objavio/la rad pod nazivom: „Efficiency of photodynamic therapy in the treatment of peri-implantitis – A three-month randomized controlled clinical trial“ (2016).

Imajući u vidu napred navedeno, Nastavno naučno veće Stomatološkog fakulteta Univerziteta u Beogradu, rešilo je kao u dispozitivu.

Odluku dostaviti: Imenovanom/oj, Univerzitetu u Beogradu, Odseku za nastavu, Veću, Komisiji (4) i Pisarnici.

Referent kadrovskog odseka
Violeta Rastović

Dekan
Stomatološkog fakulteta

Prof. dr Miroslav Vukadinović

Fakultet STOMATOLOŠKI

UNIVERZITET U BEOGRADU

Stručno veće za medicinske nauke

Broj zahteva _____

(naziv stručnog veća kome se zahtev upućuje, shodno
čl.6 Statuta Univerziteta u Beogradu i čl. 7. st.1
ovog pravilnika)

_____.god.
(Datum)

ZAHTEV

za davanje saglasnosti na izveštaj o urađenoj doktorskoj disertaciji

Molimo da, shodno članu 68. st.3. Zakona o univerzitetu ("Službeni glasnik RS" br. 20/98), date saglasnost na

izveštaj o urađenoj doktorskoj disertaciji kandidata

DRAGANE LJUBIŠA RAKAŠEVIĆ

(ime, ime jednog od roditelja i prezime)

KANDIDAT DRAGANA LJUBIŠA RAKAŠEVIĆ

prijavilo je doktorsku disertaciju pod nazivom

(ime, ime jednog od roditelja i prezime)

PROCENA EFIKASNOSTI FOTODINAMSKJE TERAPIJE KOD PERIIMPLANTITISA

Univerzitet je dana 08.07.2014. svojim aktom pod br. 61206-3036/2-14 dao saglasnost na predlog teme

doktorske disertacije koja je glasila

PROCENA EFIKASNOSTI FOTODINAMSKJE TERAPIJE KOD PERIIMPLANTITISA

Komisija za ocenu i odbranu doktorske disertacije kandidata

DRAGANE LJUBIŠA RAKAŠEVIĆ

(ime, ime jednog od roditelja i prezime)

obrazovana je na sednici održanoj 28.02.2017. odlukom fakulteta pod br. 3/10

u sastavu:

ime i prezime člana komisije:	zvanje:	naučna oblast:
<u>SAŠA JANKOVIĆ</u>	<u>PROFESOR</u>	<u>KLINIČKE STOMATOLOŠKE NAUKE</u>
<u>BOŽIDAR DIMITRIJEVIĆ</u>	<u>PROFESOR</u>	<u>KLINIČKE STOMATOLOŠKE NAUKE</u>
<u>ZORAN LAZIĆ</u>	<u>PROFESOR</u>	<u>KLINIČKE STOMATOLOŠKE NAUKE</u>
<u>JELENA ROGANOVIĆ</u>	<u>DOCENT</u>	<u>BAZIČNE STOMATOLOŠKE NAUKE</u>

Nastavno-naučno veće fakulteta prihvatilo je izveštaj Komisije za ocenu i odbranu doktorske

disertacije na sednici održanoj dana 25.04.2017.

DEKAN FAKULTETA

Prof. dr Miroslav Vukadinović

- Prilog:**
1. Izveštaj komisije sa predlogom
 2. Akt Nastavno-naučnog veća fakulteta o usvajanju izveštaja
 3. Primedbe date u toku stavljanja izveštaja na uvid javnosti, ukoliko je takvih primedbi bilo.