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SADRŽAJ/CONTENTS

<p>ORIGINALNI RAD</p> <p>ORIGINAL ARTICLE</p> <p>doi: 10.5937/asn2183125D</p>	<p>FIZIČKA I MEHANIČKA SVOJSTVA KONVENCIONALNOG GLAS-JONOMER CEMENTA SA UGRAĐENIM KATJONSKIM SUPSTANCAMA</p> <p>2125 -2135</p>
<p>ORIGINALNI RAD KLINIČKA STUDIJA</p> <p>ORIGINAL ARTICLE CLINICAL STUDY</p> <p>doi: 10.5937/asn2183136C</p>	<p>PHYSICAL AND MECHANICAL PROPERTIES OF THE CONVENTIONAL GLASS IONOMER CEMENT INCORPORATED WITH CATIONIC SUBSTANCES</p> <p><i>Aleksandar G. Dimkov, John W. Nicholson, Elizabeta S. Gjorgievska</i></p> <p>STOMATOLOŠKI TRETMAN DECE SA POSEBNIM POTREBAMA U OPŠTOJ ANESTEZIJI U KLINICI ZA DENTALNU MEDICINU U NIŠU – DESETOGODIŠNJA RETROSPEKTIVNA STUDIJA</p> <p>2136 – 2145</p>
<p>ORIGINALNI RAD KLINIČKA STUDIJA</p> <p>ORIGINAL ARTICLE CLINICAL STUDY</p> <p>doi: 10.5937/asn2183146S</p>	<p>DENTAL TREATMENT OF CHILDREN WITH SPECIAL NEEDS UNDER GENERAL ANESTHESIA AT THE CLINIC OF DENTAL MEDICINE IN NIŠ – A TEN-YEAR RETROSPECTIVE STUDY</p> <p><i>Ljiljana D. Čemerikić, Branislava B. Stojković, Miloš R. Tijanić, Žana Z. Popović</i></p> <p>MOGUĆA POVEZANOST PARODONTOPATIJE I PROSTATITISA-PILOT STUDIJA</p> <p>2146 – 2157</p>
<p>ORIGINALNI RAD KLINIČKA STUDIJA</p> <p>ORIGINAL ARTICLE CLINICAL STUDY</p> <p>doi: 10.5937/asn2183146S</p>	<p>POSSIBLE ASSOCIATION BETWEEN PERIODONTITIS AND PROSTATITIS - A PILOT STUDY</p> <p><i>Emilija S. Stefanovska, Efka N. Zabokova-Bilbilova, Snezana J. Peshevska, Stevica M. Ristoska, Sonja J. Mindova, Sasho K. Dohcev, Aleksandra V. Panovska-Petrusheva</i></p> <p>ZNANJE O ORALNOM ZDRAVLJU, STAV I PRAKSA PACIJENTA KOJI SE PRATE TOKOM PANDEMIJE COVID-19 VIRUSA</p> <p>2158 – 2167</p>
<p>ORIGINALNI RAD EPIDEMIOLOŠKA STUDIJA</p> <p>ORIGINAL STUDY EPIDEMIOLOGICAL STUDY</p> <p>doi: 10.5937/asn2183158I</p>	<p>ORAL HEALTH KNOWLEDGE, ATTITUDE AND PRACTICE AMONG PEOPLE IN MONITORING DURING COVID-19 PANDEMIC IN MAKASSAR</p> <p><i>Ayub Irmadani Anwar, Aldy Anzhari Ayu, Meilisa Yusriyanti Yusu, Andi Zulkifli Abdullah, Muhammad Ruslin</i></p> <p>IZRADA OPTURATOR PARCIJALNE PROTEZE POSLE SUBTOTALNE MAKSILEKTOMIJE - PRIKAZ SLUČAJA</p> <p>2168 – 2174</p>
<p>PRIKAZ SLUČAJA</p> <p>CASE REPORT</p> <p>doi: 10.5937/asn2183168A</p>	<p>THE MANUFACTURE OF OBTURATOR PARTIAL DENTURE AFTER MAXILLECTOMY-ACASE REPORT</p> <p><i>Maja Z. Andjelković, Ivica A. Vučković</i></p>

PRIKAZ SLUČAJA	SUVI NAČIN TRANSPORTA I ODLOŽENA REPLANTACIJA AVULZIRANOG ZUBA -TERAPIJA I ISHOD	2175 – 2185
CASE REPORT doi: 10.5937/asn2183175T	DRY EXTRAORAL STORAGE AND DELAYED REPLANTATION OF THE AVULSED TOOTH - THERAPY AND OUTCOME <i>Olivera Tričković Janjić, Mila Janjić Ranković, Branislava B. Stojković, Marija Lj. Igić, Simona M. Stojanović</i>	
INFORMATIVNI RAD	ZNAČAJ MIKRONUTRIJENATA U USNOJ DUPLJI	2186 – 2202
INFORMATIVE ARTICLE doi: 10.5937/asn2183186R	IMPORTANCE OF MICRONUTRIENTS IN THE ORAL CAVITY <i>Rajesh Ranjit, Sadaf Takalloabdali, Alexey V. Galchenko</i>	
INFORMATIVNI RAD	TERAPIJA REKURENTNIH ORALNIH ULCERACIJA KOD PACIJENATA SA HIV-om	2203 – 2212
INFORMATIVE ARTICLE doi: 10.5937/asn2183203O	MANAGEMENT OF RECURRENT APHTHOUS STOMATITIS IN HIV PATIENTS <i>Obradović R. Radmila, Kesić G. Ljiljana, Pejčić S. Ana, Marija D. Bojović, Petrović S. Milica, Stanković V. Ivana, Jovanović G. Marija, Popović Z. Žana</i>	
INFORMATIVNI RAD	AVULZIJA STALNIH ZUBA KOD DECE I ODRASLIH-TERAPIJSKE MOGUĆNOSTI ZA DUŽI OPSTANAK	2213 – 2223
INFORMATIVE ARTICLE doi: 10.5937/asn2183213S	PERMANENT TOOTH AVULSION IN CHILDREN AND ADULTS – THERAPEUTIC OPTIONS FOR LONGER SURVIVAL <i>Simona M. Stojanović, Miloš R. Tijanić, Kristina N. Burić, Nina N. Burić, Milan S. Spasić, Kosta M. Todorović, Branislava B. Stojković, Marija G. Jovanović, Milica S. Petrović, Dušan M. Mitić</i>	

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FIZIČKA I MEHANIČKA SVOJSTVA KONVENCIONALNOG GLAS-JONOMER CEMENTA SA UGRADENIM KATJONSKIM SUPSTANCAMA

PHYSICAL AND MECHANICAL PROPERTIES OF CONVENTIONAL GLASS IONOMER CEMENT INCORPORATED WITH CATIONIC SUBSTANCES

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Sažetak

Uvod: Proučavan je efekat antimikrobnih sredstava benzalkonijum hlorid (BH) i cetilpiridinium hlorid (CPH) na restauracijski glas-jonomer zubni cement Fuji IX.

Cilj: Cilj studije bio je da se proceni da li dodavanje antimikrobnih sredstava narušava fizička i mehanička svojstva komercijalnog GJC Fuji IX.

Materijali i metode: Tokom faze mešanja, dodavane su koncentracije 1%, 2% i 3% antimikrobnih sredstava BH i CPH, po težini cementa, i proučavani su različiti efekti. U većini uzoraka došlo je do blage promene vremena stvrdnjavanja. Za merenje čvrstoće na pritisak i oslobađanja jedinjenja korišćeni su uzorci prečnika 4 mm i visine 6 mm. Oslobađanje antimikrobnih jedinjenja je analizirano UV-vidljivom spektrofotometrijom na talasnoj dužini od 259 nm za CPH i 214 nm za BH, u dejonizovanoj vodi.

Rezultati: Dobijeni rezultati su pokazali da se oslobađanje odvija mehanizmom difuzije tokom prva 2-3 sata, a koeficijenti difuzije variraju u zavisnosti od koncentracije. Vrednosti se kreću od 1.97×10^{-14} do $1.78 \times 10^{-12} \text{ m}^2 \text{ s}^{-1}$. Otpuštanje antimikrobnih jedinjenja prestalo je nakon sedam dana, a ukupno otpuštanje iznosilo je između 2,15 i 4,84% početnog dodatka aditiva.

Zaključak: Oba jedinjenja imaju mali uticaj na vreme vezivanja GJC. Smanjenje čvrstoće na pritisak nije statistički značajno. Cementi koji su sadržali CHC (1 i 2%), bili su statistički značajno slabiji od onih koji sadrže BH ($p < 0,05$). Oba antimikrobna jedinjenja pokazuju konstantno oslobađanje iz GJC sa vrednostima koje su direktno proporcionalne vremenu i koncentraciji.

Cljučne reči: benzalkonijum hlorid; cetilpiridinium hlorid; kontrolisano oslobađanje; difuzija; glas-jonomer

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Abstract

Background: The effect of the antimicrobial agents benzalkonium chloride (BC) and cetylpyridinium chloride (CPC) on the restorative glass ionomer tooth cement (GIC) Fuji IX was investigated.

Aim of the study: The aim of the study was to determine whether the addition of antimicrobial compounds impairs the physical and mechanical properties of the commercial GIC Fuji IX.

Materials and Methods: The concentrations of 1%, 2% and 3% of antimicrobial agents BC and CPC, by weight of the cement, were added during the mixing phase and different effects were studied. In most samples, there was a slight change in setting time. Samples with 4 mm diameter and 6 mm height were used to measure compressive strength and release. The release of antimicrobial compounds was analysed by UV-visible spectrophotometry at a wavelength of 259 nm for CPC and 214 nm for BC, in deionized water.

Results: The obtained results showed that the release takes place through the diffusion mechanism in the first 2-3 hours, and the diffusion coefficients vary depending on the concentration. The values range is from 1.97×10^{-14} to $1.78 \times 10^{-12} \text{ m}^2 \text{ s}^{-1}$. Release of antimicrobial compound had ceased after seven days, with total release representing between 2.15 and 4.84% of the initial additive loading.

Conclusion: Both compounds have minor effect on the setting time of the GIC. The reduction of compressive strength is not statistically significant. CPC containing cements (1 and 2%), were statistically significantly weaker, than those containing BC ($p < 0.05$). Both antimicrobial compounds have shown constant release from the GIC with values which are directly proportional both to the time and to the concentration.

Key words: benzalkonium chloride, cetylpyridinium chloride, controlled release, diffusion, glass-ionomer

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Uvod

Glas-jonomer cementi (GJC) se koriste u restorativnoj stomatologiji više od četrdeset godina¹. Koriste se na razne načine i u različite svrhe. Najčešće se koriste u dečjoj stomatologiji kao direktni restaurativni materijali, ali se koriste i kao lajneri i podloge^{1,2}. U ortodonciji se mogu koristiti za cementiranje ortodontskih bravica³, a proučavani su i kao eksperimentalni koštani cementi^{4,5}.

Glas-jonomer cementi se sastoje od osnovnog stakla u prahu i vodenih rastvora poli-kiselina, tipično poli (akrilne kiseline) koji se vezuju kiselinsko-baznom reakcijom⁶. Prah je kalcijum -fluoroaluminosilikatno staklo rastvorljivo u kiselini slično onom kod silikata ali sa većim odnosom aluminijum-silikat koji povećava njegovu reaktivnost sa tečnošću. Međutim, zabeležena su i druga eksperimentalna stakla⁷.

Glas-jonomer cementi se smatraju kao najprihvatljiviji restaurativni materijali koji poseduju pozitivne karakteristike fluora značajnim u procesima remineralizacije i antimikrobnog delovanja^{1,8}. Takođe, imaju sposobnost pufera organskih kiselina, poput mlečne kiseline⁹. Ove kiseline generisane oralnim mikroorganizmima utiču na mineralnu fazu zuba - proces poznat kao demineralizacija ili erozija tvrdih zubnih tkiva¹⁰. Glas-jonomer cementi, koji poseduju pozitivne karakteristike fluora za procese remineralizacije i antimikrobnog delovanja, ističu se kao najprihvatljiviji restaurativni materijali. Jedno od najvažnijih svojstava glas-jonomer cemenata je sposobnost sporog i stalnog oslobađanja jona fluora tokom dugog perioda¹¹. Ovaj period se može povećati unošenjem fluora u prisustvu rastvorenog fluorida poreklom iz pasta za zube i/ili fluorisanih vodica za ispiranje usta¹².

Pored oslobađanja fluoridnih jona, GJC se potencijalno mogu koristiti kao osnova za kontrolisano oslobađanje drugih aktivnih antimikrobnih komponenti¹³. Najčešće analizirano antimikrobno sredstvo je hlorheksidin, opisan kao zlatni standard za antibakterijsku primenu¹⁴. Iako neki antimikrobni agensi imaju potvrđeni efekat na smanjenje kariogene flore pljuvačke kada se koriste u sistemima za ispiranje ili zubnim pastama, rezultati u vezi sa njihovom ugradnjom u glas-jonomer cemente su i dalje oskudni, osim nekoliko pokušaja ugradnje cetilpiridinium hlorida¹⁵, benzalkonijum hlorida¹⁵ i natrijuma fusidate¹⁶. Razmatrano je nekoliko aspekata dodavanja ovih supstanci.

Introduction

Glass-ionomer cements have been used in restorative dentistry for more than forty years¹. They are used in a variety of ways and for different purposes. They are most often used in paediatric dentistry as direct restorative materials, but they are also used as liners and bases^{1,2}. In orthodontics they can be used to cement orthodontic braces³, and have also been studied as experimental bone cements^{4,5}.

Glass-ionomer cements are cements that consist of a basic powdered glass and an aqueous solutions of polyacid, typically poly(acrylic acid) which are set by an acid-base reaction⁶. The powder is an acid-soluble calcium fluoroaluminosilicate glass similar to that of silicate, but with a higher alumina-silicate ratio that increases its reactivity with liquid. However, other experimental glasses have also been reported⁷.

The glass-ionomer cements distinguish themselves as most acceptable restorative materials possessing the positive characteristics of fluorine in the processes of remineralisation and antimicrobial action^{1,8}. Also, they have the ability to buffer organic acids, such as lactic acid⁹. These acids generated by the oral micro-organisms effect the mineral phase of the tooth – a process known as demineralization or eroding of hard dental tissues¹⁰. The glass-ionomer cements, possessing the positive characteristics of fluorine in the processes of remineralisation and antimicrobial action, distinguish themselves as the most acceptable restorative materials.

One of the most important properties of glass-ionomer cements is the capacity for slow and sustainable release of fluoride ions during a long period¹¹. This period can be increased by fluoride uptake in the presence of dissolved fluoride originating from toothpastes and/or fluoridated mouthwashes¹².

In addition to the release of fluoride ions, GICs can potentially be used as templates for the controlled release of other active antimicrobial components¹³. The most frequently analysed antimicrobial agent has been chlorhexidine, described as a golden standard for antibacterial application¹⁴. Although some antimicrobial agents have a confirmed effect in the reduction of the cariogenic salivary flora when used in rinses or toothpastes, the results regarding their incorporation in glass-ionomer cements are still scanty, except several attempts for incorporation of cetylpyridinium chloride¹⁵, benzalkonium chloride¹⁵ and sodium fusidate¹⁶.

I cetilpiridinium hlorid (CPH) i benzalkonijum hlorid (BH), koji su ugrađeni u GJC, pokazali su stabilno oslobađanje kao i značajna antimikrobna svojstva, ali su oslabili vreme vezivanja^{15,17}. Reakcija vezivanja hlorheksidina takođe je zabeležena sa sličnim nalazima¹⁴. Natrijum-fusidat je još jedna supstanca za koju se pokazalo da se može osloboditi iz glas-jonomer cemenata, postupkom difuzije. U literaturi postoji vrlo mali broj podataka koji se odnose na efekat natrijum-fusidata na hemiju vezivanja ili na eventualnu čvrstoću na pritisak

Cilj studije: Cilj ove studije bio je da se dobiju jasniji nalazi dodavanja katjonskih antimikrobnih jedinjenja cetilpiridinium hlorida i benzalkonijum hlorida glas-jonomer cementu.

Materijali i metode

Studije su izvedene na komercijalnom restorativnom glas-jonomernom cementu Fuji IX (GC, Japan). Korišćena su antimikrobna jedinjenja cetilpiridinium hlorid (Sigma-Aldrich, Dorset, Velika Britanija) i benzalkonijum hlorid (Fluka, Nemačka). Antimikrobna jedinjenja su prvo ugrađena u poliakrilnu kiselinu glas-jonomer cementa, a zatim je prah postepeno dodavan i mešan zajedno do potpunog zasićenja. Antimikrobno sredstvo je dodato u strogim delovima od 1, 2 i 3 % mase cementa. Prethodne analize su utvrdile da su koncentracije 1, 2 i 3% antimikrobnih sredstava jednake 0,0032 g, 0,0064 g i 0,0128 g GJC Fuji IX. Pored toga, izvedeni su eksperimenti na cementu bez aditiva, kao kontrola. Vremena vezivanja određena su za cement koji sadrži različite nivoe aditiva, kao i za cement bez aditiva, koristeći Gillmore iglu (masa od 28 g), kako je navedeno u ISO991718 (Slika 1).

Čvrstoća na pritisak utvrđena je pomoću cilindričnih uzoraka dimenzija prečnika 4 mm i visine 6 mm. Kompleti od pet takvih primeraka pripremljeni su pomoću kalupa od nerđajućeg čelika i naloženi u sveže pomešane cementne paste (Slika 2). Ivice su ravne stezanjem metalnih ploča pomoću Gstezaljke. Uzorci su očvršćavani u pećnici na 37 °C tokom 1 sata, zatim su uklonjeni iz kalupa i čuvani još 23 sata u vodi na 37 °C pre ispitivanja. Ispitivanje je izvršeno na Instron Universal Testing Machine (Model 1193, Instron Corp., USA), brzinom poprečne glave od 1 mm / min (Slika 3). Određivanje količine antimikrobnih sredstava izvršeno je pomoću spektrofotometra UV-vis VARIAN - Cari 50 Tablet (Slika 4).

Both cetylpyridinium chloride (CPC) and benzalkonium chloride (BC), which are incorporated into the GICs, have shown steady release as well as significant antimicrobial properties, but have weakened the setting time^{15,17}. The setting reaction of chlorhexidine has also been reported with similar findings¹⁴. Sodium fusidate is another substance which has also been shown to be capable of being released from glass-ionomer cements, through a diffusion process. There is a very low number of data in the literature referring to the effect of sodium fusidate on either the setting chemistry or eventual compressive strength.

Aim of study: The aim of this study was to obtain clearer findings from the addition of cationic antimicrobial compounds cetylpyridinium chloride and benzalkonium chloride in glass ionomer cement.

Materials and methods

Studies were carried out using the commercial restorative grade glass-ionomer cement Fuji IX (GC, Japan). Antimicrobial compounds used were cetylpyridinium chloride (Sigma-Aldrich, Dorset, UK) and benzalkonium chloride (Fluka, Germany). The antimicrobial compounds were first incorporated into the glass ionomer cement's polyacrylic acid and then the powder was added gradually and mixed together until complete saturation. The antimicrobial agent was added in strict portions of 1, 2 and 3 % by mass of the cement. Preceding analyses had determined the concentrations of 1, 2 and 3 % of antimicrobial agents to be equivalent to 0.0032 g, 0.0064 g and 0.0128 g of GIC Fuji IX. In addition, experiments were carried out on additive-free cement, as controls. Setting times were determined for the cement containing the various levels of additive, as well as for cement without additives, using a Gillmore needle (28g mass), as specified in ISO991718 (Figure 1).

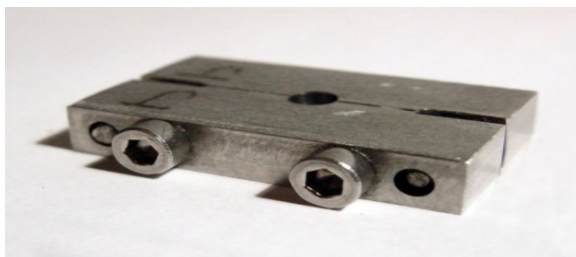
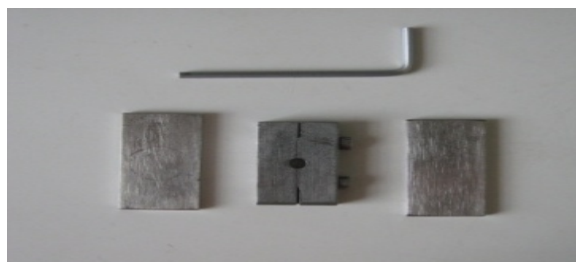
Compressive strength was determined using cylindrical specimens of dimensions 4 mm diameter x 6 mm height. Sets of five such specimens were prepared using stainless steel split moulds and loading them with freshly mixed cement pastes. Ends were made flat by clamping metal plates using a G-clamp. Specimens were cured in an oven at 37°C for 1 hour, then removed from the moulds, and stored for a further 23 hours in water at 37°C before testing. Testing was carried out on an Instron Universal Testing machine (Model 1193, Instron Corp., USA), with a cross-head speed of 1 mm/min (Figure 3). The determination of the amounts of the antimicrobial agents was done by the VARIAN

UV spektrofotometar je podešen na talasnu dužinu detekcije maksimalne apsorpcije (214 nm) za BH i 259 nm za CPH. Merenja su vršena na svakih 15 minuta tokom jednog sata, a zatim na 1, 2, 3, 4, 24 sata i 7 dana. Urtani su grafikoni M_t / M_∞ , a koeficijent difuzije je određen iz linearnog dela ovih grafikona, uzimajući nagib i zamenjujući u jednačinu $D = s^2 \pi^2 / 4$. Podaci su analizirani na statističku značajnost pomoću Statisticoprograma.

– Cary 50 Tablet UV-vis Spectrophotometer (Figure 4). The UV spectrophotometer was set to a detection wavelength of maximal absorption (214 nm) for BC, and 259 nm for CPC. The measurements were performed at every 15 min for an hour and then at 1, 2, 3, 4, 24 hours and 7 days. Graphs of M_t/M_∞ were plotted, and the diffusion coefficient was determined from the linear portion of these graphs, taking the slope and substituting into the equation $D = s^2 \pi^2 / 4$. Data were examined for statistical significance using the Statistica program.



Slika 1. Gilmoreova igla
Figure 1. Gilmore needle



Slika 2. Metalni kalupi za pripremu uzoraka
Figure 2. Metal moduls for specimens preparation



Slika 3. Univerzalni stroj za testiranje "Instron" (model 1193, Instron corp., USA)
Figure 3. Universal Testing Machine (Instron Universal Testing Machine model 1193, Instron Corp., Canton, USA)



Slika 4. UV/vis. spektrofotometar VARIAN – Cary 50 Tablet
Figure 4. UV/vis. spectrophotometer VARIAN – Cary 50 Tablet

Rezultati

Učinak različitih koncentracija antimikrobnih sredstava na vreme stvrdnjavanja prikazan je u Tabeli 1. Nije bilo jasnih trendova, mada su postojali pokazatelji da je vreme vezivanja u nekim slučajevima blago produženo. To sugerise da ovi aditivi imaju blagi inhibitorski efekat na reakciju vezivanja.

Podaci o čvrstoći na pritisak prikazani su u Tabeli 2. Ugrađivanje antimikrobnih jedinjenja u Fuji IX pokazalo je visoke vrednosti čvrstoće na pritisak kod cementa bez ugrađenog jedinjenja, koja je opadala sa porastom koncentracije ugrađenog aditiva. Ugrađivanje BH pokazalo je smanjenje vrednosti sa 146 MPa za 0% na 109,51 MPa za 3% jedinjenja. Kombinacija GJC-a i CPH-a dala je paradoksalne rezultate. Vrednosti dodataka od 1% i 2% su se kontinuirano smanjivale, dok su se drastično povećavale za 3% antimikrobnog jedinjenja.

Results

The effect of the different concentrations of antimicrobial agents on the setting time is shown in Table 1. There were no clear trends, though there was some indication that setting time was extended slightly in some cases. This suggests that these additives have a slight inhibitory effect on the setting reaction.

The data from compressive strength are shown in Table 2. The incorporation of the antimicrobial compounds into the Fuji IX, showed high values of compressive strength for the cement with no compound incorporated, which declined with the increase of the concentration. The incorporation of BC showed decreasing of values from 146 MPa for 0% down to 109.51 MPa for 3% of the compound. The combination of GIC with CPC, gave paradoxical results.

Tabela 1. Vreme stvrdnjavanja Fuji IX sa različitim nivoima dodavanja
Table 1. Setting time of Fuji IX with varying levels of addition

Aditiv/Additive	Vreme stvrdnjavanja/Setting time
None	4 min 35 s
1% BAC	4 min 40 s
2% BAC	4 min 30 s
3% BAC	4 min 30 s
1% CPC	4 min 38 s
2% CPC	4 min 45 s
3% CPC	4 min 25 s

Tabela 2. Prosečne vrednosti i statistička analiza pri određivanju čvrstoće na pritisak GJC (vrednosti u MPa)

Table 2. Average values and statistical analysis when determining the compressive strength of GIC(values in MPa)

	Fuji IX + B.Chloride Prosek/average± (SD)	Fuji IX + CPC Prosek/average± (SD)
0%	146.29(8.57)	139.33(29.62)
1%	137.78(5.33)	90.10(10.79)
2%	119.72(10.78)	77.10(16.21)
3%	109.51(7.48)	126.04(4.14)
P	0.000010	0.000119
	Significant (p=0.000)	Significant (p<0.05)
Tukey HSD test	0% : 2% 0% : 3% 1% : 2% 1% : 3% 2% : 3%	0% : 1% 0% : 2% 1% : 2% 1% : 3% 2% : 3%

Ipak, prosečne vrednosti čvrstoće na pritisak bile su veće za kombinaciju Fuji IX - BC. Statistička analiza vrednosti (ANOVA) pokazala je postojanje statistički značajnih razlika u prosečnim vrednostima. Prema Tukey HSD testu, takođe su postojale statistički značajne razlike u prosečnim vrednostima za obe kombinacije.

Rezultati oslobađanja oba dodata antimikrobna sredstva prikazani su u Tabelama 3 i 4, kao i na Grafikonima 1 i 2. Analiza varijanse otpuštanja BH iz konvencionalnog Fuji IX GJC pokazala je statistički značajne razlike u prosečnim vrednostima za 1 i 2% antimikrobnog jedinjenja i beznačajne razlike za kombinaciju od 3%.

The values for the additions of 1% and 2% continually decreased whereas they drastically increased for 3% of the antimicrobial compound. Nevertheless, the average values of the compressive strength were higher for the combination Fuji IX - BC. The statistical analysis of the values (ANOVA) showed the existence of statistically significant differences in the average values. According to Tukey HSD test there were also statistically significant differences in the average values for both combinations.

The results from the release of both antimicrobial agents are shown in Tables 3 and 4 and in Graphs 1 and 2.

Tabela 3. Otpuštanje 1%, 2% i 3% cetilpiridinium hlorida ugrađenog u Fuji IX (podaci dobijeni u jedinicama apsorbancije)

Table 3. Release of Cetylpyridinium Chloride 1%, 2% and 3%, incorporated in Fuji IX (data obtained in absorbance units)

Vreme/Time	Fuji IX + CPC 1% Prosek/average± (SD)	Fuji IX + CPC 2% Prosek/average± (SD)	Fuji IX + CPC 3% Prosek/average± (SD)
15 min.	0.01(0.00)	0.09(0.05)	0.17(0.10)
30 min.	0.02(0.00)	0.09(0.04)	0.20(0.11)
45 min.	0.02(0.00)	0.12(0.04)	0.22(0.11)
1 hour	0.02(0.00)	0.12(0.03)	0.23(0.11)
2 hours	0.02(0.00)	0.14(0.04)	0.25(0.10)
3 hours	0.02(0.00)	0.16(0.04)	0.27(0.10)
4 hours	0.02(0.00)	0.17(0.04)	0.29(0.10)
24 hours	0.04(0.01)	0.18(0.04)	0.32(0.10)
7 days	0.10(0.02)	0.23(0.05)	0.32(0.06)
P	0.000000	0.000009	0.000000
	Signifikantno/Significant (p<0.05)	Signifikantno/Significant (p<0.05)	Signifikantno/Significant (p<0.05)
Tukey HSD test	7d.:15',30',45',1,2,3,4,24h. 15':24h. 30':24h.	7d.:15',30',45',1h.,2h. 15':24h. 30':24h.	7d.:15',30',45',1,2,3h. 15',30':2,3,4,24h. 45':24h.,7d.

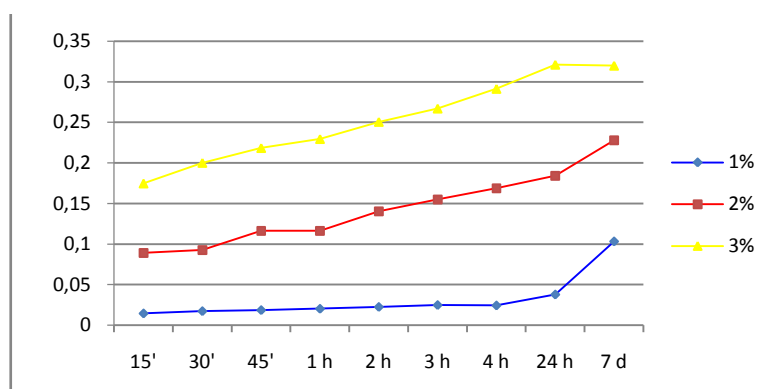
Tabela 4. Otpuštanje 1%, 2% i 3% benzalkonijum hlorida ugrađenog u Fuji IX (podaci dobijeni u jedinicama apsorbanције)

Table 4. Release of Benzalkonium Chloride 1%, 2% and 3%, incorporated in Fuji IX (data obtained in absorbance units)

Vreme/Time	Fuji IX + Benzalkonium Chloride 1% Prosek/average± (SD)	Fuji IX + Benzalkonium Chloride 2% Prosek/average± (SD)	Fuji IX + Benzalkonium Chloride 3% Prosek/average± (SD)
15 min.	0.25(0.06)	0.15(0.05)	0.17(0.10)
30 min.	0.26(0.06)	0.15(0.04)	0.20(0.11)
45 min.	0.23(0.05)	0.14(0.04)	0.29(0.11)
1 hour	0.28(0.06)	0.18(0.05)	0.23(0.11)
2 hours	0.29(0.06)	0.20(0.04)	0.25(0.10)
3 hours	0.28(0.06)	0.22(0.04)	0.27(0.10)
4 hours	0.29(0.06)	0.21(0.04)	0.29(0.10)
24 hours	0.35(0.05)	0.22(0.04)	0.32(0.10)
7 days	0.30(0.04)	0.28(0.04)	0.32(0.06)
P	0.040697	0.000012	0.162707
Tukey HSD test	Significant (p<0.05) 15':24h. 45':24h.	Significant (p<0.05) 7d.:15',30',45',1h. 4h.:24h.	

Grafikon 1. Prosečne vrednosti 1%, 2% i 3% cetilpiridinium hlorida ugrađene u Fuji IX tokom vremena

Chart 1. Average values na Cetylpyridinium Chloride 1%, 2% and 3%, incorporated in Fuji IX, over time



Grafikon 2. Prosečne vrednosti 1%, 2% i 3% benzalkonijum hlorida ugrađene u Fuji IX tokom vremena

Chart 2: Average values of released Benzalkonium Chloride 1%, 2% and 3%, incorporated in Fuji IX, over time

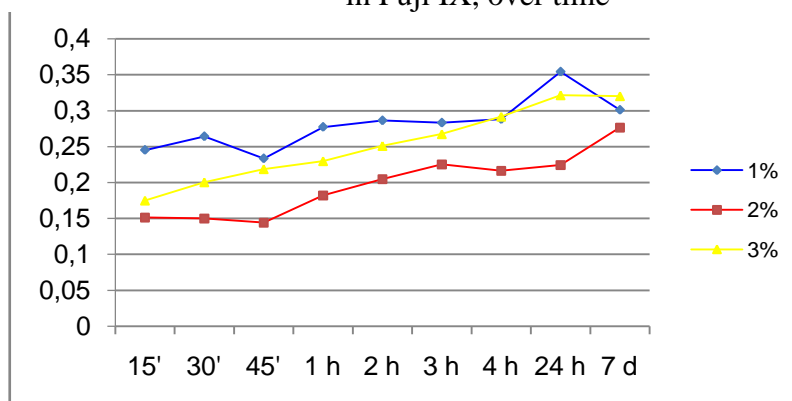


Tabela 5. Jednačine lenearne regresije i koeficijent korelacije za grafikone Mt / M_{∞} vs $\sqrt{t/s}$
Table 5. Linear regression equations and correlation coefficient for plots of Mt/M_{∞} vs $\sqrt{t/s}$.

Aditiv (količina i tip)/ Additive (amount and type)	Jednačina/Equation	Koeficijent korelacije/ Correlation coefficient
1% Benzalkonium chloride	$y = 2.607 \times 10^{-4}x + 0.038$	0.988
2% Benzalkonium chloride	$y = 1.585 \times 10^{-4}x + 0.047$	0.996
3% Benzalkonium chloride	$y = 4.208 \times 10^{-4}x + 0.066$	0.992
1% Cetylpyridinium chloride	$y = 1.53 \times 10^{-3}x + 0.181$	0.991
2% Cetylpyridinium chloride	$y = 1.078 \times 10^{-3}x + 0.218$	0.925
3% Cetylpyridinium chloride	$y = 8.858 \times 10^{-4}x + 0.173$	0.995

Tabela 6. Koeficijent difuzije aditiva na različitim nivoima dodavanja
Table 6. Diffusion coefficient of additives at various levels of addition

Aditiv (količina i tip)/ Additive (amount and type)	Koeficijent difuzije/ Diffusion coefficient ($m^2 s^{-1}$)
1% Benzalkonium chloride	5.34×10^{-14}
2% Benzalkonium chloride	1.97×10^{-14}
3% Benzalkonium chloride	1.39×10^{-13}
1% Cetylpyridinium chloride	1.78×10^{-12}
2% Cetylpyridinium chloride	9.13×10^{-13}
3% Cetylpyridinium chloride	6.16×10^{-13}

Rezultati oslobađanja druge kombinacije (CPH i Fuji IX) pokazali su velike razlike u prosečnim vrednostima između analiziranih koncentracija. Oslobađanje se uglavnom odvijalo stabilno tokom istraženog perioda. Tokom tog vremenskog intervala, oslobađanje agenasa je bilo više ili manje uravnoteženo. Uzorci koji su sadržali veće koncentracije antimikrobnog jedinjenja, oslobodili su veću količinu jedinjenja. Urtavanje podataka u obliku Mt/M_{∞} dalo je prave linije tokom prvih 2-3 sata, kao što je prikazano u Tabeli 5.

Jednačine lenearne regresije i koeficijent korelacije za grafikone Mt / M_{∞} vs $\sqrt{t/s}$ i koeficijent difuzije aditiva na različitim nivoima sabiranja prikazani su u Tabelama 5 i 6.

Iako nije bilo određene sekvence u dobijenim rezultatima, najveća vrednost se dogodila za 3% GIC napunjenog BH. Suprotno tome, u kombinaciji Fuji IX i CPH, najveća vrednost se dogodila sa nivoom dodavanja od 1% i smanjila se redom od 1% do 3%.

The analysis of the variance from the release of BC from the conventional Fuji IX GIC showed statistically significant differences in the average values for 1 and 2% of the antimicrobial compound, and insignificant differences for the 3% combination. The results from the release of the other combination (CPC and Fuji IX) showed large differences in the average values between the analysed concentrations.

Release generally occurred steadily over the investigated period. During that time interval, the releasing of the agents was more or less equilibrated. The samples which contained higher concentrations of the antimicrobial compound, released larger amount of the compound. Plotting the data in the form of Mt/M_{∞} gave straight lines for the first 2-3 hours, as shown in Table 5.

Linear regression equations and correlation coefficient for plots of Mt/M_{∞} vs $\sqrt{t/s}$ and diffusion coefficient of additives at various levels of addition are shown in Tables 5 and 6.

Although there was no specific sequence in the results obtained, the highest value occurred for a 3% GIC loaded with BC. By contrast, in the combination of Fuji IX and CPC, the highest value occurred with the 1% level of addition, and decreased in order from 1% to 3%.

Diskusija

Postoji niz studija koje opisuju efekat antimikrobnih jedinjenja na GJC¹⁵⁻¹⁹. U svim njima je zabeleženo poboljšanje antimikrobnih efekata GJC-a, ali takođe je primećeno i blago produženo vreme vezivanja i smanjenje čvrstoće na pritisak. Iako su proučavane razne vrste jedinjenja, čini se da je najviše proučavan hlorheksidin u različitim koncentracijama i kombinacijama (kombinacija sa diacetatom¹⁴ i natrijum-fusidatom¹⁶). Takođe su proučavana kationska jedinjenja, posebno jedinjenja kvaternarnog amonijuma.

Sve druge vrste aditiva, manje ili više, inhibiraju vreme stvrdnjavanja GJC-a, kao što smo primetili. Smatra se da kvartarna amonijum jedinjenja, uključujući katjonska antimikrobna sredstva analizirana u ovom radu, inhibiraju vreme stvrdnjavanja interakcijom sa komponentom poli (akrilne kiseline)^{20,21}. Međutim, inhibitorski efekat je primećen kod nekih drugih vrsta, kao što su metanol²², 2-hidroksitil metakrilat²² i natrijum hlorid²³. Bez obzira na hemijsko poreklo, inhibicija vremena vezivanja je široko rasprostranjena i povezana je sa smanjenjem čvrstoće na pritisak. Ranije je zabeležen efekat kvaternarnih amonijumovih jedinjenja na čvrstoću na pritisak na konvencionalni glas-jonomer cement Fuji IX¹⁷. U toj studiji tom prahu je dodat CPH, a BH u tečnoj fazi cementa. Za razliku od uzoraka u ovoj studiji, bili su visoki 6 mm i 3 mm u prečniku. Iako je analiza rađena nakon 7 dana (uzorci su uskladišteni), za razliku od rada u trenutnoj studiji gde je čvrstoća na pritisak merena nakon 24 sata, čak i za nivo dodavanja od 1%, smanjenje čvrstoće je bilo izuzetno značajno ($p < 0,05$). Uočavanje značajnih razlika otežalo je i veliko standardno odstupanje u vrednosti čvrstoće na pritisak na uzorak cementa bez aditiva.

Oslobađanje antimikrobnih jedinjenja ugrađenih u GJC pojačava antibakterijsku aktivnost cementa¹⁷. Korišćenjem metode difuzije agara, ovo je eksperimentalno prikazano merenjem zone inhibicije oko cementnih diskova smeštenih u agar Petri posudama bakterijskih kultura¹⁷. U sadašnjem radu, oslobađanje BH i CPH mereno je direktno korišćenjem UV /vidljive spektrofotometrije. Analiza rezultata pokazala je da se rano oslobađanje antimikrobnih jedinjenja (2-3 sata) zasnivalo na difuziji, sa koeficijentima difuzije u opsegu. Ranije je pokazano da se oslobađanje nekih antimikrobnih jedinjenja, poput hlorheksidin-diacetata i natrijum-fusidata, javlja difuzijom u ranim fazama^{14,16}. Koeficijenti difuzije natrijum-fusidata kretali su se između 3,0 i 4,4 $\times 10^{-12} \text{ m}^2 \text{ s}^{-1}$ i bili su

Discussion

There are a number of studies describing the effect of antimicrobial compounds on GJC¹⁵⁻¹⁹. In all of them an improvement of the antimicrobial effects of GICs was noted, but slightly extended setting time and decrease in compressive strength were also noted. Although various types of compounds have been studied, chlorhexidine in different concentrations and combinations seems to be the most studied (the combination with diacetate¹⁴ and sodium fusidate¹⁶). Cationic compounds, especially quaternary ammonium compounds, have also been studied.

All other types of additives, more or less inhibit the setting time of the GIC, as we have observed. Quaternary ammonium compounds, including the cationic antimicrobial agents analysed in this paper, are thought to inhibit the setting time by interaction with the poly(acrylic acid) component^{20,21}. However, an inhibitory effect has been observed in some other species, such as methanol²², 2-hydroxyethyl methacrylate²² and sodium chloride²³. Regardless of chemical origin, inhibition of setting time is widespread and is associated with a reduction in compressive strength.

The effect of quaternary ammonium compounds on compressive strength of the conventional glass-ionomer cement Fuji IX has been reported previously¹⁷. In that study, CPC was added to the powder, and BC was added in the liquid phase of the cement. Unlike the samples in this study, they were 6 mm high x 3 mm in diameter. Although the analysis was done after 7 days (the samples were stored), in contrast to the work in the current study where the compressive strength was measured after 24 hours, even for the 1% level of addition, reduction in strength was highly significant ($p < 0.05$). Observing significant differences was also hampered by the large standard deviation in the compressive strength value for the cement sample without additive.

The release of antimicrobial compounds incorporated into the GIC enhances the antibacterial activity of cements¹⁷.

Using the agar diffusion method, this was shown experimentally by measuring the zone of inhibition around cement discs placed in agar Petri dishes of bacterial cultures¹⁷. In the current work, release of BC and CPC was measured directly using UV/visible spectrophotometry. The analysis of the results showed that the early release of antimicrobial compounds (2-3 hours) was based on diffusion, with diffusion coefficients in the range.

nešto viši od onih koji su navedeni u BH i CPH u ovoj studiji. Ukupno oslobađanje antimikrobnih sredstava dobijenih u ovoj studiji bilo je između 2 i 5% od početne koncentracije, za razliku od natrijum fusidata koji je otpustio koncentraciju oko 20-22% od početnog opterećenja¹⁶.

Rezultati dobijeni u ovoj studiji potvrđuju korisnost GJC-a kao potencijalnih materijala sa kontrolisanim oslobađanjem, posebno za antimikrobna sredstva. Modifikovani GJC mogu se široko koristiti u tehnici atraktivnog restorativnog tretmana u nerazvijenim zemljama¹⁹ ili kod pacijenata sa invaliditetom i pacijenata sa posebnim potrebama čija je oralna higijena ugrožena.

Zaključak

Obe antimikrobne supstance imaju samo manje efekte na vreme vezivanja, tj. reakcija vezivanja je u određenoj meri inhibirana.

Utvrđeno je da je čvrstoća na pritisak u kontrolnoj grupi mnogo niža od tvrdnje proizvođača. Čvrstoća na pritisak se smanjivala sa porastom koncentracije antimikrobnih jedinjenja, ali ne u statistički značajnoj meri.

Uzorci koji sadrže CPH od 1 i 2% bili su slabiji do statistički značajne mere od onih koji sadrže BH ($p < 0,05$).

Antimikrobna jedinjenja BH i CPH neprekidno su se oslobađala iz glas-jonomer cemenata sa vrednostima koje su bile direktno proporcionalne vremenu i koncentraciji. Ova jedinjenja su puštena u dejonizovanu vodu pomoću mehanizma difuzije tokom prvih 2-3 sata. Koeficijenti difuzije varirali su u zavisnosti od koncentracije i kretali su se u opsegu $1,97 \times 10^{-14}$ - $1,78 \times 10^{-12} \text{ m}^2 \text{ s}^{-1}$. Ukupno oslobađanje variralo je sa koncentracijom i bilo je vrlo nisko, tj. između 2,15 i 4,84% početnog dodatka aditiva.

Previously, the release of some antimicrobial compounds such as chlorhexidine diacetate and sodium fusidate has been shown to occur by diffusion in the early stages^{14,16}. The diffusion coefficients for sodium fusidate ranged between 3.0 and $4.4 \times 10^{-12} \text{ m}^2 \text{ s}^{-1}$, and were slightly higher than those specified for BC and CPC in this study. Total release of antimicrobial agents obtained in this study was between 2 and 5% from the initial concentration, unlike sodium fusidate which released concentration was at around 20-22% of initial loading¹⁶.

The results obtained in this study confirm the usefulness of GICs as potential controlled release materials especially for antimicrobial agents. Modified GICs can be widely used in Atraumatic Restorative Treatment technique in underdeveloped countries¹⁹, or in patients with disabilities and special needs patients whose oral hygiene is compromised.

Conclusion

Both antimicrobial substances have only minor effects on the setting time, i.e., the setting reaction was inhibited to an extent.

The compressive strength in the control group was found to be much lower than the manufacturer's claim. The compressive strength decreased with the increase in the concentration of the antimicrobial compounds, but not to a statistically significant extent.

Specimens containing CPC at 1 and 2% were weaker to statistically significant extent than those containing BC ($p < 0.05$).

The antimicrobial compounds BC and CPC were continually released from the glass-ionomer cements with values which were directly proportional both to the time and to the concentration. These compounds were released into deionized water by a diffusion mechanism for the first 2-3 hours. Diffusion coefficients varied with concentration and were in the range 1.97×10^{-14} - $1.78 \times 10^{-12} \text{ m}^2 \text{ s}^{-1}$. Total release varied with concentration, and was very low, i.e. between 2.15 and 4.84% of the initial additive loading.

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STOMATOLOŠKI TRETMAN DECE SA POSEBNIM POTREBAMA U OPŠTOJ ANESTEZIJI NA KLINICI ZA DENTALNU MEDICINU U NIŠU – DESETOGODIŠNJA RETROSPEKTIVNA STUDIJA

DENTAL TREATMENT OF CHILDREN WITH SPECIAL NEEDS UNDER GENERAL ANESTHESIA AT THE CLINIC OF DENTAL MEDICINE IN NIŠ – A TEN-YEAR RETROSPECTIVE STUDY

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Sažetak

Uvod: Oralno zdravlje dece sa posebnim potrebama najčešće je narušeno, uz visoku zastupljenost karijesa i komplikacija koje izaziva. Zbog nemogućnosti uspostavljanja adekvantog kontakta deteta i stomatologa, samim tim i stomatologa i velikog broja karijesom destruiranih zuba, stomatološko zbrinjavanje u opštoj anesteziji često je indikovano u ovoj populaciji dece.

Cilj: Izvršiti sveobuhvatnu analizu stomatološkog tretmana dece sa posebnim potrebama, pruženog u opštoj anesteziji na Klinici za dentalnu medicinu u Nišu tokom perioda od deset godina.

Materijal i metode: Retrospektivnom studijom analizirana je stomatološka dokumentacija dece sa posebnim potrebama kod koje je sanacija zuba u opštoj anesteziji izvršena na Klinici za dentalnu medicinu u Nišu u periodu od 01.01.2010. godine do 31.12.2019. godine.

Rezultati: Od 1943 deteta sa posebnim potrebama, primljenih u Službu za Preventivnu i dečju stomatologiju Klinike za dentalnu medicinu u Nišu tokom analiziranog perioda, u opštoj anesteziji, stomatološki je zbrinuto njih 286 (14,7%), poreklom iz Nišavskog, Jablaničkog, Pčinjskog, Topličkog, Rasinskog i drugih upravnih okruga Srbije. U drugoj polovini desetogodišnjeg perioda praćenja, sanirano je skoro duplo više dece u odnosu na prvih pet godina. Restaurirano je 1754 zuba, endodontski tretirano 28 zuba, dok je ekstrahovano 1417 zuba.

Zaključak: Visok procenat dece sa posebnim potrebama stomatološki zbrinutih u opštoj anesteziji, i konstantan porast u broju ove dece jugoistočnog dela Srbije kod kojih je indikovana stomatološki tretman u opštoj anesteziji, sugerišu na neophodnost bliske saradnje stomatologa zdravstvenih ustanova jugoistočnog dela Srbije sa stomatolozima Klinike za dentalnu medicinu u Nišu, kao centru tercijernog nivoa stomatološke zdravstvene zaštite prema kome gravitiraju pacijenti ovog dela Srbije.

Cljučne reči: deca sa posebnim potrebama; sanacija zuba; opšta anestezija

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Abstract

Introduction: The oral health of children with special needs is most often impaired, with a high prevalence of caries and its complications. Due to the impossibility of establishing an adequate child-dentist contact and a large number of carious teeth, dental treatment under general anesthesia is often indicated in this population of children.

Aim: To perform a comprehensive analysis of the dental treatment of children with special needs under general anesthesia at the Clinic of Dental Medicine in Niš over a period of ten years.

Material and methods: A retrospective study analyzed the dental documentation of children with special needs in whom dental treatment was performed under general anesthesia at the Clinic of Dental Medicine in Niš in the period from January 1, 2010 to December 31, 2019.

Results: 286 children with special needs (14.7%) out of a total number of 1943 admitted at the Department for Preventive and Pediatric Dentistry of the Clinic of Dental Medicine in Niš during the analyzed period, originally from Nišava, Jablanica, Pčinja, Toplica, Rasina, and other administrative districts of Serbia, were treated under general anesthesia. In the second half of the ten-year follow-up period, almost twice as many children were treated regarding the first five years. The records show that 1754 teeth were restored, 28 endodontically treated, and 1417 extracted.

Conclusion: A high percentage of children with special needs treated under general anesthesia and a constant increase in the number of such children in Southeastern Serbia suggest the need for close cooperation between dentists of health care centers in Southeastern Serbia and dentists at the Clinic of Dental Medicine in Niš, a tertiary dental health care center towards which patients of this part of Serbia gravitate.

Key words: children with special needs; tooth restoration; general anesthesia

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Uvod

Dete sa posebnim potrebama Svetska zdravstvena organizacija (SZO) definiše kao ono dete koje u određenom vremenskom periodu nije u stanju, fizički ili mentalno, da u potpunosti učestvuje u normalnim aktivnostima svoje uzrasne grupe^{1,2}. Stoga, u najširem smislu termin „deca sa posebnim potrebama“ odnosi se na različite kategorije dece: decu sa smetnjama u razvoju (fizička, mentalna, senzorna ometenost), decu sa različitim hroničnim i drugim oboljenjima, deca sa emocionalnim poremećajima, decu bez roditeljskog staranja, darovitu decu³.

Sa stomatološkog aspekta, dete sa posebnim potrebama“ je ono dete koje zbog različitih medicinskih, fizičkih, mentalnih ili emocionalnih poremećaja ne može biti tretirano na uobičajen način². U tom smislu, od posebnog je značaja stomatološki tretman dece sa smetnjama u psiho-motornom razvoju (mentalnim poremećajima, cerebralnom paralizom, autizmom, Daunovim sindromom.)⁴. Prema zvaničnim podacima, u Republici Srbiji 0,7% celokupne populacije dece čine deca sa smetnjama u psiho-fizičkom razvoju⁵. Međutim, procenjuje se da je taj procenat ipak nešto veći i da se godinama konstantno beleži njegov porast u našoj populaciji dece.

Stanje oralnog zdravlja dece sa posebnim potrebama najčešće je narušeno. U ovoj populaciji dece mogu biti prisutne oralne manifestacije koje su u vezi sa osnovnim oboljenjem, ili što je značajno češće, koje osnovno oboljenje čini podložnijim razvoju drugih različitih oralnih oboljenja. Epidemiološke studije ukazuju na to da je uz gingivo-parodontalna oboljenja, u ovoj populaciji dece karijes najučestalije oralno oboljenje i da je njegova prevalencija uglavnom veća u odnosu na prevalenciju karijesa u populaciju zdrave dece⁶⁻⁸. Visoka učestalost karijesa u ovoj populaciji dece se osim sa osnovnim oboljenjem, dovodi se u vezu i sa neurednom, često i odsutnom, oralnom higijenom praćenom velikom akumulacijom dentalnog biofilma, lošim navikama u ishrani, učestalim ortodontskim nepravilnostima, konzumiranjem lekova koji su u vezi sa osnovnom bolešću i slabom motivisanošću roditelja za očuvanjem oralnog zdravlja ove dece. Neblagovremena sanacija početnih karijesnih lezija, uz otežanu saradnju sa stomatologom, čine pulpite, gangrene, parodontite, dentogene infekcije čestim komplikacijama karijesa, te je ekstrakcije zuba česta terapija izbora u stomatološkoj sanaciji ove dece. Sve se to negativno odražava na kvalitet života ove dece i njihovih porodica^{9,10}.

Introduction

According to the World Health Organization (WHO), a child with special needs is defined as a child who is not able to, in a certain period, physically or mentally, fully participate in the normal activities of his/her age group^{1,2}. Therefore, in the broadest sense, the term "children with special needs" refers to different categories of children: children with developmental disabilities (physical, mental, sensory impairment), children with various chronic and other diseases, children with emotional disorders, children without parental care, gifted children³.

From the dental point of view, a "child with special needs" is a child who, due to various medical, physical, mental, or emotional impairments, cannot be treated in the usual way². In that sense, dental treatment of children with psychomotor developmental disorders (mental disorders, cerebral palsy, autism, Down syndrome, etc.) is of special importance⁴. According to official data, 0.7% of the total population of children in the Republic of Serbia are children with disorders in psycho-physical development⁵. However, it is estimated that this percentage is slightly higher and that it has been on the increase in our population of children for years.

The oral health of children with special needs is frequently disturbed. In this population of children, oral manifestations related to the underlying disease may be present, or, more often, the underlying disease makes them more susceptible to the development of various oral diseases. Epidemiological studies indicate that in addition to gingival-periodontal diseases, caries is the most common oral disease in this population of children and that its prevalence is generally higher compared to healthy children⁶⁻⁸. The high incidence of caries in this population of children is associated not only with the underlying disease, but also with irregular, often absent oral hygiene accompanied by a large accumulation of dental biofilm, poor eating habits, frequent orthodontic irregularities, consumption of drugs related to the underlying disease, and weak motivation of parents to preserve the oral health of their children. Untimely restoration of initial carious lesions, along with difficult cooperation with the dentist, results in pulpitis, gangrene, periodontitis, and odontogenic infections as common complications of caries,

Stomatološki tretman dece sa posebnim potrebama vrlo je često kompleksan posao i predstavlja veliki izazov u svakodnevnoj stomatološkoj praksi. Iako je sanacija oralnih oboljenja kod ove dece u ambulantnim uslovima od prioritetnog značaja², vrlo je često indikovano njihovo stomatološko zbrinjavanje u opštoj anesteziji, kada je moguće kompletnu sanaciju izvršiti u jednoj seansi. Ovo najčešće proizilazi iz nemogućnosti uspostavljanja adekvantog kontakta deteta i stomatologa, uslovljeno prirodom osnovne bolesti, ali i često velikim brojem karijesom destruiranih i gangrenoznih zuba, koje je teško sanirati u ambulantnim uslovima.

Stomatološko zbrinjavanje dece sa posebnim potrebama pod opštom anestezijom radi se u hirurškim salama, u kojima je prisutna ili u koje se donosi transportabilna stomatološka oprema. Priprema pacijenta za sanaciju u ovakvim uslovima kompleksna je uz stomatološku pripremu pacijenta zahteva prikupljanje kompletne medicinske dokumentacije pacijenta kao i anesteziološku pripremu. Stoga, sanacija oboljenja usta i zuba u opštoj anesteziji zahteva angažovanje i timski rad velikog broja zdravstvenih radnika: pedijatra, stomatologa specijaliste dečje stomatologije, stomatološke sestre, anesteziologa i anestetičara i oralnog hirurga sa svojom ekipom.

Cilj studije bio je da se izvrši sveobuhvatna analiza stomatološkog tretmana dece sa posebnim potrebama, pruženog u opštoj anesteziji na Klinici za dentalnu medicinu u Nišu tokom perioda od deset godina.

Materijal i metode

Za realizaciju postavljenog cilja, sprovedena je retrospektivna studija, kojom je analizirana stomatološka dokumentacija dece sa posebnim potrebama koja su radi sanacije oboljenja usta i zuba primnjena na Kliniku za dentalnu medicinu u Nišu u periodu od 01.01.2010.godine do 31.12.2019. godine. Studija je obuhvatila samo decu sa posebnim potrebama kod kojih je sanacija zuba izvršena u opštoj anesteziji. Iz studije su isključena deca koja su imala samo medicinski hendikep, odnosno prisustvo neke sistemske bolesti kao što su oboljenja kardiovaskularnog sistema, krvne diskrazije, bubrežna oboljenja i sl., a koja predstavljaju rizik za rutinski stomatološki tretman. Iz stomatoloških kartona selektovane dece izvučeni su sledeći podaci: pol i datum rođenja deteta, stalno prebivalište, opšta dijagnoza deteta prema Međunarodnoj klasifikaciji bolesti (MKB), datum intervencije, broj obavljenih stomatoloških

thus making tooth extraction common therapy of choice in these children. All this negatively affects the quality of life of these children and their families^{9,10}.

Dental treatment of children with special needs is often very complex and represents a great challenge in everyday dental practice. Even though the treatment of oral diseases in these children in outpatient conditions is of utmost importance², their dental treatment under general anesthesia is frequently indicated, especially in cases when it is possible to complete the treatment in one session. This usually results from the impossibility of establishing an adequate child-dentist relationship due to the nature of the underlying disease, but also often due to a great number of carious and gangrenous teeth that are difficult to treat in an outpatient setting.

Dental treatment of children with special needs under general anesthesia is performed in operating rooms where transportable dental equipment is present or brought. The preparation of the patient for treatment in such conditions is complex. In addition to dental preparation, it requires the preparation of the patient for anesthesia, as well as the collection of complete medical documentation of the patient. Therefore, the treatment of oral and dental diseases under general anesthesia requires the engagement and teamwork of a large number of healthcare workers, pediatricians, pediatric dentists, dental technicians, anesthesiologists and anesthesiologists, and oral surgeons with their teams.

The aim of the study was to perform a comprehensive analysis of the dental treatment of children with special needs under general anesthesia at the Clinic of Dental Medicine in Niš over a period of ten years.

Material and methods

To meet the set goal, we conducted a retrospective study to analyze dental documentation of children with special needs admitted to the Clinic of Dental Medicine in Niš between January 1, 2010 and December 31, 2019 for the treatment of oral and tooth diseases. The study included only children with special needs in whom dental restoration was performed under general anesthesia. Children with a medical disorder, i.e. the presence of a systemic disease such as cardiovascular disease, blood dyscrasias, renal disease, etc., who pose a risk for routine dental treatment, were excluded from the study. The following data were taken from the dental records of selected children: sex and date of birth, permanent residence,

intervencija u opštoj anesteziji, vrsta i broj pruženih stomatoloških usluga u toku intervencije.

Statistička obrada podataka izvršena je u MC Excel programu. Dobijeni podaci prikazani su tabelarno i grafički. Starost ispitanika u trenutku intervencije određena je na osnovu datuma rođenja deteta i datuma obavljene stomatološke intervencije u opštoj anesteziji.

Rezultati

U analiziranom desetogodišnjem periodu u Službi za preventivnu i dečju stomatologiju Klinike za dentalnu medicinu u Nišu od 1943 primnjena deteta sa posebnim potrebama, u opštoj anesteziji stomatološki je sanirano njih 286 (14,70%). U proseku, svake godine stomatološki je sanirano 30 dece sa posebnim potrebama, najmanje 2011. godine (17), a najviše 2018. godine (49). U drugoj polovini desetogodišnjeg praćenja, sanirano je skoro duplo više dece sa posebnim potrebama u odnosu na prvih pet godina praćenja (Grafikon 1).

Prosečna starost analizirane populacije dece iznosila je 12,76 godina. Najmlađe sanirano dete bilo je staro 3 godine. Najveći procenat sanirane dece imao je stalnu denticiju (58,21%). U analiziranom periodu, u opštoj anesteziji sanirano je znatno više dečaka sa posebnim potrebama ($n = 175$) u odnosu na devojčice ($n = 111$). Starosna i polna struktura dece sa posebnim potrebama sanirane u opštoj anesteziji tokom desetogodišnjeg praćenja prikazana je na Grafikonu 2.

Najveći procenat analizirane populacije dece poreklom je iz Nišavskog okruga (37,1%), iza čega slede deca poreklom iz Jablaničkog (20,98%) i Pčinjskog okruga (12,24%), a zatim i Topličkog okruga i ostalih delova južne i istočne Srbije i sa Kosova (Tabela 1).

Sanirana deca sa posebnim potrebama različitog su spektra dijagnoza. Kod najvećeg procenta dece bili su prisutni mentalni poremećaji različitog stepena, od lake do duboke mentalne ometenosti u razvoju, najčešće udružene sa još nekim poremećajem poput epilepsije, cerebralne paralize ili u sklopu nekih sindroma (Grafikon 3). Tokom perioda praćenja, beležen je konstantan porast broja dece sa autizmom, kod kojih je sanacija zuba izvršena u opštoj anesteziji.

general diagnosis according to the ICD classification, date of intervention, number of performed dental interventions under general anesthesia, type and number of provided dental services during the intervention.

Statistical data processing was performed in MC Excel. The obtained data are presented in tables and charts. The age of subjects at the time of the intervention was determined on the basis of the date of birth of the child and the date of the performed dental intervention under general anesthesia.

Results

During the analyzed ten-year period at the Department for Preventive and Pediatric Dentistry of the Clinic of Dental Medicine in Niš, 286 out of 1943 children with special needs (14.70%) had dental treatment under general anesthesia. On average, 30 children with special needs were treated a year, the least in 2011 (17), and the most in 2018 (49). In the second half of the ten-year follow-up period, almost twice as many children with special needs were treated compared to the first five years of the monitoring period (Graph 1).

The average age of the analyzed population of children was 12.76 years. The youngest treated child was 3 years old. The largest percentage of treated children had permanent dentition (58.21%). In the analyzed period, significantly more boys with special needs ($n = 175$) were treated under general anesthesia than girls ($n = 111$). The age and gender structure of children with special needs treated under general anesthesia in the ten-year follow-up period is shown in Graph 2.

The largest percentage of the analyzed population of children was from the Nišava district (31.7%), followed by the Jablanica (20.98%) and Pčinja (12.24%) districts, as well as and the Toplica district and other districts of the Southeastern Serbia and Kosovo (Table 1).

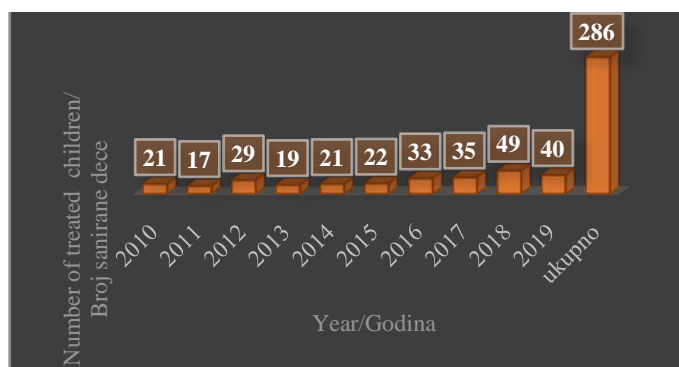
The treated children with special needs exhibited a range of diagnoses. The majority was diagnosed with mental disorders of varying degrees, from mild to severe mental disability, most often accompanied by another disorder such as epilepsy, cerebral palsy, or as part of some syndromes (Graph 3). During the follow-up period, there was a constant increase in the number of children with autism in whom dental restoration was performed under general anesthesia.

U desetogodišnjem periodu praćenja, od analiziranih 286 dece sa posebnim potrebama, kod 74,8% je stomatološki tretman u opštoj anesteziji izvršen samo jednom, kod 17,48% dece dva puta, dok je kod preostalih 7,72% analizirane dece sa posebnim potrebama stomatološka sanacija izvršena tri i više puta (Tabela 2).

Stomatološka sanacija dece u oštoj anesteziji, uz obavezno uklanjanje mekih naslaga, obuhvatila je uklanjanje čvrstih zubnih naslaga, konzervativni tretman zuba i ekstrakciju zuba. Čvrste zubne naslage uklonjene su kod 28 dece (10%). Restaurirano je 1754 zuba, endodontski tretirano i restaurirano 28 zuba (Slika 1). Ekstrahovano je 1417 zuba (730 mlečnih i 692 stalna zuba) (Grafikon 4). U proseku, svako sanirano dete imalo je 6,13 restauriranih i 4,95 ekstrahovanih zuba.

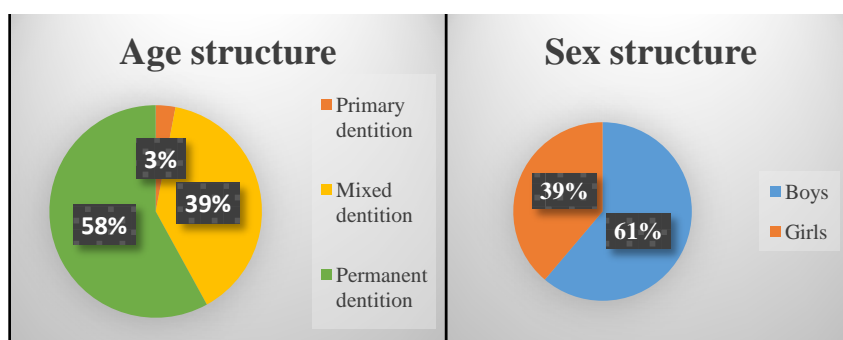
In the ten-year follow-up period during which 286 children with special needs were treated, 74.8% of children underwent dental treatment under general anesthesia only once, 17.48% of them twice, whereas in the remaining 7.72% of the analyzed children with special needs dental treatment was performed three or more times (Table 2).

Dental treatment of children under general anesthesia, with the obligatory removal of soft plaque, included the removal of hard dental plaque, conservative dental treatment, and tooth extraction. Hard dental plaque (tartar) was removed in 28 children (10%), 1754 teeth were restored, 28 teeth were endodontically treated and restored (Figure 1), and 1417 teeth were extracted (730 deciduous and 692 permanent teeth) (Graph 4). On average, each treated child had 6.13 restored and 4.95 extracted teeth.



Grafikon 1. Broj dece sa posebnim potrebama sanirane u opštoj anesteziji na Klinici za dentalnu medicinu u Nišu tokom desetogodišnjeg perioda praćenja

Graph 1. Number of children with special needs treated under general anesthesia at the Clinic of Dental Medicine in Niš during the ten-year follow-up period

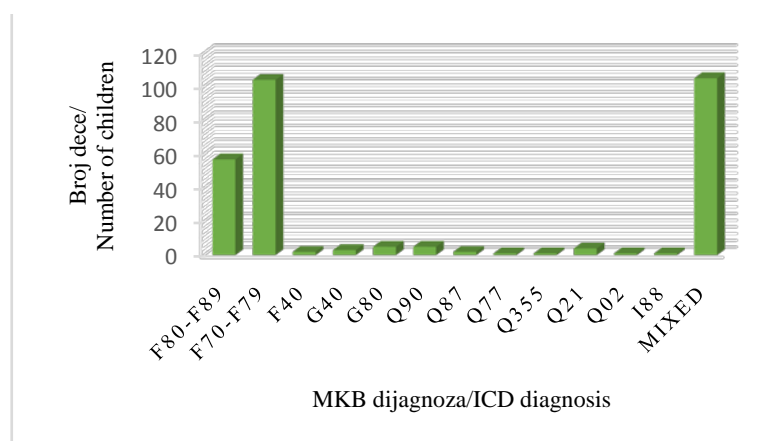


Grafikon 2. Starosna i polna struktura analizirane populacije dece

Graph 2. Age and sex structures of the analyzed population of children

Tabela 1. Distribucija analizirane populacije dece po upravnim okruzima
Table 1. Distribution of the analyzed population of children by administrative districts

Okrug (sedište okruga) / District (district center)	Broj / Number	%
Nišavski okrug (Niš) / Nišava district (Niš)	106	37,1
Jablanički okrug (Leskovac) / Jablanica district (Leskovac)	60	20,98
Pirotski okrug (Piroć) / Piroć district (Piroć)	22	7,69
Pčinjski okrug (Vranje) / Pčinja district (Vranje)	35	12,24
Toplički okrug (Prokuplje) / Toplica district (Prokuplje)	21	7,34
Zaječarski okrug (Zaječar) / Zaječar district (Zaječar)	10	3,5
Borski okrug (Bor) / Bor district (Bor)	10	3,5
Rasinski okrug (Kruševac) / Rasina district (Kruševac)	13	4,54
Pomoravski okrug (Jagodina) / Pomoravlje district (Jagodina)	2	0,7
Šumadijski okrug (Kragujevac) / Šumadija district (Kragujevac)	2	0,7
Kosovo	4	1,4
Mačvanski okrug (Šabac) / Mačva district (Šabac)	1	0,35



Grafikon 3. Zastupljenost dece u odnosu na dijagnozu po Međunarodnoj klasifikaciji bolesti (MKB)

Graph 3. Representation of children regarding the diagnosis according to the International Classification of Diseases (ICD)

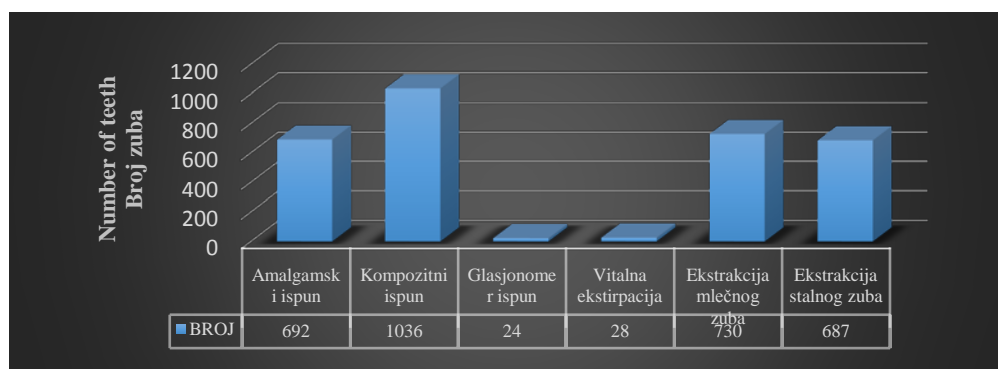
Tabela 2. Broj stomatoloških sanacija u opštoj anesteziji u analiziranoj grupi dece
Table 2. Number of dental treatments under general anesthesia in the analyzed group of children

Broj stomatoloških sanacija u opštoj anesteziji / Number of dental treatments under general anesthesia	Broj dece / Number of children	%
Jednom / One	214	74,8
Dva puta / Two	50	17,48
Tri puta / Three	13	4,54
Četiri puta / Four	4	1,4
Pet puta / Five	2	0,7
Šest puta / Six	2	0,7



Slika 1. Endodontski tretman (vitalna ekstirpacija) i restauracija frakturiranih frontalnih zuba pacijenta sa posebnim potrebama u opštoj anesteziji. Fotografija iz kolekcije dr Ljiljane Čemerikić

Figure 1. Endodontic treatment (vital extirpation) and restoration of fractured front teeth of a patient with special needs under general anesthesia



Grafikon 4. Izvršene konzervativne intervencije i ekstrakcije zuba u opštoj anesteziji u analiziranoj populaciji dece

Graph 4. Conservative interventions and tooth extractions performed under general anesthesia in the analyzed population of children

Diskusija

Sprovedena studija imala je za cilj da izvrši desetogodišnju retrospektivnu analizu stomatološkog zbrinjavanja dece sa posebnim potrebama u opštoj anesteziji na Klinici za dentalnu medicinu u Nišu. Dobijeni rezultati ukazuju na to da je od ukupnog broja dece sa posebnim potrebama koju su u analiziranom desetogodišnjem periodu primili lekari Službe za preventivnu i dečju stomatologiju Klinike za dentalnu medicinu u Nišu, oko 15% njih stomatološki zbrinuto u opštoj anesteziji. Najveći procenat dece poreklom je iz Nišavskog okruga. Međutim, nije zanemarljiv broj dece koja potiču iz drugih upravnih okruga Republike Srbije, uglavnom iz njenog jugoistočnog dela. U odnosu na Međunarodnu klasifikaciju bolesti¹¹, kod najvećeg procenta pacijenata bili su prisutni mentalni poremećaji različitog stepena, najčešće udruženi sa još

Discussion

The conducted study aimed to perform a ten-year retrospective analysis of the dental treatment of children with special needs in general anesthesia at the Clinic of Dental Medicine in Niš. The obtained results indicate that about 15% of the total number of children with special needs admitted to the Department of Preventive and Pediatric Dentistry of the Clinic of Dental Medicine in Niš during the ten-year period were treated under general anesthesia. The largest percentage of children was from the Nišava district. However, the number of children coming from other administrative districts of the Republic of Serbia, mainly from its southeastern part, is not negligible. According to the International Classification of Diseases¹¹, the largest number of children suffered from mental disorders of

nekim poremećajem poput epilepsije, cerebralne paralize ili u sklopu nekih sindroma.

Pod opštom anestezijom izvršena je klasična sanacija zuba kod dece sa posebnim potrebama, koja je obuhvatila restauraciju karijesom destruiranih zuba i ekstrakciju zuba, a kod određenog broja pacijenata i endodontski tretman primenom metode vitalne ekstirpacije. Jedinstveni protokol za pružanje stomatološkog tretmana u opštoj anesteziji kod dece sa posebnim potrebama još uvek nije usvojen¹². Međutim, uobičajno je, ukoliko to okolnosti dozvoljavaju, da se uz sistematski stomatološki pregled odradi i radiografsko snimanje pacijenta (ortopantomografsko snimanje, CBCT) na osnovu čega se pravi plan terapije, uzimajući u obzir pri tome i druge faktore kao što su opšte zdravstveno stanje pacijenta, motivisanost roditelja za očuvanje oralnog zdravlja dece i sl. Redosled stomatološkog tretmana uglavnom podrazumeva najpre uklanjanje mekih i čvrstih zubnih naslaga, zalivanje fisura i endodontsko-konzervativnu restauraciju zuba, i na kraju oralno-hirurške intervencije, najčešće ekstrakcije zuba, ali je moguće izvršiti i resekciju vrha korena zuba, i/ili cistektomije. Pri restaurativnim terapijskim procedurama zuba dece sa posebnim potrebama u opštoj anesteziji većina autora se zalaže za princip radikalnosti^{2,12}. U mlečnoj denticiji, višeseansne terapijske procedure retko su indicovane, te je u velikom broju slučajeva ekstrakcija zuba metod izbora. U stalnoj denticiji, endodontski tretman zuba suženog je indikacijskog opsega i ograničan na vitalne metode, kada se proceni da nema rizika od pojave mogućih komplikacija, kao što je to bio slučaj sa malim brojem analiziranih pacijenata Klinike za dentalnu medicinu u Nišu.

Interesantno je to da studija tokom godina beleži porast broja dece sa posebnim potrebama, koja su stomatološki tretirana u opštoj anesteziji na Klinici za dentalnu medicinu u Nišu, pri čemu je u drugoj polovini desetogodišnjeg praćenja tretirano skoro duplo više dece sa posebnim potrebama u odnosu na prvu polovinu celokupnog perioda praćenja. Vrlo je verovatno da je potreba za tretmanom ove dece daleko veća. Ovakav rezultalt indirektno ukazuje na porast broja dece sa posebnim potrebama koje zahtevaju intervenciju stomatološkog zbrinjavanja u opštoj anesteziji na Klinici za dentalnu medicinu u Nišu, kao centru tercijerne zdravstvene zaštite prema kome gravitira oko 1.500.000 ljudi jugoistočne Srbije.

varying degrees, most often accompanied by another disorder such as epilepsy, cerebral palsy, or as part of some syndromes.

Dental treatment under general anesthesia was performed in children with special needs and it included the restoration of carious teeth and tooth extraction, and in certain number of patients, endodontic treatment using the method of vital pulp extirpation. A uniform protocol for providing dental treatment under general anesthesia in children with special needs has not been adopted yet¹². However, if the circumstances allow, the usual order of dental treatment involves to perform a systematic dental examination and radiographic recording of the patient (orthopantomographic recording, CBCT) on the basis of which a treatment plan is made, taking into account other factors such as the general health of the patient, motivation of parents to preserve the oral health of children, etc. The order of dental treatment usually involves first removing soft and hard dental plaque, followed by filling fissures and endodontic-conservative tooth restoration, and finally oral surgery, most often tooth extraction, but it is also possible to perform resection of the tooth root tip, and/or cystectomy. In the restorative therapeutic procedures of the teeth of children with special needs in general anesthesia, most authors advocate the principle of radicalism^{2,12}. In primary dentition, multi-session therapeutic procedures are rarely indicated, and in a large number of cases, tooth extraction is the method of choice. In permanent dentition, endodontic dental treatment has a narrowed indication range, and is limited to vital methods, when it is assessed that there is no risk of possible complications, as was the case with a small number of analyzed patients at the Clinic of Dental Medicine in Niš.

The study recorded an increase in the number of children with special needs treated under general anesthesia at the Clinic of Dental Medicine in Niš, especially in the second half of the ten-year follow-up period, in which almost twice as many children with special needs were treated with regard to the first half of the follow-up period. The need for treatment of these children is likely far greater. This result indirectly indicates an increase in the number of children with special needs who require dental treatment under general anesthesia at the Clinic of Dental Medicine in Niš, a tertiary health care center of Southeastern Serbia to which nearly 1.500.000 people gravitate.

S druge strane, ovakav rezultat ukazuje i na neophodnost intenzivnog preventivno-profilaktičkog tretmana sa ciljem očuvanja i unapređenja oralnog zdravlja ove dece. Međutim, iako period nakon zbrinjavanja deteta sa posebnim potrebama predstavlja idealnu priliku da se roditeljima ukaže na značaj primene preventivnih mera sa ciljem sprečavanja budućih pojava karijesa i gingivo-parodontalnih oboljenja, potreba za pružanjem ovakvih informacija ipak je neophodna od najranijeg detinjstva. Zbog toga se nameće potreba za intenzivnim zdravstveno-vaspitnim radom sa roditeljima ove dece¹³. Neophodno je podizanje svesti roditelja ove dece o značaju očuvanja oralnog zdravlja, kao i blagovremeno preduzimanje svih preventivno-profilaktičkih mera i postupaka koje imaju za cilj sprečavanje oralnih oboljenja u ovoj osetljivoj populaciji dece. U tom smislu od esencijalnog je značaja uloga stomatologa iz zdravstvenih ustanova primarne i sekundarne zdravstvene zaštite jugoistočnog dela Srbije, što nužno zahteva i njihovu saradnju sa lekarima Klinike za dentalnu medicinu u Nišu, kao centru tercijernog nivoa stomatološke zdravstvene zaštite.

Zaključak

Rezultati sprovedene retrospektivne desetogodišnje studije pokazuju visok procenat dece sa posebnim potrebama, kod kojih sanacija zuba u opštoj anesteziji predstavlja terapijski metod izbora. Osim toga, sprovedena studija ukazuje i na konstantan porast broja dece sa posebnim potrebama koja zahtevaju stomatološki tretman u opštoj anesteziji na Klinici za dentalnu medicinu u Nišu. Ovakvi rezultati sugerišu na neophodnost uspostavljanja bliske saradnje stomatologa zdravstvenih ustanova primarne i sekundarne zdravstvene zaštite jugoistočnog dela Srbije sa lekarima Klinike za dentalnu medicinu u Nišu, kao centru tercijernog nivoa stomatološke zdravstvene zaštite, prema kome gravitiraju pacijenti ovog dela Srbije.

On the other hand, this result also suggests the necessity of intensive preventive and prophylactic treatment to preserve and improve the oral health of these children. However, although the follow-up period of a child with special needs is an ideal opportunity to point out to parents the importance of preventive measures to prevent caries and gingival periodontal diseases in the future, providing such information is crucial from early childhood. Therefore, there is a need for intensive health-educational work with the parents of these children¹³. It is necessary to raise their awareness about the importance of preserving the oral health of their children, as well as timely preventive and prophylactic measures and procedures aimed at preventing oral diseases in this sensitive population of children. In that sense, the role of dentists from primary and secondary health care institutions in Southeastern Serbia is essential, which requires their cooperation with dentists at the Clinic of Dental Medicine in Niš, a tertiary dental health care center.

Conclusion

The results of the conducted retrospective ten-year study suggest a high percentage of children with special needs in whom dental treatment under general anesthesia is the therapeutic method of choice. In addition, the study indicates a constant increase in the number of children with special needs who require dental treatment under general anesthesia at the Clinic of Dental Medicine in Niš. These results suggest the need to establish close cooperation between dentists of primary and secondary health care in the Southeastern Serbia with dentists at the Clinic of Dental Medicine in Niš, a tertiary dental health care center towards which patients of this part of Serbia gravitate.

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MOGUĆA POVEZANOST PARODONTOPATIJE I PROSTATITISA - PILOT STUDIJA

POSSIBLE ASSOCIATION BETWEEN PERIODONTITIS AND PROSTATITIS – A PILOT STUDY

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Sažetak

Uvod: Prostatitis je hronično oboljenje često povezano sa parodontopatijom. Nivo prostata specifičnog antigena (PSA) u serumu može biti povišen u nemalignom stanju, kao što je simptomatski i asimptomatski prostatitis. Sličnost u inflamatornoj etiopatogenezi ovih bolesti evidentna je kroz prisustvo gram-negativne bakterije, koja zauzvrat može biti moguća veza između ova dva stanja.

Cilj: Proceniti moguću povezanost između hronične parodontopatije i prostatisa, praćenjem nivoa PSA kod pacijenata sa umerenom i teškom formom parodontopatije.

Materijal i metode: Studija je obuhvatila 40 pacijenata hospitalizovanih na Univerzitetskoj urološkoj klinici Medicinskog fakulteta u Skoplju sa dijagnostikovanim prostatitisom i utvrđenim PSA nivoom ($\geq 4 \text{ ng/ml}$). Na osnovu nivoa pripojnog epitela pacijenti su podeljeni u dve grupe. Prvu grupu činilo je 20 pacijenata sa nivoom pripojnog epitela NPE $\geq 3 \text{ mm}$ odnosno umerenom formom parodontopatije, a drugu grupu 20 pacijenata sa NPE $\geq 5 \text{ mm}$, odnosno teškom formom parodontopatije. Izvršena je procena plak indeksa (PI), indeksa inflamacije gingive (IGI), indeksa krvarenja gingive (IKG) i nivoa pripojnog epitela (NPE), procenjen je PSA nivo i analizirana je njegova korelacija sa ispitanim parodontalnim parametrima, sa svakim ponaosob. Razlike u srednjim vrednostima, kao i statistička značajnost, analizirani su Studentovim t-tesom. Povezanost PSA nivoa sa svim ispitivanim kliničkim parametrima analizirana je upotrebom Pearsonove korelacione analize.

Razultati: Između ispitivanih grupa pacijenata, utvrđena je statistički značajna razlika ($p < 0,05$) između vrednosti ispitivanih parodontalnih indeksa (PI, IGI, IKG, NPE) i vrednosti PSA nivoa. Utvrđeno su više vrednosti PSA nivoa kod pacijenata sa teškom formom parodontopatije u odnosu na pacijente sa umerenom formom parodontopatije. Pearsonova korelaciona analiza pokazala je to da nema statistički značajne povezanosti ispitivanih parodontalnih indeksa (PI, IGI, IKG, NPE) sa PSA nivoom između ispitivanih grupa pacijenata.

Zaključak: Utvrđeno je da pacijenti sa teškom formom parodontopatije imaju više vrednosti PSA nivoa u odnosu na pacijente sa umerenom parodontopatijom. Klinički parodontalni parametri i povišeni PSA nivo ukazuju na moguću vezu između ispitivanih bolesti.

Cljučne reči: parodontopatija; prostata specifični antigen; prostatitis

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Abstract

Introduction: Prostatitis is one of the most chronic diseases which is often associated with periodontitis. The serum Prostate Specific Antigen (PSA) levels can be elevated in a non-malignant condition such as symptomatic and asymptomatic prostatitis. Similarity in the inflammatory etiopathogenesis of these diseases is evident through the presence of Gram negative bacteremia, which in turn may be the possible link between these two conditions.

Aim: To estimate the possible association between chronic periodontitis and prostatitis, evaluating the PSA levels in patients with moderate and severe periodontitis.

Material and methods: 40 patients with prostatitis and elevated Prostate Specific Antigen (PSA) levels ($\geq 4 \text{ ng/ml}$) that participated in the study were hospitalized at the University Urology Clinic at the Faculty of Medicine in Skopje. Patients were divided into two groups on the basis of the levels of periodontal clinical attachment. First group of 20 patients with Clinical attachment level (CAL) $\geq 3 \text{ mm}$, moderate periodontitis and other group of 20 patients with CAL $\geq 5 \text{ mm}$, severe periodontitis. Dental plaque index (DPI), Index of gingival inflammation (IGI), Gingival bleeding index (GBI) and Clinical attachment level (CAL) were recorded and an assessment of PSA values was done and correlation to periodontal parameters, respectively. Differences in means, as statistically significant, were analyzed using Student's t- test. The relationship between PSA scores with all clinical parameters was done using Pearson's correlation coefficient technique.

Results: Statistically significant differences were noted, ($p < 0.05$) between periodontal index values (DPI, IGI, GBI, CAL) and PSA levels within the two examined groups. Higher PSA levels were recorded in patients with severe periodontitis than in those with moderate periodontitis. Pearson coefficient test among these periodontal indices (DPI, IGI, GBI and CAL) and PSA levels in two examined groups showed no statistically significant correlation.

Conclusion: Patients with severe periodontitis were found to have higher PSA levels than those with moderate periodontitis. The clinical parameters of periodontitis and elevated PSA levels indicated a probable link between the two diseases.

Key words: periodontitis; prostate specific antigen; prostatitis

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Uvod

Parodontalno oboljenje predstavlja kompleksnu polimikrobnu inflamaciju potpornog aparata zuba izazvanu određenim mikroorganizmima ili grupama takvih mikroorganizama, što dovodi do kontinuiranog uništavanja parodontalnog ligamenta i alveolarne kosti¹.

Razumevanje patogenetskog mehanizma parodontalne bolesti omogućuje bolje razumevanje oboljenja. Istraživanja ukazuju na potencijalnu vezu parodontopatije i sistemskih oboljenja, kao što su dijabetes, koronarna bolest srca, infarkt, nepovoljna stanja vezana za trudnoću, oboljenja pluća i druga oboljenja. Prostatitis je jedno od oboljenja kod koga je utvrđena povezanost sa parodontopatijom. Oba oboljenja, i prostatitis i parodontopatija, spadaju u oboljenja koje se vezuju za starost osobe, i pogađaju na milione ljudi širom sveta. Ovakvi nalazi doveli su do razvoja i proširenja mnogih perspektiva u upravljanju parodontopatijama, kao nove discipline u oblasti parodontalne medicine².

Benigna hiperplazija prostate (BHP), kao jedno od najučestalijih oboljenja kod muškaraca, definiše se kao iregularna proliferacija vezivnog tkiva, glatkih mišića i glandularnog epitela unutar tranzicione zone prostate. Prostatitis se klinički manifestuje bolnim mokrenjem, otežanim pražnjenjem bešike, učestalom potrebom za mokrenjem, bolovima u penisu, testisima, čak i tokom ili nakon ejakulacije, povezanih sa groznicom i jezom³.

Prostata specifični antigen (PSA) je glikoprotein koji proizvede uglavnom epitelijalne ćelije duž acinusa i duktusa prostatne žlezde. On je biološki ili tumor marker za stanja kao što su benigna hiperplazija prostate, karcinom prostate, i pokazao se korisnim za skrining i potvrđivanju dijagnoze kod značajnog broja pacijenata sa karcinomom prostate⁴. Prostata specifični antigen test rutinski se koristi za skrining karcinoma prostate u SAD još od ranih devedesetih godina prošlog veka. Serumski PSA nivo normalno je veoma nizak. Kada su normalne strukture prostate narušene kao usled oboljenja prostate, inflamacije i traume, tada dolazi do lakšeg ulaska PSA u sistemsku cirkulaciju. Serumski PSA koncentracija ≥ 4 ng/ml generalno se smatra indikatorom karcinoma prostate; kada se sumnja na postojanje ovog karcinoma potrebno je uraditi biopsiju prostate kako bi se potencijalna dijagnoza potvrdila ili odbacila. Serumski PSA test ima suboptimalne specifikacije, s obzirom na to da PSA nivo može biti povećan i kod nemalignih stanja kao što su simptomatski i asimptomatski prostatitis⁵⁻⁸.

Introduction

Periodontal disease is a complex polymicrobial inflammation of the tissues supporting the teeth, caused by certain particular micro organisms or clusters of such microorganisms, leading to the continuous destruction of the periodontal ligament and the alveolar bone¹.

The importance of understanding the mechanisms of pathogenesis of periodontal disease will provide a better understanding of the disease. Research findings point to the potential links between periodontitis and systemic disorders, such as diabetes, coronary heart disease, stroke, pregnancy related adverse conditions, lung disorders and others. Prostatitis is one of the disorders that has shown to have a relationship with periodontitis. Both periodontal disease and prostatitis are age-related diseases that affect millions of people worldwide. These findings together have led to many developments and broadening perspectives about managing periodontitis, as a new discipline of periodontal medicine².

Benign prostatic hyperplasia (BPH), as one of the most common disease in men is defined as unregulated proliferation of connective tissue, smooth muscle and glandular epithelium within the prostate transition zone. Prostatitis clinically presents with painful urination, difficulty in emptying the bladder, frequent tendency to urinate, pain in penis, testicles, even during or after ejaculation, associated with fever and chills³.

Prostate specific antigen (PSA), is a glycoprotein produced mainly by the epithelial cells along the acini and ducts of the prostate gland. It is a biological or tumor marker for conditions such as benign prostatic hyperplasia, prostate cancer, and the screening of which has proven to be beneficial in the confirmatory diagnosis of substantial numbers prostate cancer patients⁴. The prostate specific antigen PSA test has been routinely used for prostate cancer screening in the US since the early 1990s. The serum PSA levels are normally very low. When the normal prostatic structure is disrupted, like prostatic disease, inflammation or trauma, it permits the entry of more PSA to the systemic circulation. A serum PSA concentration ≥ 4 ng/ml is generally considered an indicator for a prostate biopsy to be made in order to confirm or deny the diagnosis of prostate cancer. The serum PSA test has suboptimal specifications because PSA concentration can be elevated in non-malignant condition such as symptomatic and asymptomatic prostatitis⁵⁻⁸.

Etiologija hroničnog prostatitisa zavisi od inflamatornih faktora domaćina, kao što su proinflamatorni citokini, interleukina (IL 1 β) i tumor nekrosis faktora α (TNF α). Povećanje nivoa proinflamatornih citikona i anti-inflamatornih citokina povezano je sa patogeneom parodontopatija kao i prostatitisa. Sličnost etiopatogeneze ovih oboljenja sugerise na moguću povezanost ovih oboljenja, što može biti u vezi i sa povišenim novoom PSA⁹. Predloženi mehanizam povezanosti parodontopatije i prostatitisa uključuje i bakterijemiju nastalu usled oslabljenog parodontalnog epitela i sistemsku imunološku disregulaciju. Veruje se da disbioza mikrobioma kod parodontalne bolesti dovodi i do imunološke invazije i do proinflamatornog stanja^{10,11}. Razumevanje niza zdravstvenih stanja i izloženosti koja utiču na serumski PSA nivo potrebno je kao pomoć pri donošenju odluke za skrining i izvođenje biopsije prostate. Jedno od takvih zdravstvenih stanja je parodontopatija. Budući da parodontopatija i prostatitis imaju gram-negativne bakterije kao ekološke agense⁹, mnoge studije ispitivale su moguću povezanost parodontopatije i PSA kod muškaraca, koji su bili podvrgnuti biopsiji prostate ili su imali hroničnu parodontalnu bolest^{12,13}.

Stoga, sprovedli smo ovu studiju da ispitamo povezanost klinički procenjene parodontalne bolesti i PSA kod muškaraca starosti 50 i više godina i uporedimo nivo PSA u serumu sa parodontalnim kliničkim parametrima koji uključuju plak indeks (PI), indeks inflamacije gingive (IGI), indeks krvarenja gingive (IKG), nivo pripojnog epitela (NPE) između pacijenata ispitivanih grupa.

Cilj studije bio je proceniti moguću povezanost hronične parodontopatije i prostatitisa, praćenjem nivoa PSA kod pacijenata sa umerenom i teškom formom parodontopatije.

Materijal i metode

Studija je sprovedena na Stomatološkom fakultetu u Skoplju, Klinici za parodontologiju i oralnu medicinu i Medicinskom fakultetu u Skoplju, kao i na Klinici za urologiju. Svih 40 studijom obuhvaćenih pacijenata bilo je hospitalizovano na Klinici za Urologiju sa dijagnostikovnim prostatitisom i procenjenim PSA nivoom. Svi pacijenti dobili su informacije o istraživanju i dali su pisanu saglasnost o učešću. Uključujući kriterijumi bili su starost pacijenta ≥ 40 godina, broj zuba ≥ 12 , procenjeni PSA nivo ≥ 4 ng/ml, i nepodvrgnutost oralnoj profilaksi u predhodnih 6 meseci. Pacijenti koji su u anamnezi imali medicinski kompromitovana stanja, kao što

Etiology of chronic prostatitis depends on the inflammatory factors of multiple hosts' such as pro inflammatory cytokines, interleukin (IL 1 β) and tumor necrosis factor α (TNF α). Increased levels of pro-inflammatory and anti-inflammatory cytokines have been associated with the pathogenesis of periodontitis as well as prostatitis. Similarity in the etiopathogenesis of these diseases denotes a possible relationship between the two, which may be apparent with the elevated PSA values in circulation⁹. Proposed mechanisms for the association between periodontitis and prostatitis include the bacteremia secondary to the weakened periodontal epithelium and systemic immune dysregulation. The dysbiosis microbiome in periodontal diseases is believed to create both an immune-invasion and a proinflammatory state^{10,11}. Understanding the array of health conditions and exposures that influence serum PSA is needed to aid in clinical decision-making for screening and for performing a prostate biopsy. One possible health condition is periodontal disease. Since both periodontal disease and prostatitis have Gram-negative bacteria as etiologic agents⁹, many studies have investigated the association between periodontal disease and PSA among men who underwent prostate biopsy or had chronic periodontal disease^{12,13}.

Therefore, we performed the current study to evaluate the association between clinically assessed periodontal disease and PSA in men aged 50 and older and compare the serum PSA levels with periodontal clinical parameters which include Dental plaque index (DPI), Index of gingival inflammation (IGI), Gingival bleeding index (GBI) and Clinical attachment level (CAL) between the study groups.

The aim of the study was to estimate the possible association between chronic periodontitis and prostatitis, evaluating the PSA levels in patients with moderate and severe periodontitis.

Material and methods

The study was performed in the Faculty of Dentistry in Skopje, Clinic for Periodontology and Oral medicine and Faculty of Medicine, Urology Clinic in Skopje. Forty patients who attended in the study were hospitalized in the Urology Clinic of the Faculty of Medicine in Skopje and diagnosed with prostatitis and elevated PSA levels. All the participants in the study were informed about the research and they gave their written consent to participate in the research.

su infarkt miokarda, moždani udar, transplantacija organa u predhodnih 6 meseci bili su isključeni iz studije. Izvršen je parodontološki pregled pacijenata kojim su registrovani sledeći indeksi: plak indeks (PI) po Silness-Loe¹⁴, indeks inflamacije gingive (IGI) po Silness-Loe¹⁵, indeks krvarenja gingive (IKG) po Ainamo Bayu¹⁶, kao i nivo pripojnog epitela (NPE)¹⁷. Za svakog pacijenta obuhvaćenog studijom, iz anamnestičkog zdravstvenog kartona uzeti su podaci o PSA nivou i dijagnostikovanim oboljenjem.

Statistička analiza

Istraživanje je sprovedeno deskriptivnom statističkom analizom. Razlika u srednjim vrednostima, kao i statistička značajnost analizirana su Studentovim t-testom. Povezanost PSA skora sa kliničkim parametrima procenjena je Pearsonovom korelacionom analizom.

Rezultati

Prema težini parodontalne bolesti, pacijente smo podelili u dve grupe, grupu pacijenata sa umerenom parodontopatijom i grupu pacijenata sa teškom parodontopatijom, po 20 u svakoj grupi. Pacijenti sa umerenom parodontopatijom bili su prosečne starosti 52 godine, dok su pacijenti sa teškom parodontopatijom bili prosečne starosti 62 godine (Figura 1). U prvoj grupi, od 20 pacijenata njih 16 (80%) bili su sa benignom hiperplazijom prostate, dok je 4 pacijenta (20%) bilo sa znacima maligniteta. Nasuprot tome, u drugoj grupi 17 pacijenata (85%) je bilo sa znacima maligniteta, dok su 3 pacijenta (15%) bila sa benignom hiperplazijom prostate. Utvrđene su statistički značajne razlike ($p < 0,05$) između vrednosti parodontalnih indeksa (PI, IIGI, IKG, NPE) i PSA nivoa između ispitivanih grupa, pacijenata sa umerenom parodontopatijom (Tabela 1) i naročito kod pacijenata sa teškom parodontopatijom (Tabela 2). Takođe detektovali smo porast nivoa PSA sa progresijom bolesti. Pearson ova korelaciona analiza između parodontalnih indeksa i PSA nivoa u dve ispitivane grupe pacijenata nije pokazala statistički značajnu korelaciju u obe ispitivane grupe (Figura 2,3,4,5,6,7,8,9).

Inclusion criteria were that patients aged ≥ 40 , with ≥ 12 teeth, with elevated serum PSA ≥ 4 ng/ml had not undergone oral prophylaxis in the previous six months. Those with any history of systematically compromised conditions such as myocardial infarction, stroke and organ transplantation during the previous 6 months were not covered in the study. We performed periodontal examination on all respondents and noted the following index parameters: DPI of Silness-Loe¹⁴, IGI of Loe-Silness¹⁵, GBI of Ainamo and Bay¹⁶ and CAL¹⁷. In each of them, data on PSA values and the appropriate diagnosis were taken from the anamnestic health card.

Statistical analysis

The present study was carried out by descriptive statistical analysis. Difference in means as statistically significant was analyzed using Student's t-test. The relationship between PSA scores with all clinical parameters was assessed using Pearson's correlation coefficient technique.

Results

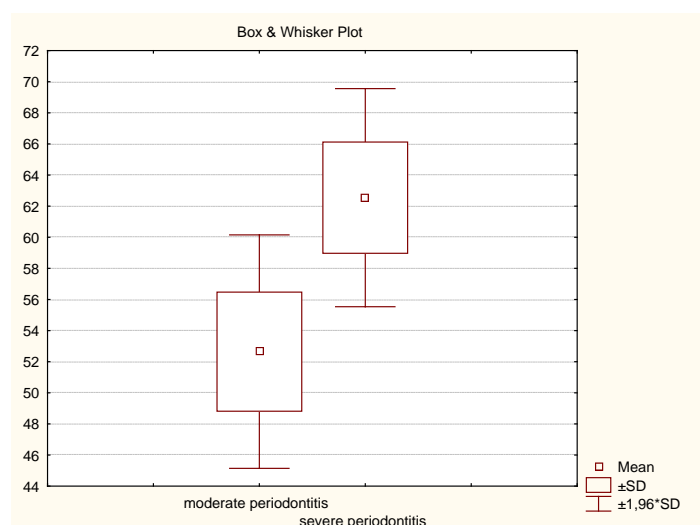
We divided the patients into two groups according to the severity of the periodontal disease, patients with moderate and patients with severe periodontitis, 20 in each group. Patients with moderate periodontitis were at an average age of 52 years, and those with severe, at 62 years. (Figure 1). In the first group of 20 patients, 16 patients (80%) were with benign prostate hyperplasia, and 4 patients (20%) with signs of malignancy. Conversely, in the second group, 17 patients (85%) had signs of malignancy and 3 patients (15%) had benign prostate hyperplasia. Statistically significant differences were noted, ($p < 0.05$) between periodontal index values (DPI, IGI, GBI, CAL) and PSA levels within the two examined groups, patients with moderate periodontitis, (Table 1) and specifically in patients with severe periodontitis, (Table 2), where we consequently noted higher periodontal index values than those with a moderate form. We also detected an increase in PSA values with disease progression. Pearson coefficient test among periodontal indices (DPI, IGI, GBI and CAL) and PSA levels in two examined groups showed statistically no significant correlation in the both examine groups (Figure 2,3,4,5,6,7,8,9).

Tabela 1. Parodontalni indeksi (PI, IGI, IKG, NPE) i PSA nivo kod pacijenata sa umerenom parodontopatijom**Table 1.** Periodontal indices (DPI, IGI, GBI,CAL) and PSA levels in patients with moderate periodontitis

<i>Moderare parodontopatija / Umerena periodontitis</i>	X	SD	N	Diff	Std Diff	t	df	p
DPI/PI	1.4	0.50						
PSA/PSA	7.2	1.43	20	-5.8	1.47	-17.6	19	0.000000
IGI/IGI	1.9	0.55						
PSA/PSA	7.2	1.43	20	-5.3	1.38	-17.7	19	0.000000
GBI/IKG	1.9	0.55						
PSA/PSA	7.2	1.43	20	-5.3	1.41	-16.7	19	0.000000
CAL/NPE	3.5	0.82						
PSA	7.2	1.43	20	-3.7	1.83	-9.0	19	0.000000

Tabela 2. Parodontalni indeksi (PI, IGI, IKG, NPE) i PSA nivo kod pacijenata sa teškom parodontopatijom**Table 2.** Periodontal indices (DPI, IGI, GBI, CAL) and PSA levels in patients with severe periodontitis

<i>Teška parodontopatija/Severe periodontitis</i>	X	SD	N	Diff	Std Diff	t	df	p
DPI/PI	2.2	0.61						
PSA/PSA	13.7	2.00	20	-11.5	2.11	-24.31	19	0.000000
IGI/IGI	2,4	0,5						
PSA/PSA	13.7	2.00	20	-11.3	1.94	-25.92	19	0.000000
GBI/IKG	2.8	0.41						
PSA/PSA	13.7	2.00	20	-10.9	2.17	-22.42	19	0.000000
CAL/NPE	5.3	0.8						
PSA	13.7	2.00	20	-8.4	2.18	-17.18	19	0.000000

**Figura 1.** Prosečna starost pacijenata sa umerenom i teškom parodontopatijom
Figure 1. Average age values in patients with moderate and severe periodontitis

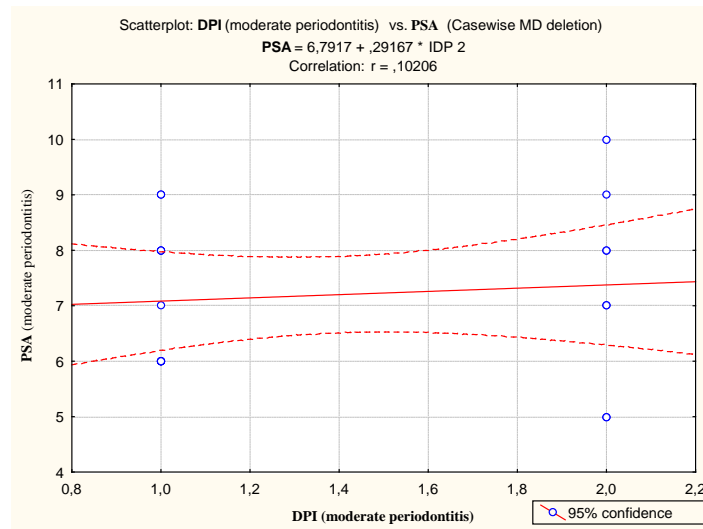


Figura 2. Pearsonov korelacioni koeficijent za vrednosti PI prema PSA kod pacijenata sa umerenom parodontopatijom ($r = 0,10206$)

Figure 2. Pearson's correlation coefficient value DPI vs. PSA in patients with moderate periodontitis ($r = 0.10206$)

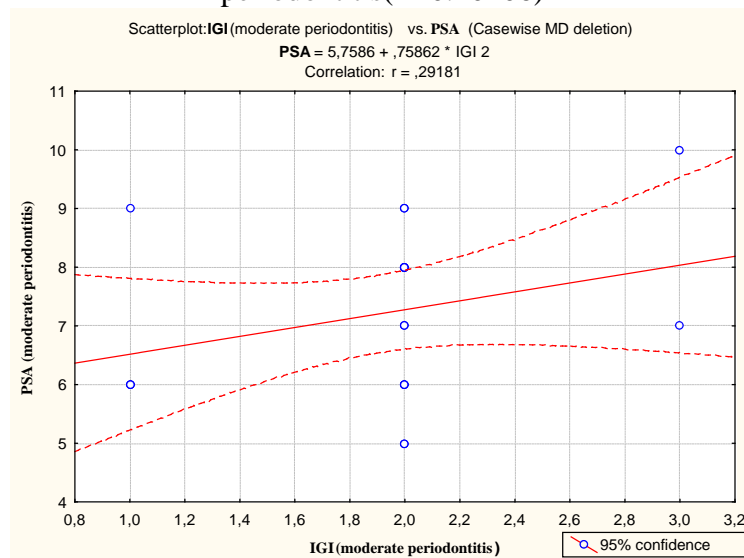


Figura 3. Pearsonov korelacioni koeficijent za vrednosti IGI prema PSA kod pacijenata sa umerenom parodontopatijom ($r = 0,29181$)

Figure 3. Pearson's correlation coefficient value IGI vs. PSA in patients with moderate periodontitis ($r = 0.29181$)

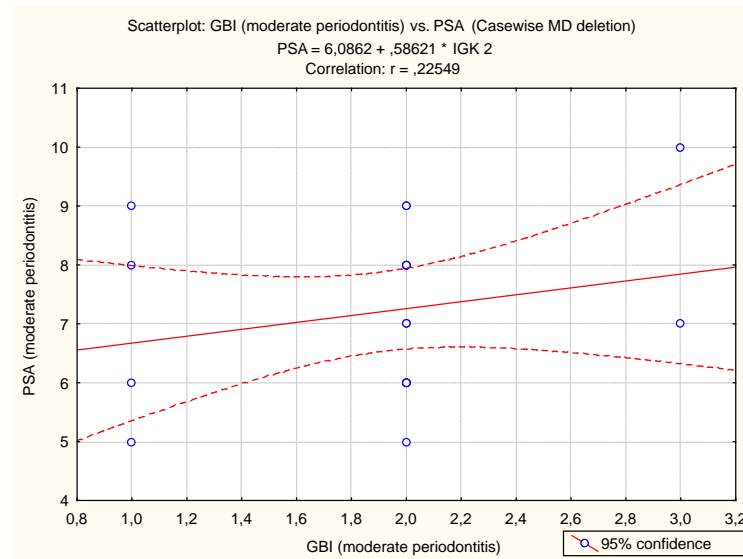


Figura 4. Pearsonov korelacioni koeficijent za vrednosti IKG prema PSA kod pacijenata sa umerenom parodontopatijom ($r = 0,22549$)
Figure 4. Pearson's correlation coefficient value GBI vs. PSA in patients with moderate periodontitis ($r=0.22549$)

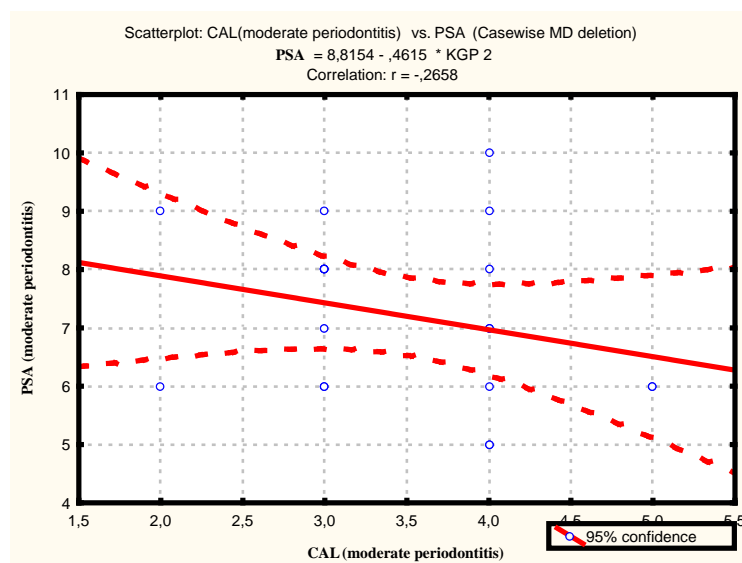


Figura 5. Pearsonov korelacioni koeficijent za vrednosti NPE prema PSA kod pacijenata sa umerenom parodontopatijom ($r = 0,2658$)
Figure 5. Pearson correlation's coefficient value CAL vs. PSA in patients with moderate periodontitis ($r=0,2658$)

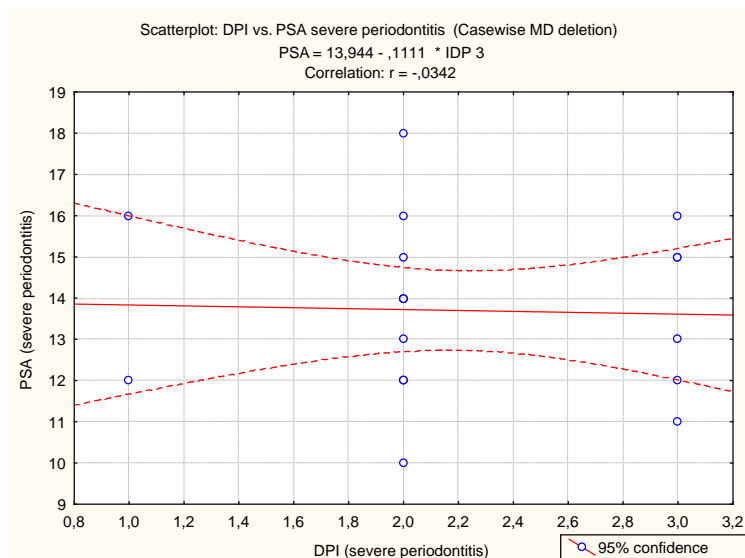


Figura 6. Pearsonov korelacioni koeficijent za vrednosti PI prema PSA kod pacijenata sa teškom parodontopatijom ($r = -0,0342$)

Figure 6. Pearson's correlation coefficient value DPI vs. PSA in patients with severe periodontitis($r=-0.0342$)

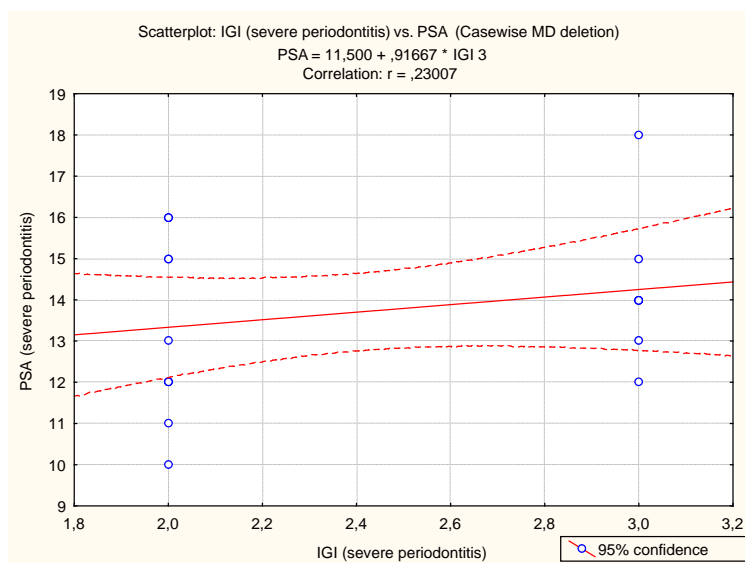


Figura 7. Pearsonov korelacioni koeficijent za vrednosti IGI prema PSA kod pacijenata sa teškom parodontopatijom ($r = 0,23007$)

Figure 7. Pearson's correlation coefficient value IGI vs. PSA in patients with severe periodontitis($r=0.23007$)

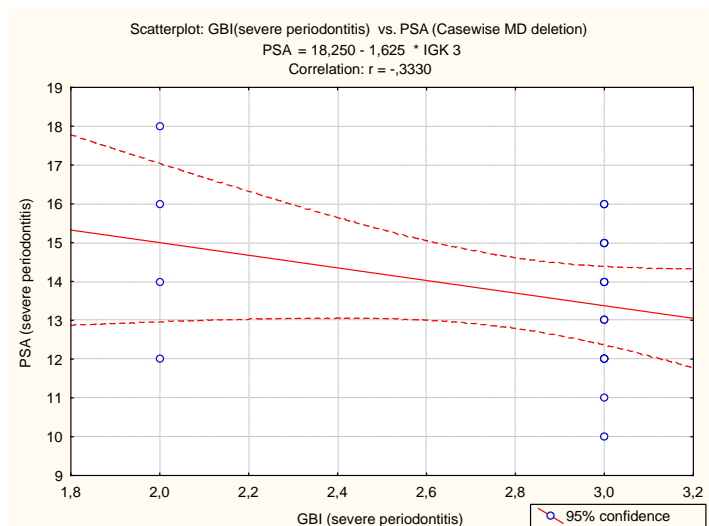


Figura 8. Pearsonov korelacioni koeficijent za vrednosti IKG prema PSA kod pacijenata sa teškom parodontopatijom (r = - 0,3330)

Figure 8. Pearson's correlation coefficient value GBI vs. PSA in patients with severe periodontitis(r=-0.3330)

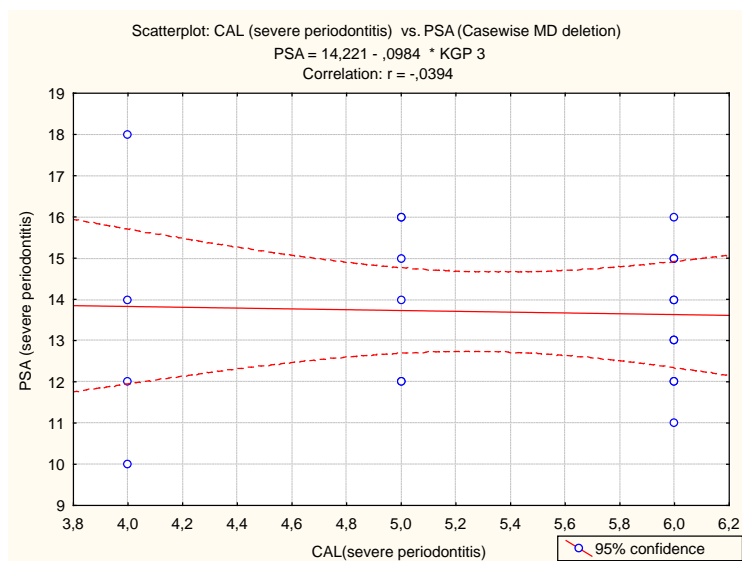


Figura 9. Pearsonov korelacioni koeficijent za vrednosti NPE prema PSA kod pacijenata sa teškom parodontopatijom (r = - 0,0394)

Figure 9. Pearson's correlation coefficient value CAL vs. PSA in patients with severe periodontitis(r=-0.0394)

Diskusija

Studijom je ispitivana povezanost parodontopatije i prostatitisa. Parodontopatija je sistemsko stanje koje doprinosi inflamatornoj reakciji domaćina kroz povećani nivo proinflammatoryh citokina. Proinflammatory citokini od značaja su u patogenezi i parodontopatije i prostatitisa. Parodontalno oboljenje dovodi do porasta proinflammatoryh citokina kao što su IL-1, IL6 i TNF, koji su takođe pronađeni u serumu muškaraca sa dijagnostikovanim prostatitisom. U tom smislu, parodontopatija indirektno doprinosi prostatitisu i to povećanim inflamatornim odgovorom na prostatitis^{18,19}. Povišeni nivo proinflammatoryh citokina zabeležen je kod muškaraca sa prostatitisom u odnosu na nivo ovih citokina kod zdravih muškarca^{20,21}.

Joshi i sar.⁹ pokazali su to da su pacijenti koji su istovremeno imali prostatitis sa umerenom ili teškom formom parodontopatije imali viši nivo PSA u odnosu na pacijente koji su imali samo jednooboljenje, bilo koje, od ovih oboljenja. Oni su sugerisali da parodontopatija širenjem proinflammatoryh citokina može poremetiti integritet epitela žlezda prostate i dovesti do prostatitisa, što delimično objašnjava povišeni PSA nivo u serumu. Postoji još jedno objašnjenje. Periodoncijum kao udaljeni izvor koji nije u vezi sa prostatitisom, može se smatrati odgovornim za povišeni PSA u serumu²². U ovoj studiji registrovali smo pozitivnu povezanost između PSA nivoa i težine parodontopatije. Pacijenti sa teškom formom parodontopatije imali su viši PSA nivo u odnosu na pacijente sa umerenom formom parodontopatije, što implicira da vrednosti PSA nivoa rastu sa težinom parodontopatije i prostatitisa. U grupi pacijenata sa teškom formom parodontopatije najveći procenat, tačnije 85% bili su sa znacima maligniteta prostate. U grupi pacijenata sa umerenom formom parodontopatije, 80% pacijenata bili su sa znacima benigne hiperplazije prostate. Ovakav nalaz u skladu je sa rezultataima Joshi N. i sar. koji su zaključili da pacijenti koji su imali komorbitet sa NPE > 2,7mm i umerenom i teškom formom parodontopatije imali povišeni nivo PSA u odnosu na one sa samo jednim stanjem⁹. Oni su takođe istakli to da tretiranje parodontopatije dovodi do redukcije PSA nivoa što može biti odraz smanjenja intraprostatke upale.

Discussion

The association between periodontitis and prostatitis is yet to be established. Periodontal disease is a systemic condition that contributes to an inflammatory reaction on the host through increased levels of pro-inflammatory cytokines. The role played by pro-inflammatory cytokines in the pathogenesis of periodontitis and prostatitis has been recognized. Periodontal disease leads to increased levels of pro-inflammatory cytokines such as IL-1, IL-6 and TNF, which were found in the blood serum of men with prostatitis. In that regard, periodontitis indirectly contributes to prostatitis by increasing inflammatory response to prostatitis^{18,19}. Elevated levels of pro-inflammatory cytokines are reported in men with prostatitis and compared to those of healthy individuals^{20,21}.

Joshi et al.⁹ showed that patients with prostatitis and moderate and severe periodontitis have higher PSA levels than those with either condition alone. They suggested that periodontitis through dissemination of pro-inflammatory cytokines may disrupt the integrity of prostate glandular epithelium and lead to prostatitis, so in that way, it partly explains increased serum PSA levels. There is another possibility. Periodontium, as a distant non prostatitis source of PSA may also be considered responsible for the increase in serum PSA levels²². In the present study we noted a positive relationship between PSA levels and the severity of periodontitis. Patients with severe periodontitis have a higher PSA levels than those with moderate periodontitis, implying that PSA values go up with the severity of periodontitis and prostatitis. In the group with severe periodontitis most of the patients, 85% of them exactly, were with signs of prostate malignancy. The other group with moderate periodontitis, 80% of patients were with signs of benign prostate hyperplasia. This observation is in agreement with Joshi N et al. which concluded that patients having comorbidity of CAL > 2.7mm and moderate or severe prostatitis had higher levels of PSA than those with one of these conditions⁹. They also reported that treating the periodontal disease reduced PSA levels, which may be a reflection of a reduction of intraprostatic inflammation. Elimination of periodontal pathogens through periodontal therapy may reduce the exposure of the prostate to bacteria toxins.

Eliminacija parodontalnih patogena tokom terapije parodontopatije može redukovati izloženost prostate bakterijskim toksinima.

Značajno poboljšanje registrovano je u IPSS u periodu između 4 nedelje i 8 nedelja nakon parodontalnog tretmana, što može biti rezultat smanjenja PSA u serumu i nivoa inflamatornih citokina, kao što su CRP i IL-1 beta, nakon nehirurškog tretmana kod muškaraca sa hroničnom parodontopatijom, sa istovremenim smanjenjem veličine žlezda prostate²³.

U našoj studiji, 85% muškaraca sa teškom formom parodontopatije bili su sa znacima maligniteta prostate. Sa druge strane, u grupi pacijenata sa umerenom formom parodontopatije 80% njih je bilo sa znacima benigne hiperplazije prostate. Ovakav nalaz takođe je u skladu sa nalazom Kandira i sar., koji su pokazali to da pacijenti koji pate od umerenog ili teškog prostatitisa imaju viši PSA nivo u odnosu na pacijente sa blagom formom ili bez ovog oboljenja. Patohistološkom analizom biopsiranog uzorka oni su utvrdili i vezu između nivoa PSA u serumu i asertivnosti inflamacije prostate²⁴.

Zaključak

Rezultate treba razmotriti sa aspekta dizajna studije. Uprkos ograničenjima naše studije kao što su veličina uzorka i nedostatak kontrolne grupe, studija je pružila podatke o uzročnoj povezanosti parodontopatije i visokog nivoa PSA u serumu. Drugo ograničenje predstavljalo je određivanje nivoa PSA izvršeno u određenom trenutku, te nivo PSA nije praćen tokom dužeg vremenskog perioda. Neophodna je dobro kontrolisana longitudinalna studija sa većom veličinom uzorka, kao i praćenje inflamatornih citokina u patogenezi parodontopatije i prostatitisa kako bi se dodatno razjasnila povezanost ove dve bolesti.

Significant improvements were noticed in IPSS for a period of 4–8 weeks after periodontal treatment, which may be the result of a reduction in the serum PSA and inflammatory cytokine levels such as CRP and IL-1 beta, after nonsurgical treatment in men with chronic periodontitis, also resulting in the shrinking of the prostate gland in size²³.

In our study, 85% of the patients in the group with severe periodontitis were with signs of prostate malignancy. On the other side, the group with moderate periodontitis, 80% of patients were with a sign of benign prostate hyperplasia. This is also in confirmatory with the findings of Kandira et al., who showed higher PSA levels in patients suffering from moderate to severe prostatitis in comparison with those with mild or no condition of the same. They also approved the affirmative association between the serum PSA levels and the assertiveness of inflammation of prostate glands, through the histopathological findings from the biopsy²⁴.

Conclusion

Findings should be considered in terms of the study designed. Despite the limitations of our study due to the size of the sample and the lack of control group, it does not fail to provide a causal affiliation to periodontitis and high serum PSA levels. Another limitation is that the PSA levels determination were taken at one point in time rather than over a longer time period. A well-controlled longitudinal study with a larger sample size as well as monitoring the inflammatory cytokines in the pathogenesis of periodontitis and prostatitis is warranted to further clarify the association between these two diseases.

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ZNANJE O ORALNOM ZDRAVLJU, STAV I PRAKSA PACIJENTA KOJI SE PRATE TOKOM PANDEMIJE COVID- 19 VIRUSA U MAKASARU

ORAL HEALTH KNOWLEDGE, ATTITUDE AND PRACTICE AMONG PEOPLE IN MONITORING DURING COVID-19 PANDEMIC IN MAKASSAR

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Sažetak

Uvod: Održavanje oralnog zdravlja je bitno za imuni sistem u borbi protiv korona virusnog oboljenja, (COVID)-19 infekcije, zbog prisustva IgA u pljuvački. Na oralno zdravlje utiču znanje, stavovi i praksa.

Cilj: Ispitivanje znanja o oralnom zdravlju, stavovi i praksa pacijenata među pacijentima koji se prate (PKSP), tokom covid-19. **Materijali i metode:** Populacija ove studije su bili stanovnici Makasara koji su bili identifikovani kao pacijenti koji se prate (PKSP). Online upitnik je poslat preko Google forme, da bi se vrednovalo znanje, stavovovi i praksa.

Rezultati: U pogledu znanja o oralnom zdravlju, stavovima i praksi među 72 PKSP u Makasaru, 25%, 50% i 25% ispitanika je kategorizovano sa lošim, umerenim i dobrim znanjem, redom. U pogledu varijable stava o oralnom zdravlju 40.3%, 34.7% i 25% ispitanika je kategorizovano sa lošim, umerenim i dobrim stavom, redom. U pogledu prakse oralnog zdravlja, bilo je 26.4%, 38.9% i 34.7% ispitanika sa lošom, umerenom i dobrom praksom, redom.

Zaključak: Većina PKSP ima nizak nivo znanja o oralnom zdravlju i stavovima, a srednji nivo prakse oralnog zdravlja.

Gljučne reči: COVID-19, oralno zdravlje pacijenata koji se prate, nivo znanja, stavovi

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Abstract

Introduction: Oral health maintenance is essential in the immune system against corona virus disease (COVID)-19 infection due to the presence of IgA in saliva. Oral health is affected by knowledge, attitudes, and practices.

Aim of study is to investigate the oral health, knowledge, attitudes and practice among people in monitoring (PiM) during the covid 19 pandemic in Makassar.

Materials and methods: The population of this study was Makassar citizens who have been identified as people in monitoring (PiM). Online questionnaire was sent via Google form to assess the knowledge, attitudes, and practice.

Results: In the category level of oral health knowledge, attitudes and practices among 72 PiM in Makassar, 25%, 50%, and 25% respondents were categorized as having poor, moderate and good knowledge, respectively. In the category of oral health attitude variable, 40.3%, 34.7% and 25% respondents were categorized as poor, moderate and good, respectively. In the category of oral health practices, there were 26.4%, 38.9% and 34.7% of respondents with low, moderate and good oral health practices, respectively.

Conclusion: Most PiM in had low oral health knowledge, low oral health attitude and medium oral health practices.

Key words: COVID-19, oral health, people in monitoring, level of knowledge, attitudes

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Uvod

Oboljenje izazvano korona virusom (COVID-19) identifikovano je kao uzrok respiratorne pandemije koja je počela 2019 godine. Patogen koji je uzorkovao oboljenje Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), član je porodice korona virusna¹⁻³.

Prema podacima koji su zabeleženi do maja 2020 godine, oboljenje SARS-CoV-2 raširila se među 207 zemalja i više miliona ljudi širom sveta zaraženo je COVID-19 virusom. Jedanaestog marta 2020 godine, WHO (World health organization / Svestska zdravstvena organizacije) proglasila je širenje pandemije COVID-19 virusa^{4,7}.

Ova pandemija, koja je počela u Wuhanu (provincija Hubei, Kina) donela je mnoge izazove, naročito na polju javnog zdravstva u mnogim zemljama, uključujući Indoneziju. Indonezija je četvrta najnaseljenija zemlja na svetu i predviđeno je da će se suočavati sa pandemijom u dužem periodu u poređenju sa manje naseljenim zemljama^{8,9}.

Kada je Kina doživela najteži udar pandemije COVID-19 virusa u decembru 2019. godine, sve do februara 2020. godine, Indonezija još uvek nije prijavila ni jedan slučaj infekcije izazvane COVID-19 virusom. Međutim, 2. marta, potvrđena su dva slučaja infekcije COVID-19 virusom, prijavljena u Indoneziji. Drugog aprila bilo je 1790 potvrđenih slučajeva infekcije COVID-19 virusom, od kojih 113 novih slučajeva, 170 smrtnih slučajeva i 112 izlečenih bolesnika⁹.

Makasar kao glavni grad južnog Sulavesija, jedne od najvećih pokrajina u Indoneziji takođe je pogođen epidemijom COVID-19 virusa, od 11. maja. Na osnovu podataka Kancelarije za javno zdravlje južne pokrajine Sulavesija, bilo je 397 potvrđenih slučajeva infekcije COVID-19 virusom, 160 smrtnih slučajeva, 1229 PPK (pacijenta pod kontrolom) i 4413 PKSP (pacijenti koji se prate)^{10,11}.

Virus COVID-19 može se širiti preko pljuvačke (kapljično) kada inficirani ljudi kašlju i kijaju oko 6 stopa udaljenosti od zdravih osoba ili dodirivanjem površina gde se virus zadržao, kao na primer prilikom držanja za ruke, telefona ili dodirivanja kvake na vratima¹². Na osnovu sprovedene studije od strane Liu i sar., angiotensin konvertujući enzim II (ACE2) odgovoran je receptor za COVID-19 virus u ljudskom telu¹³.

U usnoj duplji, ACE2 receptori češće se nalaze na jeziku u poređenju sa bukalnom sluzokožom i gingivom. To ukazuje na to da je sluzokoža usne duplje predstavlja potencijalni ulaz za COVID-19 virus. Zatim, COVID-19

Introduction

Corona virus disease-2019 (COVID-19) has been identified as the cause of a respiratory illness pandemic that started at the end of 2019. The pathogen that causes this disease, the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), is a member of the corona virus family¹⁻³.

According to the data recorded until May 2020, SARS-CoV-2 has spread in 207 countries and more than 4 million populations around the world have been infected by COVID-19. On March 11th, 2020, WHO declared the spread of COVID-19 as a pandemic⁴⁻⁷.

This pandemic, which started in the city of Wuhan in the province of Hubei, China, has brought many challenges, especially in the field of public health in many countries, including in Indonesia. Indonesia is the world's 4th most populous country and has been predicted to face this pandemic in a longer period of time compared to less populous countries^{8,9}.

When China experienced the most severe COVID-19 outbreak in December 2019-February 2020, Indonesia had yet to report any cases of COVID-19 infection. However, in March 2nd, 2020, two confirmed cases of COVID-19 were reported in Indonesia. In April 2nd, 2020, Indonesia had reached 1790 confirmed COVID-19 cases, 113 new cases, 170 deaths, and 112 cured cases⁹.

Makassar as the capital city of South Sulawesi, one of the largest provinces in Indonesia, is also affected by the COVID-19 outbreaks. Until May 11th, 2020, based on the data from the Public Health Office of South Sulawesi, there has been 397 confirmed cases of COVID-19 infection, 160 deaths, 1229 PiC (Patient In Control) and 4413 PiM (People In Monitoring)^{10,11}.

COVID-19 may be spread through saliva (droplet) when infected people cough or sneeze about 6 feet from the healthy or by touching the surface of object with this virus on it, such as holding hands, phone, or the handle of the door¹². Based on the study conducted by Liu et al., the angiotensin-converting enzyme II (ACE2) is the responsible receptor of COVID-19 in human body¹³.

In the oral cavity, ACE2 receptors are more commonly found in tongue than the buccal or gingival mucosa. This indicates that oral mucosa is a potential port d'entrée for COVID-19. In addition, COVID-19 may be detected through saliva secretion which contains high immunoglobulin A (IgA) towards COVID-19^{14,15}.

virus može biti detektovan preko pljuvačke, koja sadrži visoke koncentracije imunoglobulina A (IgA) zbog infekcije izazvane COVID-19 virusom^{14,15}.

IgA je glavni imunoglobulin koji igra ulogu u sekreciji, uključujući i stvaranje pljuvačke. IgA deluje kao prva linija odbrane protiv patogena koji napadaju posebno površinu sluzokože usne duplje. Salivarna IgA (s-IgA) antitela mogu pomoći imunom odgovoru usne duplje, na način što sprečavaju pripajanje patogena kao što su virusi ili bakterije za sluzokožu usne duplje. Ova antitela mogu, takođe, da budu uskladjena sa drugim faktorima kao što su lizozimi i enzim laktoferin¹⁶.

Dentalno i oralno održavanje zdravlja su bitni faktori koji pomažu imunom sistemu protiv virusa COVID-19, zbog toga što sugeriše da pljuvačka sadrži IgA antitela. Pored toga održavanje oralnog zdravlja će sigurno sprečiti mogućnost pojave karijesa i parodontalnih oboljenja, što će sprečiti potrebu posete stomatologu u toku pandemije COVID-19. Potrebno je da sprovede prevenciju kod kuće kao što je pranje zuba dva puta dnevno, korišćenje konca za zube i ispiranje vodicama za usta. To može takođe da redukuje širenje COVID-19 infekcije¹⁵⁻¹⁷.

Dentalno i oralno zdravlje i dalje su glavni javno-zdravstveni problemi u svetu, iako se velikom procentu mogu sprečiti. Karijes zuba, parodontalna oboljenja i karcinom usne duplje su veoma česta hronična stanja i glavna dentalna i oralna oboljenja. Nejednakost prevalencije se javlja u svim zemljama, ne može se objasniti razlikama u trenutnom zdravstvenom sistemu¹⁸.

Na osnovu ankete o zdravstvenoj zaštiti iz 2001. godine, među 10 najučestalijih bolesti u Indoneziji, Bolesti zuba i oralna oboljenja su na prvom mestu sa prevalencom od 61%¹⁹.

Glavna etiologija problema sa zdravljem zuba i usne duplje u zajednici je nezadovoljavajući odnos između stavova oralnog zdravlja i prakse. Na to utiče njihovo slabo znanje o značaju održavanja oralnog zdravlja. Pored toga, različiti faktori koji utiču na njihovo znanje, stav i praksu prema zdravlju zuba i usne duplje su upotreba četkice i paste, pranje zuba i poseta stomatologu²⁰.

Na osnovu prethodnog opisa, zainteresovani smo za ispitivanje znanja, stavova i praksi oralnog zdravlja među PKSP (pacijenti koji se prate) tokom pandemije COVID-19 u Makasaru.

Metode

Populacija u Makasaru koja je identifikovana kao PKSP sa kojima smo se susreli tokom COVID-19 od 12 poena.

IgA is the main immunoglobulin that plays a role in secretions, including saliva production. IgA acts as the first line of defense against pathogens that invade the mucosal surface especially in oral cavity. Saliva IgA (s-IgA) antibodies may help the oral cavity immunity by preventing the attachment of pathogens such as viruses and bacteria on mucosa. These antibodies can also synergize with other factors such as the lysozyme and lactoferrin enzyme¹⁶.

Dental and oral health maintenance are important factors that help the immune system against the infection of COVID-19 virus, because it is suggested that saliva contains IgA antibody. In addition, maintaining oral health will certainly prevent the possibility of dental caries and periodontal diseases, thus reducing the need for dental visit during COVID-19 pandemic. It is only needed to perform the dental prevention at home such as brushing teeth twice a day, using dental floss and rinsing with mouthwash. It may also be help to reduce the spread of COVID-19 virus infection¹⁵⁻¹⁷.

Dental and oral health diseases remain major public health problems in the world although they are largely preventable. Dental caries, periodontal disease and oral cancer are very common chronic conditions and the main dental and oral diseases are found present. Inequality of prevalence occurs in all countries, it cannot be explained by contemporary differences in the health care system¹⁸.

Based on the health nationwide survey in 2001, out of 10 of the most prevalent diseases in Indonesia, dental and oral health disease occupied the first place with a prevalence of 61%¹⁹.

The main etiology of dental and oral health problems in community is poor oral health attitude and practices. This is influenced by their poor knowledge of the importance of oral health maintenance. In addition, various factors that influence their knowledge, attitudes and practices towards dental and oral health are the use of toothbrush and toothpaste, brushing teeth and visit to the dentist²⁰.

Based on the description in the background, we are interested in investigating the oral health knowledge, attitudes and practices among PiM (People in monitoring) during COVID-19 pandemic in Makassar.

Methods

The population was Makassar citizen identified as PiM whom we encountered during COVID- of 12 points.

Ovaj upitnik je testiran pomoću Pirosonovg testa korelcije (r vrednost M (SD) = 0.756 (0059) za kategoriju znanja, a r vrednost M10 za program nadzora od marta-aprila, 2020.

Ispitanici su bili uključeni u ovu studiju ukoliko su odgovorili na linkove online google upitnika koji su istraživači slali putem WhatsApp-apa i poruka.

Instrumenti

Instrumenti naše studije su online upitnici koji su poslani u vidu "google" forme. Upitnici su korišćeni da se utvrdi nivo znanja o oralnom zdravlju, stavovima i praksi među PKSP u Makasaru. U pogledu varijable znanja o oralnom zdravlju, ocena 1 je data za svako tačno odgovoreno pitanje, a ocena 0 za svaki pogrešan odgovor ili odgovor „ne znam“. U pogledu varijable stava oralnog zdravlja, ocena 1 data je za svaki odgovor „da“, osim za pitanja sa datim kodom (N) ili oni koji moraju da odgovore ne bi postigli ocenu 1. U promenljivoj oralne zdravstvene prakse, svaki odgovor „da“ postigao bi 1, osim kodnih pitanja (N), ili onaj ko mora da odgovori ne bi postigao 1, postigavši maksimalnih 12 poena. Ovaj upitnik je testiran na validnost pomoću Pearsonovog testa korelacije (r vrednost M (SD) = 0,756 (0059) za kategoriju znanja, r vrednost od M (SD) = 0,755 (0053) za promenljive varijable i r vrednosti M (SD) = 0,592 (0058) za varijable prakse i njegovu pouzdanost je ispitana korišćenjem Cronbach Alpha testa (vrednost Cronbach alpha = 0,624 za promenljivu znanja, vrednost Cronbach alpha = 0,621 za varijablu stavova i vrednosti Cronbach alpha = 0 630 za varijablu prakse). Test je sproveden na prvih 30 ispitanika koji su popunili ovaj upitnik, od 72 ispitanika koji su bili uključeni u predmet našeg istraživanja.

Analiza podataka

Analiza podataka izvršena je deskriptivnom analizom kako bi se utvrdio nivo znanja o dentalnom i oralnom zdravlju, stavov i praksa među PKSP u Makasaru. Podaci u ovoj studiji predstavljeni su tabelama i figurom.

Rezultati

Od ukupno 120 ispitanika, 72 ispitanika je popunilo upitnik, njih je činilo 36 (50%) muškaraca i 36 (50%) žena. Na osnovu starosti, najviše ispitanika bili su odrasli (70 ispitanika, 97,3%), prosečne starosti 28 godina (dodatak appendix).

This questionnaire tested for validity using Pearson Correlation test (rvalue M (SD) = 0.756 (0059) for the category of knowledge, the r value of M 10 surveillance program from March - April, 2020.

Subjects were included in this study if they answered the online google form questionnaire links shared by the researchers via WhatsApp and message.

The Instruments

The instruments of our study are online questionnaires that were distributed through google form. Questionnaires were used to determine the level of oral health knowledge, attitudes, and practices among PiM in Makassar. In term of oral health knowledge, a score 1 was given for every correctly answered question and a score 0 was given for every wrong or "do not know" answer. In oral health attitude variable, a score 1 was given for every "yes" answer, except for questions with the given code (N) or those who have to answer would not score 1. In oral health practices variable, every "yes" answer would score 1 except for the code questions (N) or who must answer would not score 1, making a maximum score of 12 points. This questionnaire was tested for validity using Pearson Correlation test (rvalue M (SD) = 0.756 (0059) for the category of knowledge, the r value of M (SD) = 0.755 (0053) for attitudes variable and r values of M (SD) = 0.592 (0058) for practices variable and its reliability was tested by using Cronbach Alpha test (the value of Cronbach alpha = 0.624 for knowledge variable, the value of Cronbach alpha=0.621 for attitudes variable and values of Cronbach alpha = 0. 630 for practices variable). The test was conducted on the first 30 respondents who filled out this questionnaire, out of the 72 respondents who were included as subjects in our study.

Data analysis

The data analysis was through descriptive analysis to determine the level of dental and oral health knowledge, attitudes and practices among PiM in Makassar. The data in this study were presented in tables and narratives.

Tabela 1. Kriterijumi za procenu znanja o oralnom zdravlju, stavovima i praksi među PKSP (pacijentima koji se prate) tokom COVID-19 pandemije u Makasaru
Table 1. Criteria for Assessment of Oral health Knowledge, Attitude and Practice Among ODP (People in Monitoring) during COVID -19 pandemic in Makassar

Knowledge	
1. Održavanje zdravlja zuba i usne duplje može poboljšati imuni system u borbi protiv Covid-19? / Can maintaining the health of your teeth and mouth improveth the immune system to fight against Covid-19?	a. Da / Yes 1 b. Ne / No 0 c. Ne znam / I don't know 0
2. Da li se grgorenjem antiseptičkim rastvorom efektivno eliminiše Covid-19? / Does gargling with an antiseptic solution effectively kill the Covid-19?	a. Da / Yes 0 b. Ne / No 1 c. Ne znam / I don't know 0
3. Da li konzumiranje povrća i voća može efektivno da poboljša imuni sistem u borbi protiv Covid-19? / Can eating vegetables and fruits improveth the immune system to fight against Covid-19?	a. Da /Yes 1 b. Ne / No 0 c. Ne znam / I don't know 0
Stav / Attitude	
4. Svi mogu da posete stomatologa tokom pandemije COVID-19? / Can everyone visit the dentist during period of COVID-19 pandemic?	a. Da / Yes 0 b. Ne / No 1
5. Da li četkanje zuba istovremeno može pomoći u prenošenju COVID-19? / Does wear brush your teeth are simultaneously able to transmit COVID-19?	a. Da / Yes 1 b. Ne / No 0
6. Da li se pažljivim pranjem zuba može prevenirati transmisija COVID-19? / Brush your teeth carefully with a well can prevent the transmission of COVID-19?	a. Da/ Yes 1 b. Ne /No 0
Praksa / Practice	
7. Do you brush your teeth every day? / Da li perete zube svako dnevno?	a. Da / Yes 1 b. Ne / No 0
8. How many times is the minimum number of times to brush teeth? / Koliko puta dnevno perete zube?	a. Jednom dnevno/ Once a day 0 b. Dva puta dnevno/ Twice a day 1 c. Tri puta dnevno / Three times a day 0
9. When do you rinse your mouth? / Kada ispirate usnu duplju?	a. Ujutru/ In the morning 0
10. Do you clean your tongue? / Da li čistite jezik?	b. Ujutru i uveče pre spavanja / In the morning and evening before sleeping 0 c. Ujutru, uveče pre spavanja i nakon konzumiranja slatkiša/ / In the morning, evening before sleeping and sweets consumption 1
11. Do you use tools such as dental floss and solution of mouthwash to help cleaning the teeth and mouth? / Da li koristite pomoćna sredstva za čišćenje zuba i usne duplje kao što je konac za zube i vodicu za ispiranje usta?	a. Da /Yes 1 b. Ne /No 0
12. Did you visit the dentist during Covid-19 pandemic? / Da li ste posetili stomatologa tokom Covid-19 pandemije?	a. Da / Yes 1 b. Ne / No 0 a. Da /Yes 0 b. Ne / No 1

Tabela 2. Distribucija uzorka COVID -19 PKSP (pacijenti koji se prate) u Makasaru
Table 2. The Sample Distribution of COVID -19 ODP (People In Monitoring) in Makassar

Karakteristike	n	(%)
Pol/ Gender		
Muški/Male	36	50,0
Ženski/Female	36	50,0
Godine/Ages		
Deca/Childrens	2	2,7
Odrasli/Adults	70	97,3
Nivo obrazovanja/ Educational Levels		
Srednja škola/High school	17	23,6
Diploma/Bachelor	44	61,1
Master/Master	11	15,3
Profesije/ Professions		
Nezapošljeni/Unemployed	14	19,4
Zapošljeni privatno/ Private Employee	22	30,6
Državni službenici/Civil Servants	11	15,3
Medicinski radnici/ Medical Personnel	5	6,9
Nastavnici/ Teacher	7	9,7
Preduzetnik/ Entrepreneur	13	18,1
Bračni status/ Marital Status		
Nije u braku/ Not Married	47	65,3
U braku je/Married	25	34,7
Ukupno/Total	72	100,0

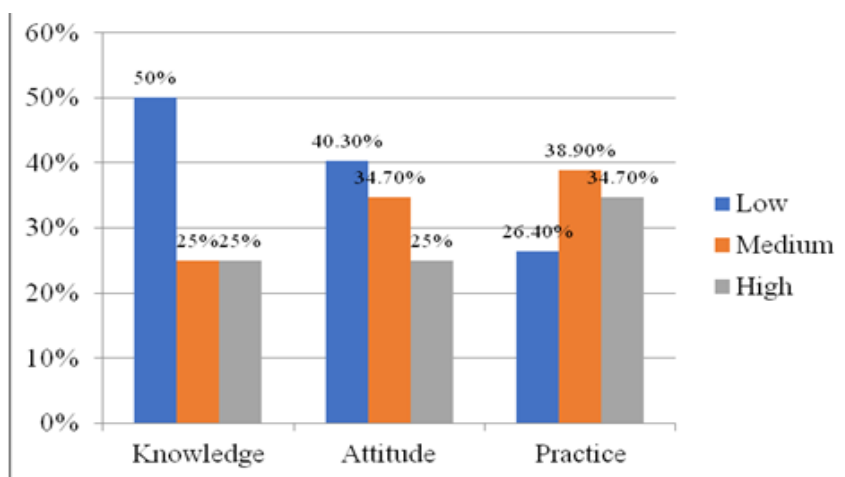


Figura 1. Totalni rezultat po kategorijama odgovora ispitanika baziranih na znanju, stavu i praksi

Figure 1. The total score category of respondents' answers is based on knowledge, attitude and practice

Većina ispitanika (44 ispitanika, 61,1%) ima bačelor diplomu. Što se tiče profesije i bračnog statusa, više ispitanika su bili privatno zapošljeni (22 ispitanika, 30,6%), a neoženjenih je bilo (47 ispitanika, 65,3%) (Tabela 2).

Distribucija odgovora na znanje o oralnom zdravlju, stavu i praksi ukazuju da je za varijablu znanja o oralnom zdravlju većina ispitanika smatrala da održavanje zdravlja zuba i usne duplje može uticati na bolji imuni odgovor u borbi protiv COVID -19, oko 42 (58,33%) ispitanika sa tačnim i pogrešnim odgovorom, a 36 (50%) sa po jednim od svakog. Što se tiče varijable "stav o oralnom zdravlju", većina ispitanika je odgovorila da ne mora da poseti zubara tokom pandemije COVID -19, oko 52 (72,22%) ispitanika bilo je sa ispravnim i pogrešnim stavovima o oralnom zdravlju, odnosno 39 (54,16%) i 33 ispitanika (45,84%). Za varijablu oralne zdravstvene prakse, većina ispitanika pere zube svaki dan, oko 55 (76,39%) ispitanika bilo je i sa ispravnim i pogrešnim stavovima o oralnom zdravlju od 43 (59,72%), odnosno 29 ispitanika (40,28%). Pored toga, većina ispitanika, 53 (73,61%) ispitanika, isto tako pretpostavlja da zube moraju da peru minimum dva puta dnevno (Tabela 3).

Slika 1 prikazuje nivo znanja o oralnom zdravlju, stavu i praksi među PKSP u Makasaru.

U pogledu znanja o oralnom zdravlju, oko 50% ispitanika je imalo slabo znanje, dok je 25% ispitanika je imao umeren, odnosno visok rezultat. U pogledu odnosa prema oralnom zdravlju, 40,3% ispitanika je dobilo nisku ocenu, 34,7% ispitanika je dobilo umerenu ocenu, a 25% visoku ocenu.

Results

Out of a total of 120 subjects, 72 respondents (36 (50%) men and 36 (50%) women) filled the questionnaire. Based on the age, most respondents were adults (70 respondents, 97.3%) with an average age of 28 years (appendix). Most respondents (44 respondents, 61.1%) had bachelor's degree. For profession and marital status, more respondents were private employees (22 respondents, 30.6%) and unmarried (47 respondents, 65.3%) (Table 2).

The answers for distribution of oral health knowledge, attitude and practice indicated that for oral health knowledge variable, the majority of respondents, 42 (58.33%) of them with correct and wrong answer, 36 (50%) of each, considered that maintaining the dental and oral health could increase the immune system to fight Covid-19. For oral health attitude variable, most respondents, 52 (72.22%) of them with right and wrong oral health attitudes, 39 (54.16%) and 33 (45.84%), respectively, answered that they did not have to visit a dentist during Covid-19 pandemic. For oral health practice variable, the majority of respondents, 55 (76.39%) of them with correct and wrong oral health attitudes, 43 (59.72%) and 29 respondents (40.28%), respectively, brushed their teeth every day. In addition, most respondents, 53 (73.61%) of them also assumed that they had to brush their teeth twice a day minimum (Table 3).

Figure 1 shows the level of oral health knowledge, attitude and practice among PiM in Makassar.

Što se tiče usmene prakse, bilo je 26,4% ispitanika sa niskim rezultatom, 38,9% ispitanika sa umerenim i 34,7% sa visokim ocenama.

Diskusija

Održavanje oralnog zdravlja jedan je od važnih faktora koji pomažu imunom sistemu protiv virusne infekcije COVID-19 putem IgA antitela u pljuvački. Takođe će sprečiti mogućnost nastanka karijesa i parodontalnih oboljenja, tako da nije potrebno ići kod stomatologa zbog stomatoloških uslugaveć bi samo trebalo da održavaju dobru oralnu higijenu kod kuće, što može pomoći u suzbijanju širenja infekcije virusom COVID-19¹⁵⁻¹⁷.

In term of oral health knowledge, about 50% of respondents had poor knowledge while 25% of respondents had moderate and high score, respectively. In term of oral health attitude, 40.3% respondents obtained low score, 34.7% of respondents obtained moderate score and 25% obtained high score. In term of oral practice, there were 26.4% of respondents with low score, 38.9% of respondents with moderate score and 34.7% of with high score.

Discussion

Maintaining the oral health is one of important factors that help the immune system against COVID-19 viral infection through IgA antibody in saliva.

Tabela 3. Distribucija odgovora: znanje o oralnom zdravlju, stav i praksa među PKSP (pacijenti koji se prate) u Makasaru
Table 3. The answer distribution of Oral health Knowledge, Attitude and Practice among COVID -19 ODP (People in Monitoring) in Makassar

	The answer/odgovor Right/Tako je		The answer/odgovor False/pogrešno/Don't Know/Ne znam	
	n	%	n	%
Knowledge/Znanje				
1. Maintain the health of your teeth and mouth can increase the immune system to against Covid-19?/ Održavanje zdravlja zuba i usne duplje može poboljšati imuni system u borbi protiv Covid-19?	42	58.33	30	41.67
2. Is gargling with an antiseptic solution effectively kill the Covid-19?/ Da li se grgorenjem antiseptičkim rastvorom efektivno eliminiše Covid-19?	38	52.78	34	47.22
3. Are eating vegetables and fruit can increase the immune system to against Covid-19?/ Da li konzumiranje povrća i voća može efektivno da poboljša imuni system u borbi protiv Covid-19?	28	38.89	44	61.11
Average Knowledge/Prosek znanja	36	50.0	36	50.0
Attitude/Stav				
4. Everyone can visit the dentist during period of Covid-19 pandemic?/ Svi mogu da posete stomatologa tokom pandemije COVID-19?	52	72.22	20	27.78
5. Does wear brush your teeth are simultaneously able to transmit Covid-19?/ Da li četkanje zuba istovremno može pomoći u prenošenju COVID-19?	25	34.72	47	65.28
6. Brush your teeth carefully with a well can prevent the transmission of Covid-19?/ Da li se pažljivim pranjem zuba može prevenirati transmisija COVID-19?	41	56.94	31	43.06
Average Attitude/ Prosek stava	39	54.16	33	45.84
Practice/Praksa				
7. Do you brush your teeth every day?/ Da li perete zube svakodnevno?	55	76.39	17	23.61
8. How many times the minimum of brushing teeth?/ Koliko puta dnevno perete zube?	53	73.61	19	26.39
9. When you rinse your mouth?/ Kada ispirate usnu duplju?	24	33.3	48	66.67
10. Do you clean your tongue?/ Da li čistite jezik?	45	62.50	27	37.50
11. Do you use a tool to help in cleaning the teeth and mouth like dental floss and solution of mouthwash?/ Da li koristite pomoćna sredstva za čišćenje zuba i usne duplje kao što je konac za zube i vodicu za ispiranje usta?	45	62.50	27	37.50
12. Did you visit the dentist during Covid-19 pandemic?/ Da li ste posetili stomatologa tokom Covid-19 pandemije?	36	50.0	36	50.0
Average Practice/Prosek prakse	43	59.72	29	40.28

Zdravlje zuba i usta je sastavni deo opšteg zdravlja čoveka koji je veoma usko povezano sa znanjem, stavom i praksom. Održavanje zdravlja zuba i usne šupljine smatra se doživotnom navikom i ključnim za zdravlje zuba i desni¹⁷. Oralna zdravstvena praksa je definisana kao oblik aktivnosti = zaštita, unapređenje ili održavanje oralnog zdravlja i prevencija oralnih oboljenja²¹.

Većina ispitanika prikazanih u tabeli 3, 38 ispitanika (52,78%), je odgovorilo da gargiranje antiseptičnih rastvora nije efikasno u suzbijanju COVID-19. To je u skladu sa nemačkom studijom koju su sprovedli Kampf i saradnici koja je sugerisala da antiseptični rastvor nije efikasan za eliminisanje COVID-19²².

Pored toga, većina ispitanika (76,39%) je prala zube svaki dan, što je u skladu sa studijom Abeer i saradnika iz Rijada koji su takođe objavili da je većina ispitanika, 66,5% pralo zube svaki dan¹⁷.

Tabela 3 takođe prikazuje raspodelu odgovora na pitanje „koliko najmanje puta peru zuba“, oko 53 ispitanika (73,61%) odgovorilo je dva puta dnevno. To je u skladu sa studijom Netty Suriyanti i sar. u Bandungu koja je izvestila da 85% ispitanika pere zube dva puta dnevno. Takođe je u skladu sa preporukom Američkog udruženja stomatologa (ADA) da se učestalost pranja zuba sprovodi dva puta dnevno²³.

Iz rezultata naše studije, tabela 3 isto tako prikazuje raspodelu odgovora na pitanje „da li četkate jezik?“ gde je 45 ispitanika (62,50%) odgovorilo „da“. Ovi rezultati studije su u suprotnosti sa studijom koju su sprovedli Netty Suriyanti i sar. koja je objavila da 60% ispitanika nikada ne četka jezik²³.

Na osnovu studije u Kini, 47% odraslih je prijavilo da informacije o oralnom zdravlju dobijaju preko radio programa ili televizije, dok je 30% dobilo informacije čitajući novine ili časopise.

Poster u bolnici ili instrukcije stomatologa obeleženi su kao izvor informacija, 15% odnosno 21%. Pored toga, obrazovanje o oralnom zdravlju u školama i lokalne zdravstvene kampanje spomenulo je 10% od ukupnog broja ispitanika. Svi izvori informacija o oralnom zdravlju su češće zabeleženi u lokalnim urbanim sredinama nego u ruralnim²⁴.

Kampanja Love-Teeth-Day (LTD) je program edukacije o oralnom zdravlju koja je formirana u Kini radi podizanja javne svesti o oralnom zdravlju i podsticanja implementacije društvene edukacije o oralnom zdravlju na nivou pokrajine. LTD kampanja dizajnirana je da pošalje poruku

It will also prevent the possibility of dental caries and periodontal diseases so people do not need to visit dentist for dental services and only need to perform oral health practices at home, which may help to suppress the spread of COVID-19 virus infections¹⁵⁻¹⁷.

Dental and oral health is an integral part of human general health which is very closely related to knowledge, attitude and practice. The maintenance of dental and oral health are both regarded as a life-long habit and central to the health of teeth and gums¹⁷. Oral health practice is defined as a form of activity = to protect, promote or maintain oral health and prevent oral disease²¹.

The majority of respondents in Table 3, 38 respondents (52.78%), answered that gargling with antiseptic solution is not effective in killing COVID-19. It is in line with a German study conducted by Kampf et al. which suggested that the antiseptic solution was not effective to kill COVID-19²².

In addition, the majority of respondents (76.39%) brushed their teeth every day, which is in line with the study by Abeer et al. in Riyadh which reported that the majority of respondents, 66.5% brushed their teeth every day¹⁷.

Table 3 also shows the answer distribution to the question "how many times is the minimum number of times to brush teeth?", 53 respondents (73.61%) answered two times a day. It is in line with the study by Netty Suryanti et al. in Bandung which reported that 85% of respondents brush their teeth two times a day. It is also in accordance with the American Dental Association's (ADA) recommendation that the frequency of brushing teeth should be two times a day²³.

From the results of our study, Table 3 also shows the answer distribution to the question "do you clean your tongue?" with 45 respondents (62.50%) who answered "yes". This result of our study is contradict with the study conducted by Netty Suryanti et al. which reported that 60% of respondents never brush their tongue²³.

Based on the study in China, 47% of the adults reported that they heard the information about the oral health on a radio program or television while 30% received the information through reading newspaper or magazine.

Poster at hospital or instruction from a dentist is indicated as a source of information by 15% and 21% of adults, respectively. In addition, oral health education in schools and local health campaigns were mentioned by 10% of total respondents. All sources of information about oral health were reported to be more frequently given in local urban areas than in rural²⁴.

društvu o oralnom zdravlju, kao što je važnost redovnih stomatoloških pregleda, pranje zuba najmanje dva puta dnevno, praksa sistematskog pranja zuba, kao i upotrebe standardne zubne paste sa četkicom i fluorom.

Studija je prijavila da samo jedna trećina odraslih Kineza pere zube najmanje dva puta dnevno i ovaj broj je mnogo manji nego što je to slučaj kod dece i adolescenata koji su učestvovali u istoj anketi. Pored toga, održavanje oralnog zdravlja je i dalje mnogo slabije u poređenju sa nalazima studije u zapadnim industrijskim zemljama i Hong Kongu²⁴.

Do danas, prema našim saznanjima, ova studija je prva koja analizira znanje, stav i praksu PKSP. Na opšti nivo znanja o oralnom zdravlju, stavove i praksu u društvu o održavanju dentalnog i oralnog zdravlja mogu uticati nekoliko faktora, kao što su socio-demografija, među drugim faktorima prikazano je okruženje, nivo obrazovanja, ekonomska situacija, tradicija i pružanje stomatoloških usluga zdravstvenih ustanova. Nivo obrazovanja može uticati na nivo dentalne i oralne higijene; ljudi nižeg obrazovnog nivoa imali su tendenciju da imaju slabije znanje o održavanju zdravlja zuba i usne duplje. Studija je pokazala da nivo obrazovanja veoma utiče na znanje o zdravom životu, stav i praksu²⁵.

Na osnovu rezultata ovog istraživanja, predložimo stvaranje programa svesti o oralnom zdravlju usmerenom na PKSP. Predloženi programi treba da se usredsrede na značaj i praktični pristup u postizanju i održavanju dobrog oralnog zdravlja među PKSP u Makasaru zbog suzbijanja širenja infekcije COVID-19.

Zaključak

Postoji još uvek veliki broj PKSP sa slabim znanjem o oralnom zdravlju, stavovima i praksi.

Love-Teeth-Day (LTD) campaign is an oral health education program which was formed in China to increase the public awareness of oral health and to encourage the implementation of oral health education-based society at the province level. The LTD Campaign has been designed to send oral health message to society, such as the importance of visiting dentist regularly, brushing the teeth at least twice a day, practice of systematic toothbrushing method, as well the use of a standard toothbrush and fluoridetoothpaste.

Study reported that only one-third of Chinese adults brush their teeth at least two times a day and this number is much lower than the observed for children and adolescents who participated in the same survey. Besides that, the oral health maintenance is still much lower compared with the findings of the study performed in west industrial countries and Hong Kong²⁴.

Until today, to our knowledge, this study is the first to analyze the knowledge, attitude, and practice of PiM. The general level of oral health knowledge, attitudes and practice among society towards maintaining the dental and oral health may be affected by several factors, such as socio-demographics, among other factors environment, level of education, economy, tradition and the provision of dental health service facilities. Education level may affect the level of dental and oral hygiene; people with lower educational level tended to have lower knowledge in dental and oral health maintenance. A study has shown that education level is very influential on the knowledge, attitude and practice of healthy living²⁵.

Based on the results of this study, we suggest creating a PiM-targeted oral health awareness program. The proposed programs should focus on the importance and practical approach in achieving and maintaining good oral health among PiM in Makassar to suppress the spread of COVID-19 infections.

Conclusion

There was still a high number of PiM with low oral health knowledge, attitude, and practice.

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IZRADA OPTURATOR PARCIJALNE PROTEZE NAKON SUBTOTALNE MAKSILEKTOMIJE-PRIKAZ SLUČAJA

THE MANUFACTURE OF OBTURATOR PARTIAL DENTURE AFTER MAXILLECTOMY-CASE REPORT

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Sažetak

Uvod: Resekcija maksile otvara oronazalnu i/ili oroantralnu komunikaciju koja ozbiljno otežava različite funkcije orofacijalnog sistema, kao što su žvakanje, gutanje i govor. Osim toga, narušen je simetričan i prijatan izgled pacijenta, narušeni su njegovo psihičko stanje, radna sposobnost i socijalni život.

Prikaz slučaja: U radu je prikazan pacijent protetički rehabilitovan nakon parcijalne maksilektomije.

Zaključak: Bliska saradnja maksilofacijalnog hirurga i specijaliste stomatološke protetike može rezultirati uklanjanjem nastalih promena na maksili i izradom opturator proteze, koja unapređuje funkcije orofacijalnog sistema i kvalitet života pacijenta uopšte.

Ključne reči: opturator proteza, maksilektomija

Abstract

Introduction: Maxillary resection opens oronasal and / or oroantral communication, which seriously complicates various functions of the orofacial system, chewing, swallowing and speech. In addition, the symmetrical and pleasant appearance of the patient, his mental state, working ability and social life are disturbed.

Case report: The manuscript shows a patient who was prosthetically repaired after a partial maxillectomy.

Conclusion: The close cooperation of a maxillofacial surgeon and a specialist in prosthodontics can result in the removal of the changes on the maxilla and the creation of an obturator denture that improves the functions of the orofacial system and the quality of life of the patient in general.

Key words: denture obturator, maxillectomy

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Uvod

Opturator proteze koriste se za zatvaranje kongenitalnih ili stečenih komunikacija dveju unutrašnjih šupljina glave, u najvećem broju slučajeva usne i nosne ili sinusne šupljine. Stečeni defekti najčešće nastaju nakon uklanjanja malignog tkiva i različitog su oblika i veličine. Komunikacije između oralnih šupljina otežavaju funkciju žvakanja i gutanja hrane, otežavaju govor, narušavaju izgled pacijenta i, samim tim, smanjuju kvalitet života pacijenta nakon uklanjanja tumora¹. Ove proteze najčešće zatvaraju otvore na koštanom tkivu, ali se mogu nastaviti i na meke oralne strukture, što predstavlja poseban izazov, s obzirom na to da se koristi akrilat, koji je tvrd i neugibljiv materijal².

Opturator proteze izrađuju se neposredno nakon operacije (hirurški ili imedijatni opturatori) kao interim ili prelazni opturatori. Privremeni opturatori koriste se tokom perioda oporavka dok se definitivni opturatori izrađuju nakon definitivnog zarastanja tkiva^{3,4}. Retencija i stabilizacija opturator proteza vrši se na preostalim zubima, a poslednjih decenija i na implantatima^{1,5}. Veći izazov mogu predstavljati opturator proteze na bezubim grebenima, jer je jako teško postići retenciju ventilnim učinkom³.

Laboratorijske faze izrade opturator proteza identične su fazama izrade parcijalne akrilatne proteze, uz modelaciju nastavka za zatvaranje komunikacije na radnom modelu. S obzirom na potpunu različitost kliničkih slučajeva, ne postoje dva ista opturatora.

Materijal za izradu opturator proteza je toplo polimerizovani akrilat⁶. Podlaganja opturatora hladno polimerizovanim akrilatom apsolutno su kontraindikovana zbog nadražajnog dejstva ovog materijala na oralna tkiva i iritirajućeg mirisa monomera. Umesto toga, do potpunog zarastanja tkiva rane izrađuju se privremeni opturatori. Definitivni opturator izrađuje se tek nakon potune stabilizacije resekcijske šupljine⁷.

Prikaz slučaja

Pacijentkinji O. Đ. staroj 43 godine, ustanovljena je dijagnoza adenocističnog karcinoma gornje vilice (Adenoid cystic carcinoma (ACC)) prilikom čega je, u sklopu terapije urađena je desna subtotalna maksilektomijana Odeljenju za maksilofacijalnu hirurgiju Klinike za dentalnu medicinu u Nišu.

Introduction

Obturator dentures are used to close congenital or acquired communications of the two internal cavities of the head, in most cases the oral and nasal or sinus cavities. Acquired defects usually occur after the removal of malignant tissue and are of different shapes and sizes. Communications between the oral cavities complicate the function of chewing and swallowing food, speech, impair the patient's appearance and, thus, reduce the patient's quality of life after tumor removal¹. These dentures usually close the openings on the bone tissue, but they can also be extended to soft oral structures, which is a special challenge, since acrylate is used, which is a hard and inflexible material².

Obturator dentures are made immediately after surgery (surgical or immediate obturators) as interim or transitional obturators. Temporary obturators are used during the recovery period while definitive obturators are made after definitive tissue healing^{3,4}. Retention and stabilization of obturator dentures is performed on the remaining teeth, and in recent decades on implants^{1,5}. A greater challenge may be the denture obturator on edentulous ridges, as it is very difficult to achieve retention by the valve effect³.

The laboratory stages of making an obturator denture are identical to the stages of making a partial acrylic denture, with the modeling of the extension to close the communication on the working model. Due to the complete diversity of clinical cases, there are no two same obturators.

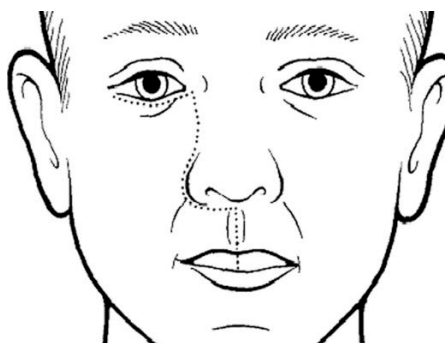
The material for making the obturator denture is hot polymerized acrylate⁶. Obturator relining with cold polymerized acrylate is absolutely contraindicated due to the irritating effect of this material on oral tissues and the irritating odor of monomers. Instead, temporary obturators are made until the wound tissue is completely healed. The definitive obturator is made only after complete stabilization of the resection cavity⁷.

Case report

Patient O.Đ. at the age of 43, was diagnosed adenoid cystic carcinoma (ACC) of maxillae, where a right subtotal maxilectomy was performed at the Department of Maxillofacial Surgery of the Clinic for Dental Medicine in Niš.

Klasični Weber–Fergussonov pristup moguće je modifikovati Dieffenbacovom incizijom u zavisnosti od prostiranja i prirode tumora. Nakon pristupanja medijalnom kantnoj regiji, inciziju je moguće proširiti lateralno inferiorno u odnosu na donji kapak u jedan od nabora kao na primeru modifikaciji⁸ (slika 1).

Nakon intervencije, u martu 2016. godine pacijentkinja je protetički zbrinuta na Odeljenju za stomatološku protetiku iste klinike. Terapija je obuhvatila izradu gornje parcijalne akrilatne opturator proteze u cilju popunjavanja defekta nastalog uklanjanjem tumora, kao i nedostatka zuba. Protetska rehabilitacija donje vilice nije bila potrebna, jer je pacijentkinja imala svoje, prirodne zube (slika 2).



Slika 1. Šema hirurškog terapijskog pristupa⁹
Figure 1. Scheme of surgical therapeutic approach⁹

Pre uzimanja preliminarnog otiska u predeo defekta postavljena je vazelinska gaza sa ciljem da se spreči zapadanje otisnog materijala u eksponirane šupljine. Odgovarajućom standardnom kašikom uzet je otisak gornje vilice ireverzibilnim hidrokolooidom (*Phas Plus, fast setting chromatic dust free, Zhermark Italy*). Istim materijalom uzet je i otisak zuba antagonista. Izlivanjem preliminarnog otiska dobijen je anatomski model na kome je izrađena individualna kašika od hladno polimerizovanog akrilata, kojom je zatim uzet precizniji funkcionalni otisak gornje vilice i defekta. Kao otisni materijal korišćeni su kondenzacioni silikoni (*Elite Hd+Light Body, Zhermark Italy*), kako bi se dobio radni model velike preciznosti. Na definitivnom radnom modelu izrađena je zagrižajna šablona, nakon čega su, u ustima pacijentkinje, određeni međuvučni odnosi, korišćenjem očuvane visine zagrižaja i habitualnog okluzalnog obrasca (slika 3).

The classical Weber – Fergusson approach can be modified by Dieffenbac incision depending on the extent and nature of the tumor. Once the medial canthal region is approached, the incision may be extended laterally inferior to the lower eyelid in one of the folds as in the modification⁸ (Figure 1).

After the intervention, in March 2016, the patient was prosthetically taken care of at the Department of Dental Prosthetics at the same Clinic. The therapy included the production of an upper partial acrylic obturator denture in order to fill the defect caused by the removal of the tumor, as well as the lack of teeth. Prosthetic rehabilitation of the lower jaw was not necessary, because the patient had her own teeth (Figure 2).



Slika 2. Defekt nastao nakon desne kompletne maksilektomije
Figure 2. Defect caused by right complete maxillectomy

Before taking the preliminary impression, a vaseline gauze was placed in the area of the defect in order to prevent the impression material from falling into the exposed cavities. The upper jaw impression was taken with an irreversible hydrocolloid (*Phase Plus, fast setting chromatic dust free, Zhermark Italy*) with an appropriate standard tray. The antagonist's tooth impression was taken with the same material. By pouring the preliminary impression, an anatomical model was obtained on which an individual tray was made of cold polymerized acrylate, which was then used to take a more precise functional impression of the upper jaw and the defect. Condensation silicones (*Elite HD + Light Body, Zhermark Italy*) were used as the impression material, in order to obtain a working model of high precision. On the definitive working model, a occlusal rim was developed, after which intermaxillary relationships were determined in the patient's mouth, using the preserved bite height and habitual occlusal pattern (Figure 3).



Slika 3. Kontakti zuba opturator parcijalne proteze i zuba antagonista u habitualnoj okluziji. Modelacija proče proteze u potpunosti imitira izgubljeno tkivo alveolarnog grebena

Figure 3. Contacts of partial denture obturator teeth and antagonist teeth in habitual occlusion. Modeling of the prosthesis completely mimics the lost alveolar ridge tissue

Nakon prenošenja modela na artikulator, postavljeni su zubi, koji su morfološki i po boji u potpunosti odgovarali preostalim zubima u gornjoj vilici¹. Nakon probe modela, u ustima pacijentkinje, proteza je definitivno izrađena od toplo polimerizovanog akrilatnog materijala (*Triplex Hot, Ivoclar Vivadent, Lihtenštajn*). Proteza je obrađena i visoko ispolirana (slika 4).

Pacijentkinji je opturator proteza nameštena uz pažljivu adaptaciju, kako se ne bi oštetila prethodno traumatizovana susedna tkiva. Retenciona kukica na desnom centralnom sekutiću i gornjem desnom prvom molaru prilagođene su konveksitetu zuba. Asimerija lica značajno je ublažena, defekt na vilici je zatvoren, a govor je bio prilično razumljiv. Pacijentkinji su data sva uputstva kako da koristi i održava opturator protezu.



Slika 4. Izrađena opturator proteza
Figure 4. Produced denture obturator

After transferring the model to the articulator, teeth were placed that morphologically and in color completely corresponded to the remaining teeth in the upper jaw¹. After testing the model in the patient's mouth, the denture was definitely made of hot polymerized acrylic material (*Triplex Hot, Ivoclar Vivadent, Liechtenstein*). The denture was machined and highly polished (Figure 4).

The denture obturator was handed over to the patient with careful adaptation, so as not to damage the previously traumatized surrounding tissues. The retention clasps on the right central incisor and upper right first molar are adjusted to the convexity of the teeth. The asymmetry of the face was significantly alleviated, the defect on the jaw was closed, and the speech was quite understandable. The patient was given all instructions on how to use and maintain the denture obturator.



Slika 5. Izgled izrađene proteze *en face* i iz profila. Postignuti optimalni estetski efekti i korigovana asimetrija lica

Figure 5. Appearance of the prosthesis made *en face* and from the profile. Optimal aesthetic effects and corrected facial asymmetry were achieved

Diskusija

Subtotalna maksilektomija težak je invaliditet pacijenta, koji, osim remećenja orofacijlnih funkcija dovodi do značajne asimetrije lica. Posledice operativnog zahvata smanjuju ili onemogućavaju radnu sposobnost pacijenta, remete njegov društveni život, otežavaju komunikaciju sa okolinom i remete psihičko stanje obolelog. Kvalitet života pacijenta ozbiljno je narušen, stoga su izrada opturator proteze i zatvaranje novonastalih komunikacija šupljina u lobanji veliki izazov koji sem zdravstvenog ima i izuzetan socijalni značaj.

Svrha terapije opturator protezom nakon parcijalne i totalne resekcije maksile jeste uspostavljanje adekvatnih funkcija žvakanja, govora i gutanja, kao i prihvatljivog izgleda pacijenta¹⁰. Prednost terapije opturator protezom je mogućnost rane inspekcije svakog nastalog oštećenja, kao i rana dijagnostika eventualnih recidivantnih promena, jeftinim sredstvom visoke efikasnosti. Ova vrsta nadoknade treba hermetički da zatvori stvorenu šupljinu i spreči nakupljanje hrane i tečnosti, kao i nastanak infekcije. Zato se od korisnika opturator proteza zahteva besprekorna higijena, posebno imajući u vidu da je akrilat porozan, hrapav i jako sklon nakupljanju biofilma¹¹. Ekstenzija opturator proteza smanjuje fluktuaciju vazduha kroz šupljinu i nazalni govor¹².

Gubitak zuba, delova alveolarnog grebena i tvrdog nepca, nakon parcijalne resekcije maksile, remete biostatičku i biodinamičku ravnotežu orofacijalnog sistema. U prikazanom slučaju unilateralnog palatomaksilarnog oštećenja, koncentracija sila najjača je u prednjem delu proteze.

Discussion

Subtotal maxillectomy is a severe disability of the patient, which, in addition to disrupting orofacial functions, leads to significant facial asymmetry. The consequences of the surgical procedure reduce or disable the patient's ability to work, disrupt his social life, make communication with the environment more difficult and disrupt the patient's mental state. The quality of life of the patient is seriously impaired, so making an obturator denture and closing the newly formed communications of the cavities in the skull is a great challenge which, in addition to health, also has an exceptional social significance.

The purpose of obturator denture therapy after partial and total resection of the maxilla is to establish adequate chewing, speech, and swallowing function, as well as an acceptable patient appearance¹⁰. The advantage of obturator denture therapy is the possibility of early inspection of any damage, as well as early diagnosis of possible recurrent changes, with a cheap high-efficiency tool. This type of compensation should hermetically close the created cavity and prevent the accumulation of food and fluids, as well as the occurrence of infection. Therefore, the user of the obturator denture requires impeccable hygiene, especially bearing in mind that acrylate is porous and rough and very prone to biofilm accumulation¹¹. The obturator denture extension reduces air fluctuation through the cavity and nasal speech¹².

Loss of teeth, parts of the alveolar ridge and hard palate after partial resection of the maxilla disturbs the biostatic and biodynamic balance of the orofacial system.

Da bi se obezbedile dobra retencija i stabilizacija opturator proteze, izrađena je kukica na susednom retencionom zubu, a korišćena je i podminiranost same komunikacije¹⁰. Prenos mastikatornog pritiska namenjenog izgubljenim zubima isključivo je gingivalan, te se mogla očekivati i dodatna resorpcija okolnog koštanog tkiva i dislokacija mekih tkiva. Gubitak optimalne retencije i stabilizacije može se rešiti podlaganjem opturator proteze ili izradom noveproteze. Podlaganje je bolje izvesti toplopolimerizovanim, nego hladno polimerizovanim akrilatom, s obzirom na moguće alergijske i toksične reakcije sluzokože sa kojom ovaj materijal dolazi u kontakt¹³.

Pacijentkinja se nakon tri meseca javila na kontrolui bila je zadovoljna funkcijom i izgledom protetske nadoknade. Nisu uočene promene na retencionom zubu kao ni na preostalim zubima. Pacijentkinja je naučila da se služi opturator protezom pri žvakanju, govoru i gutanju. Poboľšan je socijalni život pacijentkinje.

Nakon tri godine nije bilo recidiva tumora, a izrađena opturator proteza je i dalje bila funkcionalna. Pacijentkinja je bila radno sposobna i aktivno učestvovala u svim životnim aktivnostima.

Zaključak

Opturator parcijalna proteza dobro je terapijsko sredstvo za sanaciju komunikacija nastalih nakon subtotalne maksilektomije. Pacijentkinji su vraćene funkcije žvakanja, gutanja, govora, poboljšani su izgled lica i kvalitet života.

In the case of shown unilateral palatomaxillary damage, the concentration of forces is strongest in the anterior part of the denture. In order to ensure good retention and stabilization of the obturator denture, a clasp was made on the adjacent retention tooth, and the undermining of the communication itself was used¹⁰. The transmission of masticatory pressure intended for lost teeth is exclusively gingival, and additional resorption of the surrounding bone tissue and soft tissue dislocation could be expected. Loss of optimal retention and stabilization can be solved by relining an obturator denture or making a new one. The relining is better reported with warm than cold polymerized acrylate, given the possible allergic and toxic reactions of the mucous membrane with which this material comes into contact¹³.

After three months, the patient came for a check-up and was satisfied with the function and appearance of the prosthetic replacement. No changes were observed on the retention tooth as well as on the remaining teeth. The patient learned to use the denture when chewing, speaking and swallowing. The social life of the patient is improved.

After three years, there was no recurrence of the tumor, and the obturator denture was still functional. The patient was able to work and actively participated in all life activities.

Conclusion

A partial denture obturator is a good therapeutic tool for repairing communications that have occurred after subtotal maxillectomy. The patient regained the function of chewing, swallowing, speech, and improved her appearance and quality of life.

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PRIKAZ SLUČAJA
CASE REPORT
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SUVI NAČIN TRANSPORTA I ODLOŽENA REPLANTACIJA AVULZIRANOG ZUBA-TERAPIJA I ISHOD

DRY EXTRAORAL STORAGE AND DELAYED REPLANTATION OF AVULSED TOOTH- THERAPY AND OUTCOME

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Sažetak

Uvod: Cilj rada bio je da prikaže terapijski postupak i ishod replantacije avulziranog, stalnog centralnog, maksimalnog sekutića, nađenog na mestu velike kontaminiranosti, nakon ekstraoralnog perioda od 15 sati i suvog načina transporta.

Prikaz slučaja: Kliničkim pregledom utvrđeno je to da je koren dostigao punu dužinu, sa paralelnim ivicama, što je odgovaralo uzrastu devojčice od 8,5 godina. Nakon pažljivo uklonjenog nekrotičnog periodontalnog ligamenta sa korena, obavljen je ekstraoralni endodontski tretman. Uklonjena je pulpa, odustalo se od interseansnih medikamentoznih punjenja i pristupilo se definitivnoj opturaciji kanala korena zuba. Zub je vraćen u alveolu i urađena je imobilizacija žičano-kompozitnim splintom. Nakon replantacije, praćeno je stanje zuba. Zamenska resorpcija i dentoalveolarna ankiloza nastupile su posle devet meseci, a zatim je cervikalna inflamatorna resorpcija dovela do gubitka zuba nakon tri i po godine.

Zaključak: Postignuti rezultat može se smatrati uspehom, budući da je to vreme replantirani zub odgovorio razvojnim, funkcionalnim i estetskim zahtevima, što je posebno važno u periodu intenzivnog rasta i razvoja deteta.

Gljučne reči: avulzija, stalni zub, dug ekstraoralni period, replantacija, zamenska resorpcija

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Abstract

Introduction: The aim of this study was to present the therapeutic procedure and the outcome of replantation of the avulsed permanent central maxillary incisor, found at the site of high contamination, after an extraoral period of 15 hours and dry transport.

Case report: By clinical examination it was determined that the root reached the full length, with parallel edges, which corresponded to the age of the girl- 8.5 years. After carefully removing the necrotic periodontal ligament from the root of the tooth, extraoral endodontic treatment was performed. The pulp was removed, the multi-session intracanal medicament fillings were avoided and the definitive obturation of the root canal was performed. The tooth was returned to the alveolar socket and immobilized with a wire-composite splint. After replantation, the condition of the tooth was monitored. Replacement resorption and dentoalveolar ankylosis occurred after nine months, and then cervical inflammatory resorption led to tooth loss after three and a half years.

Conclusion: The achieved result can be considered as a success because during this time the replanted tooth met the developmental, functional and aesthetic requirements, which is especially important in the period of intensive growth and development of the child.

Key words: avulsion, permanent tooth, long extraoral period, replantation, replacement resorption

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Uvod

Avulzija zuba je teška povreda potpornih tkiva zuba sa prekidom neurovaskularnog snopa i kompletnim istisnućem zuba iz alveolarne čašice^{1,2}. Avulzija stalnog zuba čini 0,5% do 3,0% svih povreda zuba^{1,2}. Najčešće avulziran zub, u obe denticije, je maksilarni centralni sekutić³. U najvećem broju slučajeva javlja se avulzija jednog zuba⁴, udružena sa povredama tvrdih zubnih ili parodontalnih tkiva susednih zuba⁵.

Replantacija avulziranog zuba je tretman izbora, u odsustvu lokalnih i opštih kontraindikacija. Uspeh replantacije, pre svega zavisi od vremena koje je zub proveo u ekstraoralnoj sredini, kao i od aktivnosti preduzetih na mestu nezgode i neposredno nakon toga^{1,6,7}. Kako momentalna replantacija često nije moguća, čuvanje zuba u vlažnoj sredini i što brži odlazak stomatologu (< 60 min.) povećavaju izgleda za dugoročni uspeh terapije¹. Međutim, postoje slučajevi kod kojih su, zbog udaljenosti od mesta povređivanja, do mesta ukazivanja stručne pomoći i neprikladnog suvog transporta avulziranog zuba izgledi za uspeh terapije narušeni. Treba imati u vidu da je i u ovakvim slučajevima, posebno replantacija zuba kod dece u procesu intezivnog rasta i razvoja, od velikog značaja iz razvojnih, funkcionalnih, estetskih, fonetskih i psihoemocionalnih razloga. Stoga je i cilj ovog rada bio prikazati terapijski postupak i ishod replantacije avulziranog centralnog maksilarnog sekutića, nakon suvog ekstraoralnog perioda od 15 sati.

Prikaz slučaja

Prikaz slučaja je odobren od strane Etičkog odbora Klinike za dentalnu medicinu u Nišu u Srbiji (br. 20/10-2017-9 EO) uz poštovanje načela dobrovoljnosti Helsinške deklaracije.

Devojčica stara 8,5 godina, dolazi u pratnji roditelja na Kliniku za dentalnu medicinu u Nišu u Srbiji, zbog jednog izbijenog zuba i višestrukih povreda drugih zuba i mekih tkiva lica, nakon pada sa bicikla, 15 sati ranije.

Odmah nakon povređivanja, u večernjim satima, devojčica i roditelji javljaju se stomatologu u lokalnoj zdravstvenoj ustanovi, gde dobijaju savet da potraže zub. Izbijeni zub nalaze narednog dana u prašini prometne ulice, stavljaju u papirnu maramicu i dolaze na Kliniku.

Nakon uzete anamneze od roditelja i devojčice o načinu, mestu, vremenu povređivanja i opštem zdravstvenom stanju, obavljen je radiološki i intraoralni klinički pregled.

Introduction

Tooth avulsion is a severe injury of the tooth supporting tissues with interruption of the neurovascular bundle and complete displacement of the tooth from the alveolar socket^{1,2}. Permanent tooth avulsion comprises 0.5% to 3.0% of all tooth injuries^{1,2}. The most commonly avulsed tooth in both dentitions is the maxillary central incisor³. In most cases, avulsion of the one tooth occurs⁴, usually associated with injuries of hard dental or periodontal tissues of adjacent teeth⁵.

Replantation of an avulsed tooth is the treatment of choice, in the absence of local and general contraindications. The success of replantation, depends primarily on the time the tooth has spent in the extraoral environment, as well as on the activities undertaken at the place of the accident and immediately thereafter^{1,6,7}. As immediate replantation is often not possible, keeping tooth in a humid environment and going to the dentist as soon as possible (< 60 min.) increases the chances of long-term therapy success¹. However, there are cases when the chances for the success of the therapy are decreased due to the distance from the place of injury and the place where professional help is provided and inappropriate dry transport of the avulsed tooth. It should be considered that even in such cases, especially in children during the process of intensive growth and development, tooth replantation is a method of choice, and it is of great importance for developmental, functional, aesthetic, phonetic and psychoemotional reasons. Therefore, the aim of this study was to present the therapeutic procedure and the outcome of replantation of the avulsed central maxillary incisor, after a dry extraoral period of 15 hours.

Case report

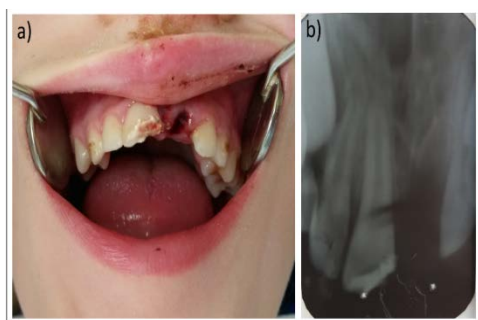
The case report was approved by the Ethics Committee of the Clinic for dental medicine, Niš, Serbia (No. 20 / 10-2017-9 EO) and it was in compliance with the principles of Helsinki Declaration.

The 8.5 year-old girl, accompanied by her parents, came to the Clinic for dental medicine, Niš, Serbia, due to one avulsed tooth and multiple injuries to other teeth and soft tissues of the face, after falling from the bicycle, 15 hours earlier.

Immediately after the injury, in the evening, the girl and her parents contacted the dentist at the local health institution, where

Utvrđeno je odsustvo levog centralnog sekutića iz alveole i utvrđena je očuvanost alveolarne kosti (Slika 1 a i b). Desni centralni sekutić imao je kosi prelom na nivou dentina bez otvaranja pulpe, u srednjoj trećini krunice i patološku pokretljivost bez dislokacije. Oba lateralna sekutića takođe su pokazivala patološku pokretljivost bez dislokacije. Test vitaliteta sva 3 sekutića^{11,12,22} bio je negativan.

Avulzirani zub imao je prelom na nivou dentina, u incizalnoj trećini krunice. Inspekcijom korena avulziranog zuba i analizom radiograma istoimenog zuba suprotne strane i susjednih zuba, definisana je, orijentaciono, dentalna starost i stepen rasta i razvoja korena avulziranog zuba. Zub je imao kompletnu dužinu korena sa paralelnim ivicama, što je po Demirijanu bilo u skladu sa uzrastom djevojčice⁸.



Slika 1. Klinička slika (a) i radiogram (b) avulziranog maksilarnog levog centralnog sekutića

Figure 1. Clinical finding (a) and radiograph (b) of the avulsed maxillary left central incisor

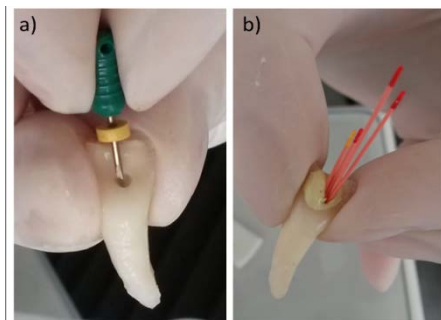
Odmah po prijemu, avulzirani zub je ispran i potopljen u 0,9% NaCl, sve do donošenja odluke da bude replantiran, bez obzira na protekli period od 15 sati, sa mesta velike kontaminiranosti i suv način transporta. Gazom natopljenom 0,9%-tnim NaCl, pažljivo su uklonjene nečistoće i nekrotična periodontalna vlakna sa korena zuba. Potom se pristupilo ekstraoralnom endodontskom tretmanu avulziranog zuba.

Držeći zub isključivo u predelu aproksimalnih površina krunice, na palatinalnoj površini napravljeni su pristupni kavitet i trepanacijski otvor. Koronarna pulpa amputirana je sterilnim svrdlom, a ostatak pulpnog tkiva je iz kanala korena ekstirpiran pomoću instrumenta po Hoedstremu (Slika 2 a). Bez mehaničke obrade kanala korena, taktilno-vizuelnom kontrolom, isključena je mogućnost zaostajanja pulnog tkiva u kanalu.

they received advice to look for a tooth at the place of the accident. The next day, they found the avulsed tooth in the dust of a street, put it in a paper tissue and came to the Clinic.

After taking anamnesis from the parents and the girl about the way, place and time of injury and general health condition, a radiological and intraoral clinical examination was performed.

The absence of the left central incisor from the alveolar socket and the preservation of the alveolar bone were determined (Figure 1 a and b). The right central incisor had an oblique fracture at the dentin level, in the middle third of the crown, without pulp involvement and pathological mobility without dislocation was observed. Both lateral incisors also showed pathological mobility without dislocation. The vitality test was negative for all 3 incisors^{11,12,22}.



Slika 2. Ekstra oralni endodontski tretman avulziranog zuba: priprema (a) i opturacija kanala korena zuba (b)

Figure 2. Extraoral endodontic treatment of the avulsed tooth: preparation (a) and obturation of the tooth canal (b)

The avulsed tooth had a fracture at the level of the dentin, in the incisal third of the crown. By inspecting the root of the avulsed tooth and analyzing the radiograph of the corresponding tooth on the opposite side, as well as the adjacent teeth, the dental age and the degree of growth and development of the root of the avulsed tooth were defined. The tooth had a complete root length with parallel edges, which was in accordance with the age of the girl according to Demirjian⁸.

Immediately upon admission, the avulsed tooth was washed and immersed in 0.9% NaCl, until a decision was made to replant it, regardless of the elapsed period of 15 hours after being collected from a site of high contamination and a dry mode of transport. Impurities and necrotic periodontal fibers were carefully removed from the tooth root using gauze soaked in 0.9% NaCl. Afterwards, extraoral endodontic treatment of the avulsed tooth was started.



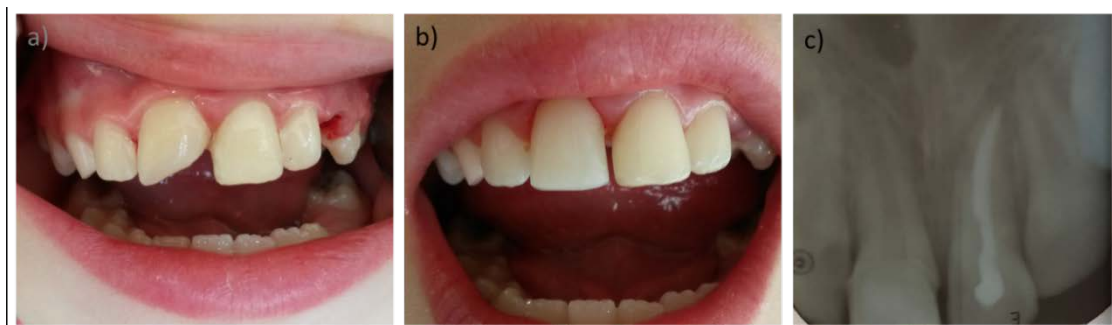
Slika 3. Izrada žičano-kompozitnog splinta na mlečnim i stalnim zubima (a) I poslednji uključen avulzirani zub (b). Žičano-kompozitni splint dve nedelje nakon traume (c)

Figure 3. Preparation of the wire-composite splint on deciduous and permanent teeth (a) and the last included avulsed tooth (b). Wire-composite splint two weeks after trauma (c)

Obilna irigacija kanala korena izvršena je 2% hlorheksidinom (Gluc-Chex 2% liquid, Cerkamed, Poland). Zidovi kanala korena su lagano, bez pritiska, osušeni papirnim poenima. Definitivno punjenje kanala obavljeno je pastom jodoform cementa (jedan deo Jodoform Prevest Den Pro Limited, India; i dva dela Cegal[®] N; normalvezujući cink-fosfatni cemet Galenika a.d. Beograd, Srbija-prah i tečnost) i gutaperka poenima (Guttapercha, #15-#40, Spident, Hand Rolled, Korea) sa koničnošću od 2%, tehnikom primene mono gutaperka poena, korigovanom akcesornim gutaperka poenima (Slika 2 b). Glavni gutaperka poen, dimenzije #40, aplikovan je širom stranom, do dentinskih ivica apeksa korena, a veliki broj akcesornih poena, dimenzije #15 i #20 u prostor preostale dve trećine dužine i širine kanala, sve do homogenizacije i vezivanja paste. Pristupni kavitet je zatvoren cink-fosfatnim cementom, čime je završena hermetička opturacija kanala korena apeksno, lateralno i koronarno. Zub je potom potopljen 20 minuta u 2% rastvor NaF. Za to vreme obavljani su priprema zuba, koji se uključuju u splint i toaleta usne duplje 3% H₂O₂ i 0,9% NaCl i obezboljeno radno polje sa 2ml anestetika Lidokain 2% adrenalin, Galenika a.d. Beograd, Srbija. Spremljena je odgovarajuća dužina fleksibilne ortodonske žice, debljine 0,25 mm (Dentaurum, Ispringen, Germany) i duplirana. Pristupilo se izradi žičano-kompozitnog splinta na mlečnim i stalnim zubima, po sledećem redosledu: 14, 53, 63, 24, 12, 22 i 11 (Slika 3 a). Zatim je uklonjen krvni ugrušak iz alveole levog centralnog sekutića, mlazom 0,9%-tnog NaCl-a, iz šprica bez igle, nakon čega je ona bila spremna za povratak i fiksaciju zuba. Uz blag pritisak prstima, bez upotrebe sile za sve vreme fiksacije kompozitom (Te-Econom[®] Plus (Ivoclar - Vivadent, Principality of Liechtenstein)), avulzirani zub uključen je

Holding the tooth in the area of the proximal surfaces of the crown, an access cavity and a trepanation opening were made on the palatal surface. The coronary pulp was amputated with a sterile bur, and the rest of the pulp tissue was extirpated from the root canal using a Hedström instrument (Figure 2 a). Without mechanical processing of the root canal, with tactile-visual control, the possibility of remaining pulp tissue in the canal is excluded.

Abundant irrigation of the root canal was performed with 2% chlorhexidine (Gluc-Chex 2% liquid, Cerkamed, Poland). The walls of the root canal were dried with paper points, lightly, without pressure. Definitive filling of the canal was done with iodoform cement paste (one part Jodoform Prevest Den Pro Limited, India; and two parts Cegal[®] N; normal binding zinc-phosphate cement Galenika ad Belgrade, Serbia-powder and liquid) and gutta-percha points (Guttapercha, # 15- # 40, Spident, Hand Rolled, Korea) with a conicity of 2%, using the technique of applying mono gutta-percha points, corrected with accessory gutta-percha points (Figure 2 b). The master gutta-percha point with dimension # 40, was applied with wider side pointing to the apex, until reaching the dentinal edges of the root apex. Additionally, a large number of accessory gutta-percha points, dimensions # 15 and # 20, were applied into the space of the remaining two thirds of the channel length and width, until full homogenization and paste binding. The access cavity was closed with zinc-phosphate cement, which completed the hermetic obturation of the root canal apically, laterally and coronally. The tooth was then immersed for 20 minutes in 2% NaF solution. During that time, teeth were prepared for the inclusion in the splint, the oral cavity was cleaned with 3% H₂O₂ and 0.9% NaCl, and local anesthesia was



Slika 4. Uklonjen žičano-kompozitni splint (a), urađene kompozitne restauracije (b) i kontrolni radiogram (c) četiri nedelje nakon traume

Figure 4. Removed wire-composite splint (a), performed composite restorations (b) and control radiograph (c) four weeks after trauma

poslednji (14, 53, 12, 11, 21, 22, 63, 24) (Slika 3 b). Potom je frakturirana površina desnog centralnog sekutića prekrivena kompozitnim zavojem (Te-Econom[®] Plus (Ivoclar - Vivadent, Principality of Liechtenstein)).

Pacijentkinji je data preporuka o ordiniranju sistemske antibiotske terapije (Benzilpenicilin Galenika A.D., Beograd, Republika Srbija, 1200 000/ 24h, 3 dana i Amoksicilin Hemofarm A.D., Vršac, Republika Srbija, 250 mg/ 8h, još 4dana) i savetovana provera antitetanusne zaštite. Dat je savet o ishrani i načinu održavanja oralne higijene za vreme nošenja splinta i zakazan kontrolni pregled narednog dana, zbog provere prilagođenosti na novonastale uslove u ustima.

Na kontrolnom pregledu kroz 2 nedelje, splint je bio stabilan, a higijena usne duplje uredna (Slika 3 c).

Test vitaliteta desnog centralnog sekutića i oba lateralna, na prijemu negativan, sada je bio pozitivan. Ti zubi (11, 12, 22) isključuju se iz splinta, a replantirani zub ostaje još dve nedelje imobilisan.

Nakon 4 nedelje uklonjen je žičano-kompozitni splint sa preostalih zuba, avulziranog zuba i susednih zuba (14, 53, 21, 63, 24) (Slika 4 a).

Urađene su definitivne kompozitne restauracije na oba centralna sekutića i kontrolni rendgen snimak (Slika 4 b i c). Uredan radiološki i klinički nalaz, potvrdili su dobijeni anamnestički podaci, koji su negirali bilo kakve subjektivne tegobe.

Na kontrolnom pregledu, nakon 9 meseci, replantirani zub bio je u okluzalnoj ravni, ali promenjene boje, sa odsustvom pokretljivosti i visokim perkutnim tonom, a radiogram je pokazao zamensku resorpciju korena (Slika 5 a). Pacijentkinja nije imala nikakve subjektivne tegobe.

Na kontrolnom pregledu nakon 16 meseci od povrede, replantirani zub bio je u infrapoziciji u odnosu na desni centralni sekutić (Slika 5 b).

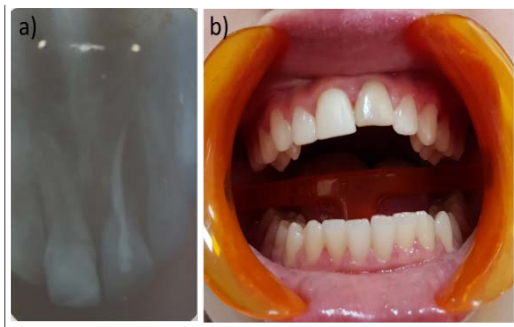
applied using 2 ml Lidocaine 2% adrenaline (Galenika a.d., Belgrade, Serbia). For fixation of the teeth an appropriate length of flexible orthodontic wire, 0.25 mm thick (Dentaurum, Ispringen, Germany) was bended and used. The wire-composite splint for inclusion of deciduous and permanent teeth was made in the following order: 14, 53, 63, 24, 12, 22 and 11 (Figure 3 a). A blood clot was then removed from the alveolar socket of the left central incisor, rising it with 0.9% NaCl using a syringe without a needle, after which it was ready for the return and fixation of the tooth. With gentle finger pressure, without the use of force for the entire time of composite fixation (Te-Econom[®] Plus (Ivoclar-Vivadent, Principality of Liechtenstein)), the avulsed tooth was included last in the splint of eight teeth (14, 53, 12, 11, 21, 22, 63, 24) (Figure 3 b). The fractured surface of the right central incisor was covered with a composite bandage (Te-Econom[®] Plus, Ivoclar-Vivadent, Principality of Liechtenstein).

A systemic antibiotic therapy was prescribed to the patient (Benzylpenicillin Galenika AD, Belgrade, Republic of Serbia, 1,200,000/24h, 3 days and Amoxicillin Hemofarm AD, Vrsac, Republic of Serbia, 250 mg/8h, for another 4 days) and checking of the antitetanus protection was advised. Additionally, the patient was advised on diet and how to maintain oral hygiene while wearing a splint, and a follow-up examination was scheduled for the next day, in order to check the adaptation to the new conditions in the mouth.

At the control examination after 2 weeks, the splint was stable, and the hygiene of the oral cavity was satisfying (Figure 3 c).

Nakon 29 meseci, na kontrolnom pregledu, pacijentkinja je bila bez subjektivnih tegoba, zub je bio nepokretljiv, u izraženijoj infrapoziciji, a radiološki nalaz pokazivao je značajnu progresiju zamenske resorpcije korena.

Posle 3 godine i 6 meseci pacijentkinja dolazi zbog luksacije replantiranog zuba. Kontrolni radiogram pokazao je izraženu cervikalnu inflamatornu resorpciju (Slika 6 a). Nakon toga, zub je ekstrahovan (Slika 6 b) i izrađen adhezivni kompozitni most u cilju daljeg očuvanja prostora (Slika 7 a i b).



Slika 5. Zamenska resorpcija vidljiva na radiogramu devet meseci nakon traume (a). Infra pozicija centralnog sekutića nakon 16 meseci od traume (b)

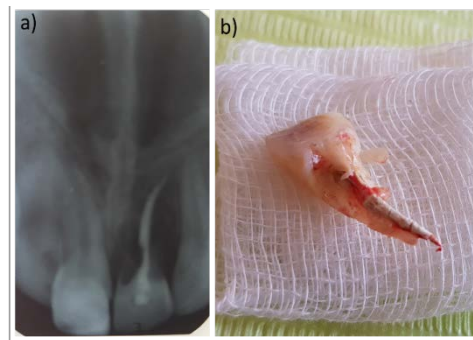
Figure 5. Replacement resorption visible on radiograph nine months after trauma (a). Infraposition of the central incisor 16 months after trauma (b)

Diskusija

Avulzija zuba najčešće se javlja kod dece u uzrastu od 7. do 9. godine², uzrasni period u kom je bila i pacijentkinja u ovom slučaju. To je period erupcije stalnih sekutića, koje u tom uzrastu karakteriše nepotpuno formiran koren i osetljivost periodontalnog ligamenta na dejstvo ekstruzivnih sila⁹. U slučaju avulzije, tok terapije, kao i prognoza, uslovljeni su stadijumom razvoja korena i apikalnog otvora, dužinom ekstraoralnog perioda i načinom transporta avulziranog zuba^{1,10,11}. Najbolja prognozaza oporavak, uz potpunu periodontalnu regeneraciju i revaskularizaciju pulpe je kod avulziranih zuba sa otvorenim apeksom, u slučaju replantacije odmah nakon traume ili najkasnije do 60 minuta nakon traume¹. U slučaju odložene replantacije zuba sa otvorenim apeksom, prognoza je gora nego kod zuba sa zatvorenim apeksom^{10,12}.

The vitality testing of the right central incisor and both lateral incisors, reported to be negative on the date of first admission, responded positively now. These teeth (11, 12, 22) were excluded from the splint and the replanted tooth stayed immobilized for another two weeks.

After 4 weeks, the wire-composite splint was removed from the remaining teeth, avulsed and adjacent (14, 53, 21, 63, 24) (Figure 4 a). Definitive composite restorations were performed on both central incisors and a control X-ray (Figure 4 b and c).



Slika 6. Cervikalna inflamatorna resorpcija vidljiva na radiogramu (a) i ekstrahovan zub (b) nakon tri godine i šest meseci

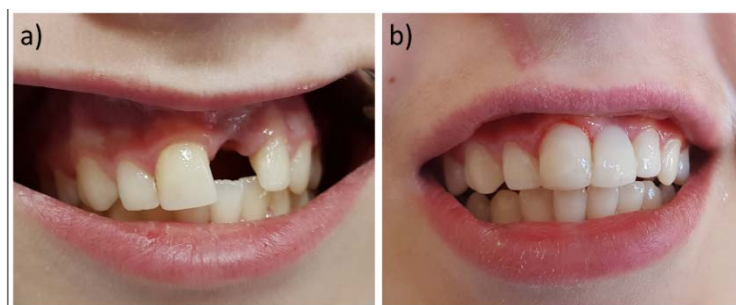
Figure 6. Cervical inflammatory resorption visible on radiograph (a) and extracted tooth (b) after three years and six months

An orderly radiological and clinical findings were confirmed by the obtained anamnestic data, excluding any subjective symptoms.

At the control examination, after 9 months, the replanted tooth was in the occlusal plane, showing the change in the color, with no mobility and high percussion tone. Additionally, replacement root resorption signs could be observed on the radiograph (Figure 5 a). The patient was symptom-free.

At the follow-up examination 16 months after the injury, the replanted tooth was in infraposition when compared to the right central incisor (Figure 5 b).

After 29 months, at the control examination, the patient was symptom free, the tooth was immobile, more pronounced infraposition could be observed. The radiological finding showed a significant progression of replacement root resorption.



Slika 7. Očuvan prostor nakon gubitka zuba (a) i izrađen adhezivni kompozitni most u cilju daljeg očuvanja prostora (b)

Figure 7. Preserved space after tooth loss (a) and an adhesive composite bridge made in order to further preserve the space (b)

U prikazanom slučaju, razvijenost korena avulziranog zuba odgovarala je G stadijumu po Demirjianu⁸, što znači da je koren dostigao punu dužinu, sa paralelnim ivicama. Bez obzira na takav status, po proceni i kliničkom iskustvu terapeuta, sproveden je plan terapije u skladu sa preporukama Anderssona i sar. za zbrinjavanje avulziranih stalnih zuba sa zatvorenim apikalnim foramenom i suvim ekstraoralnim periodom dužim od 60 minuta¹.

Pored jako dugog ekstraoralnog perioda, na visoko rizičnom infektivnom terenu, dopremljen zub u potpuno suvom okruženju bio je dodatno otežavajući činilac u ovom slučaju. Pravilan izbor medijuma za čuvanje avulziranog zuba od jako je velikog značaja, kako za očuvanje vitaliteta ćelija periodontalnog ligamenta¹³, tako i za smanjenje rizika od prevremenog javljanja komplikacija u vidu resorpcije korena. Pri izboru medijuma za čuvanje zuba prednost se daje mleku i Henkovom balansiranom slanom rastvoru¹³. Kao dobar transportni medijum pominju se i kokosova voda, propolis, probiotski rastvori, ekstrakt zelenog čaja, aloe vera i sojino mleko^{13,14}. Pijaća voda se ne preporučuje zbog neodgovarajuće osmolarnosti, jer može dodatno da doprinese oštećenju ćelija periodontalnog ligamenta i favorizuje ranu pojavu resorpcije korena^{14,15}.

S obzirom na jako dug ekstraoralni period u visokorizičnoj infektivnoj sredini (ulica), terapeut se opredelio na ekstraoralno punjenje kanala korena Jodoform cement pastom i gutaperka poenima. Pri donošenju odluke, uzeta je u obzir dostignuta puna dužina korena zuba i još uvek širok foramen. Savremena literatura preporučuje punjenje kanala korena avulziranih zuba preparatima kalcijum-hidroksida, pri čemu se, naročito kod zuba sa nekompletno zatvorenim apeksom, preporučuje upotreba bioaktivnog cementa, mineralnog trioksid agregata (MTA) u apikalnom predelu, kako bi se izbegla dodatna

After 3 years and 6 months, the patient came because of the luxation of the replanted tooth. Control radiograph showed pronounced cervical inflammatory resorption (Figure 6 a). Afterwards, the tooth was extracted (Figure 6 b) and adhesive composite bridge was made in order to further preserve the space (Figure 7 a and b).

Discussion

Tooth avulsion most often occurs in children aged 7 to 9², which corresponds to age of the patient in this case. This is the period of eruption of permanent incisors, which are at this age characterized by incompletely formed root and sensitivity of the periodontal ligament to extrusion forces⁹. In the case of avulsion, the course of therapy, as well as the prognosis, are influenced by the stage of root and apical opening development, the length of the extraoral period and the mode of transport of the avulsed tooth^{1,10,11}. The best prognosis, with complete periodontal regeneration and revascularization of the pulp, is in avulsed teeth with an open apex, in the case of replantation immediately after trauma or no later than 60 minutes after trauma¹. In the case of delayed replantation of teeth with an open apex, the prognosis is worse than in teeth with a closed apex^{10,12}.

In the case shown, the development of the root of the avulsed tooth corresponded to the Demirjian stage G⁸, which means that root reached full length, with parallel edges. Regardless of such status, according to the assessment and clinical experience of the therapist, a therapy plan was implemented in accordance with the recommendations of Andersson et al. for the care of avulsed permanent teeth with a closed apical foramen and a dry extraoral period longer than 60 minutes¹.

iritacija periapikalnog tkiva pri direktnom kontaktu sa kalcijum-hidroksidom. I pored preporuke, treba uzeti u obzir i mogući nedostatak MTA, a to je dugo vreme vezivanja i uticaj mnogih faktora okoline na tu osobinu¹⁶. Između ostalog, usled nedostupnosti pomenutog materijala, u ovom slučaju upotrebljen je jodoform cement, imajući u vidu njegova dobra antibakterijska svojstva i brzo vezivanje^{17,18}. Međutim, potrebno je uzeti u obzir i nedostatke materijala sa dodatkom jodoforma u vidu toksičnosti, koja može negativno da utiče na okolna tkiva i potencijalno ubrzu pojavu resorpcije¹⁹.

U skladu sa preporukama, primenjena je i sistemska terapija antibioticima^{1,11,2}. Gomes i sar. pokazali su to da sistemska antibiotska terapija ima pozitivan efekat na reparatorne procese nakon odložene replantacije zuba, dajući pri tome prednost upotrebi amoksicilina²¹.

Kod zuba sa produženim ekstraoralnim periodom, oporavak periodontalnog tkiva kao opcija nije moguć, a samim tim i dugoročno očuvanje zuba u ustima. Resorpcija zamene, nakon ekstenzivne nekroze periodontalnog ligamenta, neminovan je ishod^{10,12}. Ostaci nekrotičnog tkiva periodontalnog ligamenta uzrokuju inflamatornu reakciju nakon koje se nastala oštećenja nadoknađuju novim tkivom-koštanim²². Kako bi se ovaj proces što više usporio, indikovano je pažljivo i potpuno otklanjanje nekrotičnih ostataka periodontalnog ligamenta sa površine avulziranog zuba¹¹, što je u ovom slučaju i učinjeno. Izvršeno je i potapanje zuba u rastvor fluorida, takođe sa ciljem usporavanja procesa zamenske resorpcije¹. Nakon 9 meseci primećeni su znaci koji su ukazivali na postojanje zamenske resorpcije. Nedostatak pokretljivosti, visok perkutorni ton i radiografski nalaz, "kao da su zub pojeli moljci", posledica su aktivnosti osteoklasta i procesa remodelacije kosti. Tvrdo tkivo zuba u kontaktu sa alveolarnom kosti resorbovano je i zamenjeno košću. Nakon 16 meseci od povrede, kao posledica dentoalveolarne ankiloze, replantirani zub je bio u infrapoziciji.

U terminalnom stadijumu radiolološki je uočena izražena cervikalna eksterna inflamatorna resorpcija, najverovatnije uzrokovana prodorom infekcije iz sulkusnog predela, koja je dovela do patološke luksacije zuba. Nedugo zatim, a 3 godine i 6 meseci nakon traume, usledio je i gubitak zuba, koji je u tom razvojnom periodu, između ostalog, uspešno ostvario ulogu fiziološkog čuvara prostora.

In addition to a very long extraoral period, in high-risk infectious surrounding, a tooth delivery in a completely dry environment was an additional aggravating factor in this case. The correct choice of medium for the preservation of avulsed tooth is of great importance, both for preserving the vitality of periodontal ligament cells and for reducing the risk of premature complications in the form of root resorption¹³. Milk and Hank's balanced saline solution are preferred when choosing a dental care medium¹³. Coconut water, propolis, probiotic solutions, green tea extract, aloe vera, soy milk are also mentioned as good transport media^{13,14}. Drinking water is not recommended due to inadequate osmolarity, because it can additionally contribute to the damage of periodontal ligament cells and favors the early appearance of root resorption^{14,15}.

Due to the very long extraoral period in a high-risk infectious environment (street), the therapist decided on extraoral filling of the root canal with Iodoform cement paste and gutta-percha points. In making the decision, the achieved full length of the tooth root and still incompletely closed foramen were taken into account. Modern literature recommends filling the root canals of avulsed teeth with calcium hydroxide, whereby, especially in teeth with incompletely closed apex, the use of bioactive cement, mineral trioxide aggregate (MTA) in the apical region is recommended in order to avoid additional irritation of periapical tissue. In direct contact with calcium hydroxide. Despite the recommendation, the possible disadvantage of MTA should be taken into consideration, which is the long binding time and the influence of many environmental factors on this property¹⁶. Among other things, due to the unavailability of the mentioned material, iodoform cement was used in this case, considering its good antibacterial properties and fast binding^{17,18}. However, it is necessary to take into account the disadvantages of materials with the addition of iodoform in the form of toxicity that can adversely affect the surrounding tissues and potentially accelerate the occurrence of resorption¹⁹.

In accordance with the recommendations, systemic antibiotic therapy was applied^{1,11,20}. Gomes et al. have shown that systemic antibiotic therapy has a positive effect on reparative processes after delayed tooth replantation, giving preference to the use of Amoxicillin²¹.

Sličan rezultat postigli su i Sardana i sar. u prikazu slučaja replantacije centralnog sekutića nakon ekstraoralnog vremena od 15 sati, kod 12 godina starog pacijenta²³. U ovom slučaju, zub sa završenim rastom korena do javljanja lekaru je držan u mleku, endodontski tretman je izveden intraoralno, a kanal privremeno punjen Ca (OH)₂ pastom. Nakon 3 godine od replantacije zabeleženi su znaci izražene ankiloze i inflamatorne resorpcije. Savas i sar. Pratili su slučaj replantacije centralnog sekutića kod osmogodišnjeg pacijenta, tretiran protokolarno, nakon 27 sati suvog ekstraoralnog perioda, tokom 18 meseci⁹. Na kraju ovog observacionog perioda zub je bio čvrst i funkcionalan, 0,5mm u infraokluziji sa evidentnim znacima zamenske resorpcije i ankiloze na rendgenskom snimku. Ovi rezultati su u skladu sa rezultataima Anderssona i sar., koji su pokazali da replantacija zuba nakon produženog suvog ekstraoralnog perioda, kod dece starosti od 8 do 16 godina, dovodi do gubitka zuba usled zamenske resorpcije u periodu od 3 godine do 7 godina²⁴.

Zbog svih nepovoljnih okolnosti pre replantacije, u prikazanom slučaju, zadržavanje zuba u zubnom nizu tokom tri i po godine može se smatrati uspehom. S obzirom na avulziju mladog zuba sa nezatvorenim apeksom, treba naglasiti to da bi ishod terapije bio znatno bolji da je stručna pomoć ukazana neposredno nakon traume i da je zub bio u odgovarajućem transportnom medijumu. Iz tog razloga, u ovom periodu odrastanja i povećane vulnerabilnosti dece, neophodno je ukazati i na značaj infor-misanosti roditelja o pravilnom postupanju u ovakvim slučajevima.

In teeth with a prolonged extraoral period, recovery of periodontal tissue is not possible, and thus also long-term preservation of the tooth in the mouth. Replacement resorption, after extensive periodontal ligament necrosis, is an unavoidable outcome^{10,12}. Remains of necrotic tissue of the periodontal ligament cause an inflammatory reaction after which the damage is compensated by new bone tissue²². In order to slow down this process as much as possible, careful and complete removal of necrotic remainings of the periodontal ligament from the surface of the avulsed tooth is indicated¹¹, which was done in this case. The tooth was immersed in a solution of fluoride, also with the aim of slowing down the process of replacement resorption¹. After 9 months, signs that indicated the existence of replacement resorption were noticed. Lack of mobility, high percussion tone and radiographic findings, "as if the tooth was eaten by moths", are a consequence of osteoclast activity and bone remodeling process. The hard dental tissue is resorbed in contact with the alveolar bone and replaced with bone tissue. After 16 months from the injury, as a consequence of dentoalveolar ankylosis, the replanted tooth was in infraposition.

In the terminal stage, radiologically observed pronounced cervical external inflammatory resorption, most likely caused by the penetration of infection from the sulcus region, led to pathological luxation of the tooth. Shortly afterwards, and 3 years and 6 months after the trauma, tooth loss occurred. It can be considered that it successfully fulfilled the role of a physiological guardian of space, during that developmental period.

A similar result was achieved by Sardana et al. in a case report of central incisor replantation after an extraoral time of 15 hours, in a 12-year-old patient²³. In this case, the tooth with the completed root growth was kept in milk until reaching the doctor. The endodontic treatment was performed intraorally, and the canal was temporarily filled with Ca (OH)₂ paste. After 3 years from replantation, signs of pronounced ankylosis and inflammatory resorption were reported. Savas et al. followed for 18 months a case of central incision replantation in an eight-year-old patient, treated according to the protocol, after 27 hours of dry extraoral period⁹.

Zaključak

Očuvanje zuba u zubnom nizu replantacijom, makar i privremeno, u periodu intezivnog orofacijalnog razvoja deteta, od velikog je značaja za očuvanje lokalnog integriteta koštanih struktura, kao i pravilan nastavak orofacijalnog razvoja. Stoga, replantacija avulziranog zuba treba uvek da predstavlja terapiju izbora, čak i u jako nepovoljnim okolnostima, kao u ovom slučaju, gde je uspešan ishod opravdao odstupanje od preporuka za terapijski postupak, u datom slučaju.

At the end of this observation period the tooth was firm and functional, 0.5 mm in infracclusion with evident signs of replacement resorption and ankylosis on radiograph. These results are consistent with the results of Andersson et al. who showed that tooth replantation after a prolonged dry extraoral period in children aged 8 to 16 years leads to tooth loss due to replacement resorption within a period of 3 to 7 years²⁴.

Due to all unfavorable circumstances before replantation in the presented case, keeping the tooth in the dental arch for three and a half years can be considered a success. Considering the avulsion of a young tooth with an unclosed apex, it should be emphasized that the outcome of the therapy would be significantly better if professional help was provided immediately after the trauma and if the tooth was stored in an appropriate transport medium. For that reason, in this period of development and increased vulnerability of children, it is necessary to point out the importance of informing parents about the correct reactions in such situations.

Conclusion

Preservation of tooth in the dentition by replantation, even temporarily, in the period of intensive orofacial development of the child, is of great importance for preserving the local integrity of bone structures, as well as the proper continuation of orofacial development. Therefore, replantation of an avulsed tooth should always be the therapy of choice, even in very unfavorable circumstances, as in this case, where a successful outcome justified a deviation from the recommendations for the therapeutic procedure in a given case.

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ZNAČAJ MIKRONUTRIJENATA U USNOJ DUPLJI

IMPORTANCE OF MICRONUTRIENTS IN THE ORAL CAVITY

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Sažetak

Uvod: Mikronutrijenti igraju moćnu ulogu u funkcionisanju različitih sistema organizma. Za održanje optimalnog stanja usne duplje neophodno je održati adekvatan status mikronutrijenata.

Cilj: Istaći značaj različitih mikronutritijenata za normalno funkcionisanje usne duplje, kao i njihov uticaj na pojavu različitih oboljenja mekih i tvrdih tkiva usne duplje.

Zaključak: Mikronutrijentkaoštosu vitamin C, B9 i E, kalcijum, cink, bakar i gvožđe imaju osim građivnih i anti inflamatorna svojstva i deluju kao antioksidansi. Nedostatak određenih mikronutrijenata ima važnu ulogu u razvoju parodontopatije i karijesa. Osobe sa hroničnim inflamatornim oboljenjem creva, kao i deca, trudnice i dojilje obično su deficitarni u ovim vitaminima i zato često podložni razvoju inflamatornih promena na mekim tkivim usne duplje, nastanku parodontopatije i karijesa.

Cljučne reči: malnutricija, antioksidans, inflamacija, parodontopatija, karijes

Abstract

Introduction: Micronutrients play a potent role in the functioning of the different systems of the organism. It is necessary to sustain an adequate status of the micronutrients for maintaining the optimal condition of the oral cavity.

The aim: To emphasize the importance of different micronutrients for the normal functioning of the oral cavity, as well as their influence on the occurrence of various diseases of the soft and hard tissues of the oral cavity.

Conclusion: Micronutrients such as vitamin C, B9 and E, calcium, zinc, copper and iron have a role in development so as anti-inflammatory and antioxidants properties. Deficiency of certain micronutrients plays an important role in the development of periodontitis and caries. People with chronic inflammatory bowel disease, as well as children, pregnant and breastfeeding women, are usually deficient in these vitamins and therefore often susceptible to the development of inflammatory changes in soft tissues of oral cavity, periodontitis and caries.

Key words: malnutrition, antioxidant, inflammation, periodontitis, caries

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Uvod

Dovoljna količina mikronutrijenata od ključnog je značaja za zdravo oralno okruženje. Na primer, brzi imuni odgovor značajan je ukoliko postoji zapaljenski proces. To je moguće obezbediti ukoliko je telo snabdeveno odgovarajućom ishranom¹. In vitro studijama je pokazano da vitamini i supstance u tragovima imaju značajnu ulogu u svim aspektima imunološke funkcije i da njihov deficit može narušiti imunološku funkciju². Konzumiranje dovoljne količine proteina i amino-kiselina može sprečiti različita oboljenja usne duplje, s obzirom na to da njihova deficijencija može dovesti do disfunkcije pljuvačnih žlezdi³, promeniti antibakterijska svojstva pljuvačke i promeniti sposobnost zaceljenja mekih oralnih tkiva⁴. Zapravo, pljuvačka se može koristiti i kao medijum za praćenje rizika za nastanak karijsa⁵. Drugu sličnu patologiju čine oboljenja parodontijuma, kao što su gingivitis i parodontopatija, koja imaju sličan trend progresije. Osim toga, mikronutrijenti deluju kao katalizatori metaboličkih reakcija. Budući da se samo malo vrsta hrane zapravo sastoji iz mikronutrijenata, od krucijalnog je značaja održati njihov balans, što se često postiže dodavanjem suplemenata⁶. Drugi zanemareni problemi su emocionalne i psihološke smetnje povezane sa kvalitetom života osoba sa oboljenjima usne duplje^{7,8}.

I pored značajnih uloga mikronutrijenata, veliki deo populacije je u njihovom deficitu. Na primer, Svetska zdravstvena organizacija (SZO) identifikovala je to da su u mnogim zemljama regiona Srednjeg Istoka, naročito deca i žene u reproduktivnom periodu deficitarni u kalcijumu, gvožđu, cinku, vitaminima A i D, i folatima⁹. Slično, statistika pokazuje to da je oko 33% ljudi, uglavnom žena, deficitarno u gvožđu. Nadalje, 13,2 miliona predškolske dece ima nivo serumskog retinola ispod 0,7 $\mu\text{mol/L}$, i znatno niže od toga, te da oko 800 000 ljudi pati od noćnog slepila⁹.

U cilju poboljšanja kvaliteta života, trebalo bi dobro proceniti unos ugljenih hidrata, proteina i mikronutrijenata¹⁰ naročito kod dece¹¹. Međutim, treba naglasiti to da se uprkos dobro izbalansiranoj ishrani, može desiti da pojedinac i dalje ne unese preporučene dnevne doze mikronutrijenata. Pored nedovoljnog unosa usled nepravilne ishrane, do deficijencije može doći i usled poremećaja u apsorpciji, interakcijama sa lekovima, drugih hroničnih oboljenja^{12,13}. Pored inherentnog rizika od deficijentnog stanja, dugoročne posledice smanjenog unosa vitamina i elemenata mogu se odraziti na fiziološke funkcije, mogu dovesti do ćelijske neispravnosti i povećanja rizika od nastanka hroničnih oboljenja¹³⁻¹⁵.

Introduction

Sufficient supply of micronutrients is the key to having a healthy oral environment. For instance, a quick immune response is important if there is an inflammatory process. This is possible provided that the body is supplied with proper nutrition¹. It has been proved in-vitro that vitamins and trace components play an important role in all aspects of immune function and their deficiency can lead to impaired immune function². Consuming enough amounts of proteins and amino acids can prevent different diseases of the oral cavity because deficiency of them can lead to dysfunction of salivary glands³, change in an antibacterial property of saliva and wound healing capacity of soft oral tissue⁴. Indeed, saliva can be used as monitoring medium for determining the risk for caries development⁵. Other similar pathologies are diseases of the periodontium, like gingivitis and periodontitis, which have a similar course of progression. Furthermore, micronutrients act as a catalyst for all metabolic reactions. Since only a small amount of food actually consists of micronutrients, it is crucial to maintain its balance, sometimes by administering food supplements⁶. Other underestimated problems are the emotional and psychological distraught associated with the quality of life due to the oral damage^{7,8}.

Despite the important functions of the micronutrients, a big chunk of population is lacking them. For example, WHO has identified that in many countries in the Middle East region, especially children and women of reproductive age to be deficient in calcium, iron, zinc, vitamin A, vitamin D and folate⁹. Similarly, statistics show that about 33% of people, the majority of whom are women, lack iron. Furthermore, 13.2 million preschool children have their retinol serum level below 0.7 $\mu\text{mol/L}$, and even worse, about 800.000 of them are suffering from night blindness⁹.

In order to improve the quality of life, the nourishment in the form of carbohydrate, proteins and micronutrients should be well assessed¹⁰, especially in the case of children¹¹. But it is to be noted that, despite a properly balanced diet, an individual can still fall short of meeting recommended micronutrient allowances. In addition to insufficient micronutrient intakes due to poor diet, deficiencies can still be a problem due to inherent risk for deficiency states, the long-term consequence of decreased intake of vitamins and elements can be linked with physiological performance, cellular malfunction and increased risk for chronic disease¹³⁻¹⁵.

Efekti mikronutrijenata u usnoj duplji Efekti makroelemenata i elemenata u tragovima

Magnezijum

Postoje dokazi da deficit magnezijuma povećava rizik od pojave parodontopatija. Netretirana parodontopatija takođe može usloviti probleme na drugim organima organizma. Analiza zasnovana na populacionoj studiji pokazala je to da dodatak magnezijuma u vidu suplemenata može poboljšati zdravlje parodontijuma, redukujući gubitak periodontalnog pripoja¹⁷. Slično, magnezijum pomaže u aktiviranju vitamina D, koji za uzvrat reguliše homeostazu kalcijuma i fosfata koji utiču narast o održanje kostiju. Na sličan način, magnezijum utiče na stabilnost ćelijske funkcije, sintezu RNK i DNK, ćelijski oksidacioni status i ćelijsku reparaciju. Takođe, magnezijum ima značajnu ulogu u aktivaciji značajnih transporta i enzima¹⁸ i smatra se da je njegova deficijencija okidač za apoptozu¹⁹. Slično ovome, studije pokazuju to da postoji međuzavisni odnos između konzumiranja magnezijuma i karijesa²⁰.

Kalcijum

Sledeći značajan element je kalcijum. Prema podacima trećeg Nacionalnog ispitivanja zdravstvenog stanja i ishrane (NIZSI III), nizak unos kalcijuma može rezultirati težom formom parodontalnog oboljenja, a takođe može uticati i na gustinu minerala i jačinu potpornih struktura zuba²¹. Prema studiji sprovedenoj u SAD na civilnoj neinstitucionalizovanoj populaciji, povezanost niskog unosa kalcijuma sa parodontalnim oboljenjem najčešće je pronađena kod mladih muškaraca i žena (starosti 20 do 39 godina) i starijih muškaraca (starosti 40 do 59 godina)²². Druga povezanost ogleda se između niskog nivoa kalcijuma i visokog nivoa fosfata u krvi nastalog usled neadekvatne niske koncentracije parathormona (PTH). Regularan tretman hipoparatiroidizma može uključiti aktivirani vitamin D i/ili kalcijum suplemetaciju, ali ova terapija ne može u potpunosti zameniti funkciju PTH i može usloviti kratkotrajne probleme (kao što su hipokalcijemija, hiperkalcijemija i povećano izlučivanje kalcijuma putem urinarnog trakta), te je zamena PTH prikazana kao nova opcija lečenja²³. S druge strane, primarni hipoparatiroidizam može povećati nivo kalcijuma u serumu sa neprimereno nesupresioniranim nivoom PTH. Hiperkalcijemija, koja se razvija kao rezultat

Effects of micronutrients in the oral cavity

Effects of macro and trace elements Magnesium

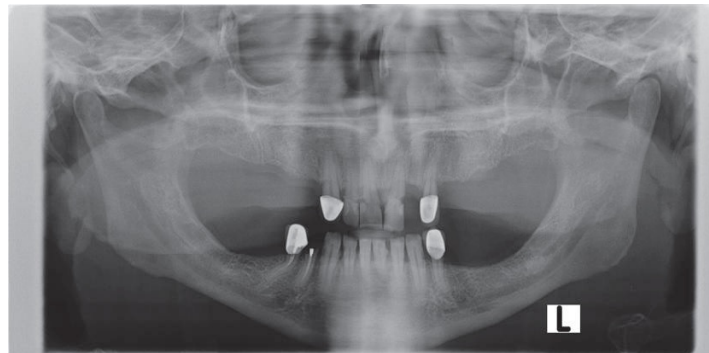
There is a piece of evidence that magnesium deficiency increases the risks for the development of periodontitis. Periodontitis, if untreated, can cause health problems in other parts of the body as well¹⁶. A population-based analysis revealed that nutritional magnesium supplementation may improve periodontal health, reducing periodontal attachment loss¹⁷. Similarly, magnesium helps in activating vitamin D, which in turn regulates calcium and phosphate homeostasis to influence bone growth and maintenance. In the same way, stability of cell function, RNA and DNA synthesis, cell's oxidation status and cell repairs are performed by magnesium. It has also a vital role in activating important transports and enzymes¹⁸, and it has been suspected that its deficiency can trigger apoptosis¹⁹. Similarly, studies show that there is an intricate link between magnesium consumption and dental caries²⁰.

Calcium

The next important element is calcium. According to data from the third National Health and Nutrition Examination Survey (NHANES III), low dietary intake of calcium may result in more severe periodontal disease as well as affect bone mineral density and strength to anchor tooth structure²¹. According to a study in U.S. civilian non-institutionalized population, the relation of lower dietary calcium intake with periodontal disease was found more often in young males and females (20 to 39 years of age), and in older males (40 to 59 years of age)²². Another assessable issue is low calcium levels and high phosphate levels in the blood due to inadequate low concentrations of parathyroid hormone (PTH). Regular treatment for hypoparathyroidism may include activated vitamin D and/or calcium supplements, but this treatment may not fully replace the functions of PTH and can lead to short-term problems (such as hypocalcaemia, hypercalcaemia and increased urinary calcium excretion), so PTH replacement has been demonstrated as a new treatment option²³. On the other hand, primary hyperparathyroidism may elevate serum calcium level with an inappropriately non suppressed PTH level. The hypercalcemia that develops as a result of primary hyperparathyroidism leads to osteoporosis (Picture 1), nephrolithiasis,

primernog hiperparatieroidizma, dovodi do pojave osteoporoze (Slika 1), nefrolitijaze, pankreatitisa i neurokognitivnih deficita kao što su poteškoće sa memorijom, koncentracijom i spavanjem²⁴. Morfometrijske analize pokazuju to da je slučajna primena PTH (40 µg/kg) uspela da zaštiti zub od koštane resorpcije izazvane parodontopatijom. Prema studiji sprovedenoj u Kini, uočen je potencijal intermitentnog PTH da stimuliše cementogenezu. Intermitentni PTH ograničio je inhibiciju cementogeneze i diferencijacije cementoblasta. Oba ova nalaza sugerišu da se intermitentni PTH može terapijski koristiti za poboljšanje prognoze resorpcije korena zuba²⁵.

pancreatitis, and neurocognitive deficits such as difficulty with memory, concentration and sleep²⁴. The morphometric analysis demonstrates that random PTH administration (40 µg/kg) was able to protect the tooth site from periodontitis-induced bone resorption. According to a study conducted in China, the potential of intermittent PTH to promote cementogenesis was observed. Intermittent PTH restrained the inhibition of cementogenesis and cementoblast differentiation by a mechanical strain. Taken together, these findings suggest that intermittent PTH can be therapeutically exploited to improve the prognosis of tooth root resorption²⁵.



Slika 1. Osteoporoza se uočava kao razređenje kostiju i proređivanje korteksa²⁶
Picture 1. Osteoporosis seen as rarefying of the bone and thinning of the cortex²⁶

Gvožđe

Gvožđe deficitarna anemija uključuje atrofiju jezičnih papila, peckanje i crvenilo jezika, angularni stomatitis, disfagiju, bledilo oralnih tkiva nastalog usled anemije²². Plummer-Vinsonov sindrom (Slika 2) je genetsko stanje povezano sa deficitom gvožđa, i manifestuje se angularnim stomatitisom, glositisom i disfagijom²⁸.

Iron

Iron deficiency anaemia includes atrophy of the lingual papillae, burning and redness of the tongue, angular stomatitis, dysphagia, and the pallor of the oral tissues due to underlying anaemia²⁷. Plummer-Vinson syndrome (Picture 2) is a genetic condition related to the deficiency of iron and presents with angular stomatitis, glossitis, and dysphagia²⁸.



Slika 2. Slučaj Plummer-Vinsonovog sindroma pokazuje angularni heilitis i gladak jezik sa gubitkom normalnih papila jezika²⁹
Picture 2. A case of Plummer-Vinson syndrome showing angular cheilitis and smooth tongue with loss of the normal tongue papillae²⁹

Cink i bakar

Deficit cinka može dovesti do promena u epitelu jezika, povećanja broja ćelija, poravnania filiformnih papila, pojave ulceracija i kserostomije²⁷. Cink poboljšava čulo ukusa i apetit; stoga deficit cinka može smanjiti čulo ukusa, što može biti povezano sa problemom malnutricije²⁵. Takođe smatra se da se može dovesti u vezu sa karijesom³¹. Cink takođe može da obezbediti zarastanje rane³² tako što učestvuje u svakoj fazi procesa zarastanja rane od reparacije membrane, koagulacije, angiogeneze, oksidativnog stresa, inflamacije imunološke odbrane, do formiranja fibroze³³. S druge strane apsorpcija bakra je direktno proporcionalna koncentraciji cinka³⁴. Postoji nekoliko dokaza da nedostatak bakra može povećati rizik od pojave karijesa. U studiji, koja je obuhvatila 60 pacijenata, uzrasta od 3 godine do 15 godina, pacijenti su bili podeljeni u dve grupe, grupu dece sa aktivnim karijesom i drugu grupu dece bez karijesa. Zapaženo je da deca bez karijesa imaju viši nivo bakra³⁵. Na glodarima je pokazano to da bakar inhibira enzime koji sadrže S-H, što može otežati proizvodnju kiselina u dentalnom plaku i stvaranje karijesa³¹. Deficit cinka i bakra povećava rizik od pojave infektivnih stanja³⁷.

Staviše, nedostatak cinka može potisnuti antiinflamatorni i imunološki odgovor mekih tkiva usne duplje²¹.

Selen

Studija sprovedena u Finskoj, gde je nedostatak selena široko rasprostranjen, pokazala je to da dodatak ovog ultramikroelementa ima sposobnost smanjenja karijesa kod mladih Finaca, jer je kolagen najvažniji komponenta organskog matriksa zuba, a selen može da zameni sumpor u vezama kolagena i smanjuje zubni karijes³⁹.

Fluor

Fluor sprečava pojavu karijesa³⁹ uglavnom svojim lokalnim dejstvom. Tokom izloženosti kiselinama fluoridi se apsorbuju za površinu kristala hidroksiapatita inhibirajući demineralizaciju (Figura 1(a), Figura 1(b)). Kada se pH ponovo uspostavi, mala količina fluorida u rastvoru učiniće rastvor visokoprezasićenim povećavajući proces remineralizacije. Na sličan način, mineral koji nastaje pod dejstvom nukleacije delimično rastvorenih minerala preferencijalno će sadržati fluor i uzimaće karbonat, čineći ga otpornijom na buduće kisele izazove⁴⁰. Osim toga, osim sprečavanja nastanka sekundarnog karijesa, fluor deluje i antimikrobno⁴¹. Stoga,

Zinc and Copper

Deficiency of zinc may cause changes to the epithelium of the tongue, increase cell numbers, flatten filiform papillae, cause ulcers and xerostomia²⁷. Zinc can improve taste and appetite; thus, deficiency of zinc also may cause a decrease in taste sensation, which can be related to the malnutrition problem³⁰. It is also considered to be associated with dental caries³¹. Zinc also can promote the healing of wounds³² by taking part in each phase of the wound healing process, ranging from membrane repair, coagulation, angiogenesis, oxidative stress, inflammation and immune defence, to fibrosis formation³³. On the other hand, the absorption of copper is inversely proportional to the concentration of zinc³⁴. There is a shred of evidence that the lack of copper can increase the risks of caries. In the study conducted on 60 patients aged 3-15 years, patients were divided into two groups: one with active caries and the other without caries. The observation showed that the caries-free group had a higher level of copper³⁵. It has been shown to inhibit S-H containing enzymes on rodents, which may impede acid production in dental plaque and caries³⁶. Deficiency of zinc and copper increases the risk of infectious diseases³⁷. Moreover, zinc deficiency can depress anti-inflammatory and immune response of oral soft tissue²¹.

Selenium

A study conducted in Finland, where selenium deficiency is widespread, demonstrated that the supplementation of this ultra-trace element has the capability to reduce caries in young Finns since collagen is the most important component of the organic matrix of the teeth and selenium can replace sulphur in bonds of collagen and reduce dental caries³⁹.

Fluorine

Fluorine prevents tooth decay³⁹ mainly by its topical effect. During the acidic challenge, fluoride is absorbed to the surface of the apatite crystals which inhibits demineralization (Fig. 1(a), 1(b)). When the pH is re-established, a small amount of fluoride in solution will make it highly supersaturated in comparison with fluorhydroxyapatite, increasing the process of remineralization. Similarly, the mineral formed under the nucleating action of the partially dissolved minerals will then preferentially include fluoride and exclude carbonate, rendering the enamel more resistant to future acidic challenges⁴⁰.

stomatolozi koriste fluore u lečenju karijesa⁴².

Istovremeno, treba da budemo svesni toksičnih efekata fluore, koji mogu dovesti do pojave fleka na zubima od blagih, bele boje (Slika 3), do ekstremno izraženih, braonkaste prebojenosti i doprineti formiranju rupica u gleđi³⁶. Kao što je pomenuto, nedostatak fluore može dovesti do povećanja zubnog karijesa, ali ne utiče na sluzokožu.

Moreover, besides preventing secondary caries⁴¹, it also has an antimicrobial action. So dental professionals use fluorides in caries management⁴².

At the same time, we should be aware of toxic effects of fluorides that can lead to mottling of the enamel ranging from mild white flecks (Picture 3) to extreme brown discoloration and enamel pitting⁴³. As mentioned, deficiency of fluorides can lead to increase indental caries but it does not affect mucous membranes.

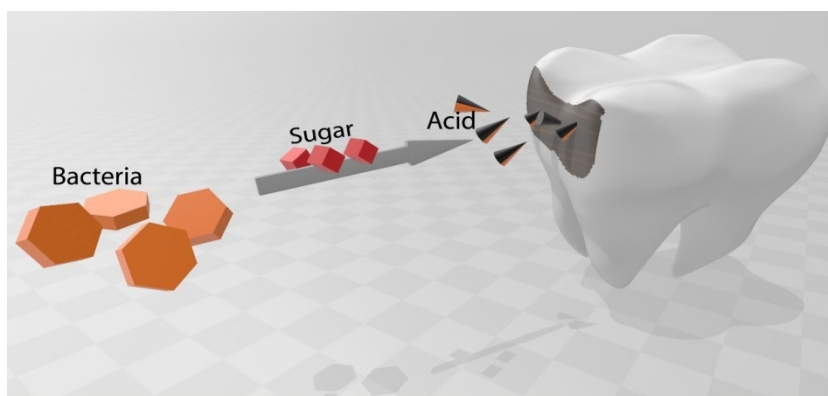


Figura 1 (a). Kiselina, prodire u običan sloj hidroksiapatita ($\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$), uslovljavajući pojavu karijesa

Figure 1 (a). Acid, penetrating the usual layer of hydroxyapatite ($\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$), eventually leading to caries

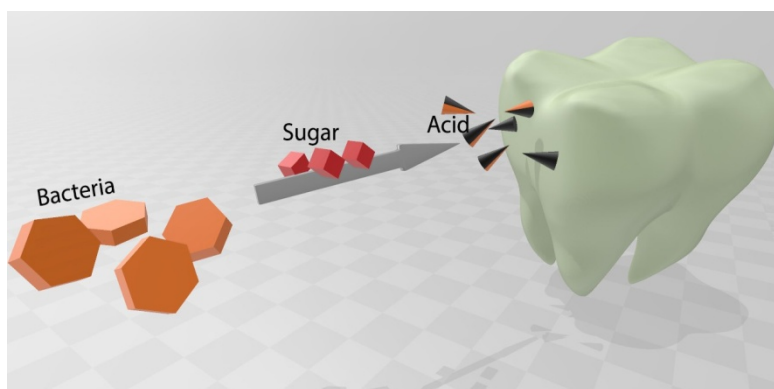


Figura 1 (b). Kiselina, nesposobna da prodre u film fluorapatita ($\text{Ca}_{10}(\text{PO}_4)_6\text{F}_2$), što na prvom mestu sprečava formiranje karijesa

Figure 1 (b). Acid, unable to penetrate the film of fluorapatite ($\text{Ca}_{10}(\text{PO}_4)_6\text{F}_2$), preventing the formation of caries in the first place



Slika 3. Bele mrlje kao rezultat prekomernog unosa fluorida⁴⁴
Picture 3. White flecks as a result of fluorine overdose⁴⁴

Efekti vitamina Folna kiselina

Deficit folne kiseline je učestala pojava. Prema Vogelju i sar. deficit folne kiseline povezuje se sa teškom formom inflamacije gingive⁴⁵. Osim toga, epitelne ćelije ne mogu efikasno da se dele bez folne kiseline⁴⁶. Iako povezanost između folne kiseline i formiranja i razvoja parodontalnih džepova još uvek nije dovoljno jasna, prema nekim studijama upotreba folne kiseline može biti od značaja za prevenciju inflamacije gingive⁴⁷ i patoloških promena na jeziku koje su vezi sa time kao što su poremećaj govora i mastikacije⁴⁸. Folna kiselina takođe može redukovati patološke promene na jeziku kao što su glossitis i papilarna atrofija⁴⁹. Prema Esakiju i sar., povezanost upotrebe folne kiseline i krvarenja gingive u grupi nepušača u Japanu pokazala je da upotreba folne kiseline može biti značajan indikator krvarenja gingive kod odraslih osoba i može obezbediti promociju zdravlja gingive⁵⁰.

Vitamin B₁₂

Kohortna studija koju su sproveli Zong i sar., pokazala je to da je serumski vitamin B₁₂ obrnuto povezan sa progresijom parodontalnog oboljenja i gubitkom zuba⁵¹. Druga studija preseka sprovedena na deci uzrasta od 10 do 14 godina pokazala je to da sistemski deficit vitamina B₁₂ je bio glavni krivac porasta karijesa zuba kod dece i istaknuta je povezanost sa gingivalnim problemima kod ove dece⁵². Slično ovome, deficit vitamina B₁₂ odgovoran je i za pojavu glossitisa, kao i atrofiju filiformnih papila²¹.

Vitamin C

Vitamin C takođe ima značajnu ulogu u protekciji parodontalnih tkiva (Slika 4). Amaliya i sar. pronašli su negativnu povezanost nivoa askorbata u plazmi i oštećenja parodonta⁵³.

Effects of vitamins Folic acid

Deficiency of folic acid is a common issue. According to Vogel et al., folic acid deficiency is related to severe gingival inflammation⁴⁵. Besides it, epithelial cells do not divide properly without folic acid⁴⁶. Although the relation among folic acid, the periodontal pocket formation and development is not quite understood, according to some studies, use of folic acid could be important for the prevention of gingival inflammation⁴⁷ and pathologies related to it, like impeded speech or mastication⁴⁸. Folic acid can also reduce pathologies of the tongue like glossitis and papillary atrophy²¹. A healthy gingiva maintains a healthy periodontal condition⁴⁹. According to Esaki et al., a correlation between intake of folate and gingival bleeding in the non-smoking group in Japan revealed that intake of folic acid could be an important indicator of gingival bleeding in adults and may provide a lead to promote gingival health⁵⁰.

Vitamin B₁₂

In a cohort study conducted by Zong et al., it was revealed that serum vitamin B₁₂ was inversely associated with periodontal progression and risk of tooth loss⁵¹. In another cross-sectional study done on children from 10 to 14 years old, it was found that systemic vitamin B₁₂ deficiency was the main culprit which increased dental caries and associated gingival problems in those children⁵². Similarly, lack of vitamin B₁₂ is also responsible for glossitis and filiform papillary atrophy²¹.

Vitamin C

Vitamin C may also play a significant role in the protection of periodontal tissues (Picture 4). Amaliya et al. have found a negative correlation between plasma ascorbate levels and periodontal breakdown⁵³.



Slika 4(a). Slika parodontalnog tkiva slikana pre davanja askorbinske kiseline. Uočava se rekurentno urastanje gingive nakon druge gingivektomije i pre davanja askorbinske kiseline. Bela polja ukazuju na tipična mesta rekurentnog gingivalnog urastanja⁵⁵

Picture 4(a). Periodontal images taken before ascorbic acid supplementation. Recurrent gingival overgrowth observed after the second gingivectomy and before ascorbic acid supplementation. The white arrows indicate typical sites of recurrent gingival overgrowth⁵⁵



Slika 4 (b). Slika parodontalnog tkiva slikanja 9 meseci nakon uzimanja askorbinske kiseline⁵⁵

Picture 4 (b): Periodontal images taken after 9 months of ascorbic acid supplementation⁵⁵

Paillaud i sar. pružili su drugi dokaz o povećanom riziku od nastanka parodontalnih oboljenja usled deficita vitamina C⁵⁴. Osim toga, pronađeno je to da blagi deficit vitamina C je povezan sa obimnim urastanjem gingive u prisustvu metaboličkog sindroma i teške parodontalne infekcije⁵⁵. Kao dodatak ovome, autori su pokazali i povezanost deficijencije vitamin C sa gingivitisom, ulceracijama u usnoj duplji, i nekoliko abnormalnosti gingive (sunderasta gingiva, krvarenje, izrazito crvena gingiva)^{21,53}. Deficit vitamina C takođe može biti značajan nezavisni faktor rizika od pojave oralne kandidijaze⁵⁶, međutim potrebno je više studija kako bi se utvrdo tačan uticaj pojedinačnog antioksidansa na prevenciju parodontopatije. Velika parodontalna studija sprovedena na Medicinskom i dentalnom univerzitetu u Tokiju pokazala je to da askorbinska kiselina može pojačati aktivnost i povećati ekspresiju $\alpha\beta 1$ integrina.

Paillaud et al. discovered another evidence of increased risks of periodontitis caused by vitamin C deficiency⁵⁴. Moreover, it has been found that mild deficiency of vitamin C is associated with extensive gingival outgrowth in the presence of metabolic syndrome and severe periodontal infection⁵⁵. In addition to it, authors have shown an association among deficiency of vitamin C and gingivitis, ulcer in the oral cavity and several gingival abnormalities (spongy, bleeding, abnormal redness)^{21,53}. Vitamin C deficiency can also be one of the most significant independent risk factors for oral candidiasis⁵⁶. But more studies are needed to understand the impact of every exact antioxidant in periodontitis prevention. In a huge study of periodontology atTokyo Medical and Dental University, it was found thatascorbic acid may enhance alkaline phosphatase activity in periodontal ligament cells and also may increase the expression of $\alpha\beta 1$ integrin.

To je veliki receptor za kolagen tip I, koji može da obezbedi osteoplastnu diferencijaciju ćelija parodontalnog ligamenta modulacijom interakcije kolagen tipa I- α 2 β 1 integrin⁵⁷. Shiga i sar., sugerišu to da askorbinska kiselina dovodi do novog pojačanja u nivou kolagane tip I, ali ne može da poveća aktivnost alkalne fosfataze ili osteoklaste m RNK u ćelijama parodontalnog ligamenta⁵⁸.

Vitamin A

Vitamin A je od značaja za očuvanje epitelnih tkiva, te njegova deficijencija može dovesti do gingivitisa, gingivalne hipoplazije, proliferacije vratnog epitela i resorpcije alveolarnih delova vilice⁵⁹. Prema Chapple i sar., ispitivanjem 11.480 odraslih osoba tokom trećeg Nacionalnog ispitivanja zdravstvenog stanja i ishrane (NIZSI III), utvrđeno je da je teška forma parodontopatije povezana sa likopenom, α -karotenom, β -karotenom, β -kriptoksantinom i deficitom vitamina A⁶⁰. Analiza četvrtog Korejskog Nacionalnog ispitivanja zdravstvenog stanja i ishrane pokazala je to da deficit vitamina A može biti povezana sa parodontopatijom kod mladih žena⁶¹. Proteini, malnutricija i deficit vitamin A mogu izazvati atrofiju pljuvačnih žlezda, što redukuje protok pljuvačke i puferski kapacitet pljuvačke, sa mogućim smanjenjem uloge pljuvačke u čišćenju usne duplje i puferskog uticaja na kiseline dentalnog plaka. Slično, tome deficit vitamina A, vitamina D i protein-energetska malnutricija (PEM) mogu se dovesti u vezu sa glednom hipoplazijom⁶². Deficit vitamina A može usloviti i kserostomiju, smanjiti otpornost na infekcije, narušiti antiinflamatorni odgovor i narušiti rast zuba^{21,43}. S druge strane, višak vitamina A dovodi do heilitisa, gingivitisa i narušava zarastanje rana⁶³.

Vitamin D

Primarna funkcija vitamina D je povećanje intestinalne apsorpcije kalcijuma i resorpcije kalcijuma na nivou bubrega, kao i regulacija metabolizma kostiju²⁴. Na sličan način vitamin D povećava mineralizaciju gleđi i dentina zuba. Vitamin D ne samo da utiče na mineralnu gustinu kostiju, već ima antiinflamatorna svojstva kao i sposobnost da stimulise produkciju antiinflamatornih peptida⁶⁴. Slično tome, na razvoj karijesa u prisustvu ugljenih hidrata mogu uticati mikronutrijenti kao što je vitamin D₃.

It is a major receptor of type I collagen, which can promote the osteoblastic differentiation of periodontal ligament cells by modulating type I collagen- α 2 β 1 integrin interaction⁵⁷. Shiga et al. suggest that ascorbic acid causes substantial enhancement in levels of type I collagen but is unable to increase alkaline phosphatase activity or osteocalcin messenger RNA in periodontal ligament cells⁵⁸.

Vitamin A

Vitamin A is important in maintaining the epithelial tissues and a deficiency of it can cause gingivitis, gingival hypoplasia, proliferation of crevicular epithelium and resorption of alveolar parts of jaws⁵⁹. According to Chapple et al., by examining 11.480 adults from the third National Health and Nutrition Examination Survey (NHANES III), severe periodontitis was associated with lycopene, α -carotene, β -carotene, β -cryptoxanthine and vitamin A deficiency⁶⁰. In an analysis of the Fourth Korean National Health and Nutrition Examination Survey, a deficiency of vitamin A could be associated with periodontitis in young women⁶¹. Protein, energy malnutrition and vitamin A deficiency can cause atrophy of the salivary glands, which reduces the flow of saliva and buffering capacity, eventually decreasing the cleansing action of saliva and ability to buffer plaque acids. Similarly, lack of vitamin A, vitamin D and protein-energy malnutrition (PEM) can be associated with enamel hypoplasia⁶². Vitamin A deficiency can also lead to xerostomia, reduced resistance to infections, depressed anti-inflammatory response and also impaired growth of the teeth^{21,43}. On the other hand, excess of vitamin A can lead to cheilitis, gingivitis and impaired healing⁶³.

Vitamin D

The primary function of vitamin D is to increase intestinal calcium absorption and calcium reabsorption from kidneys and to regulate bone metabolism²⁴. In the same way, vitamin D increases teeth dentin and enamel mineralization. Vitamin D not only affects bone mineral density but also has anti-inflammatory actions and the ability to stimulate the production of anti-microbial peptides⁶⁴. Similarly, the development of caries in the presence of carbohydrates may be influenced by micronutrients such as vitamin D₃.

Postoje dokazi da se vitamin D može dovesti u vezu i sa povećanim rizikom za pojavu hronične parodontopatije⁶⁵. Prema Van der Veldenu i sar., svakodnevno konzumiranje hrane koja sadrži dovoljno antioksidanasa, vitamina D i kalcijuma može sprječiti i lečiti parodontopatiju⁶⁶. Antiinflamatorni efekat vitamina D može pozitivno uticati na parodontalna tkiva, smanjiti parodontopatiju i gubitak zuba⁶⁷ (jačanjem potpornih struktura zuba²¹) kao i inflamacije gingive⁶⁸. Takođe, kalciferol poseduje imunomodulatornu aktivnost, koja može da utiče na parodontalno oboljenje, dok parodontopatija utiče na sistemski imuni odgovor⁶⁹.

Vitamin E

Vitamin E je antioksidans čiji nedostatak može biti povezan sa oralnim kancerom²⁷. Srećom, nedostatak vitamina E je retka pojava i simptomi nedostaka ovog vitamina retko se viđaju kod zdravih osoba koja dobijaju samo malu količinu vitamina E putem hrane⁷⁰. Deficit vitamina E, sekundarno u odnosu na abetalipoproteinemiju dovodi do problema kao što je slabost mišića, loša transmisija nervnih impulsa, i degeneracija retinala koja dovodi do slepila⁷¹. Slično tome njegova deficijencija može dovesti do supresije antiinflamatornog sistema i depresije imunog odgovora mekih oralnih tkiva²¹.

Rizične grupe od deficijencije mikronutrijentima

Postoji dosta mikronutrijenata koji su potrebni za normalno funkcionisanje usne duplje. Postoje određena stanja prilikom kojih određene grupe ljudi mogu biti u većem riziku od deficita specifičnih vitamina ili elemenata.

Grupa ljudi sa određenim bolestima

Velika deo ove grupe ljudi čine ljudi sa inflamatornim oboljenjem creva, kao što je Kronova bolest i celijakija ili osobe koje su podvrgnute hirurškim zahvatima na želucu. Ovi ljudi su uskraćeni za apsorpciju određenih nutrijenata unetih hranom i u čestom su deficitu kao što je bakar⁷², cink^{73,74}, kalijum⁷⁵, magnezijum⁷⁶, vitamin D⁷⁷, vitamin E⁶⁴, vitamin B₁₂⁷⁸, vitamin B₉⁷⁹, vitamin C⁸⁰ i vitamin B₁⁸¹.

Osobe sa oboljenjem bubrega takođe su u deficitu od pojedinih nutrijenata na primer vitamin C⁸², vitamin B₆⁸³ i selen⁸⁴ imaju niže

There is an evidence that vitamin D can be related to increased risk of chronic periodontitis⁶⁵. According to Van der Velden et al., consuming enough daily nutrition that covers sufficient antioxidants, vitamin D and calcium can prevent and treat periodontitis⁶⁶. Anti-inflammatory effects of vitamin D may have positive effects in periodontal tissues, in decreasing periodontal disease and tooth loss⁶⁷ (by increasing strength to anchor tooth structure²¹) as well as gingival inflammation⁶⁸. Also, calciferols have an immunomodulatory activity that can affect the periodontal disease as well, while periodontitis influences the systematic immune response⁶⁹.

Vitamin E

Vitamin E is an antioxidant whose deficiency may be associated with oral cancer²⁷. Fortunately, vitamin E deficiency is a rare situation and deficiency symptoms have not been found in healthy people who obtain even little vitamin E from their diets⁷⁰. Vitamin E deficiency, secondary to abetalipoproteinemia causes problems like muscle weakness, poor transmission of nerve impulses, and retinal degeneration that leads to blindness⁷¹. Similarly, its deficiency can lead to suppressed anti-inflammatory system and depressed immune response of oral soft tissue²¹.

Risk groups for micronutrient deficiencies

There are a lot of micronutrients that are required for the proper functioning of the oral cavity. There exist certain conditions, when a particular group of people could be at higher risk of being deficit in specific vitamins or elements.

Groups with certain diseases

One of the major group of people is individual with inflammatory bowel disease, like Crohn's disease and celiac disease, or an individual who has undergone through gastric surgery. These people are abstained from absorbing proper nutrients from the consumed food and frequently lack copper⁷², zinc^{73,74}, potassium⁷⁵, magnesium⁷⁶, vitamin D⁷⁷, vitamin E⁶⁴, vitamin B₁₂⁷⁸, vitamin B₉⁷⁹, vitamin C⁸⁰ and vitamin B₁⁸¹.

People suffering from kidney failures are also in the risk of lacking some nutrients.

serumske vrednosti kod pacijenta sa terminalnim bubrežnim oboljenjem jer se određena količina selen eliminise hemodijalizom. Vitamin C i aktivna forma vitamina B₆ takođe ima pojačani gubitak putem mokraće kada je funkcija bubrega narušena^{82,83}.

Dijabetes je sledeće oboljenje koje može usloviti deficit u pojedinim nutrijentima. Kod dijabetičara, postoji povećani klirens vitamina B₁⁸⁵ i magnezijuma⁸⁶. Slično, pacijenti sa uznapredovalim karcinomima gube veliku količinu krvi, što dovodi do gubitka gvožđa⁸⁷. Osim toga, odrasle osobe mogu imati deficit vitamina B₁ usled smanjene apsorpcije^{88,89} odnosno vitamina D usled smanjene sposobnosti kože da ovaj vitamin sintetiše efikasno, kao što je to slučaj kod mlađih osoba⁹⁰.

Grupa ljudi sa posebnim fiziološkim stanjima

Veliki deo grupe ljudi sa posebnim fiziološkim stanjima čine trudnice i novorođenčad. Trudnice imaju veliku potrebu za određenim vitaminima i hranljivim sastojcima, koje, ako se ne nadoknade, lako mogu dovesti do deficita vitamina A⁹¹, vitamina B₉⁹², vitamina B₁₂⁹³, gvožđa⁹⁴ i cinka⁹⁵. S druge strane, novorođenčad ima mali depo nekih vitamina i hranljivih sastojaka, a zbog njihove specifične ishrane oni su u velikom riziku od nedostatka vitamina C⁹⁶, vitamina B₁₂⁹³, vitamina E⁹⁷, vitamina A^{98,100}, vitamina D¹⁰¹ i gvožđa^{102,103}.

Druga grupa pojedinaca povezana je sa široko rasprostranjenim društvenim problemom, alkoholizmom. Poremećaji upotrebe alkohola obično sprečavaju prekid metabolizma cinka¹⁰⁴, vitamina B₁¹⁰⁵, folata¹⁰⁶. Hronični alkoholizam takođe može dovesti do povraćanja, dijareje i bubrežne disfunkcije, što rezultira gubljenjem hranljivih sastojaka poput magnezijuma¹⁰⁷, folata¹⁰⁶. Konačno, metaboliti alkohola mogu se takmičiti sa aktivnim oblicima nekih vitamina, poput vitamina B₆, te postaje podložan hidrolizi¹⁰⁸.

Vegetarijanci i vegani

Nemoguće je zanemariti još jednu grupu, tačnije dve grupe, koje su u riziku od nedostatka mikroelemenata - vegetarijanci i vegani¹⁰⁹. Nedostatak ribe u ishrani u velikoj meri povećava rizik od nedostatka vitamina D kod vegana¹¹⁰. Vegetarijanci delimično ispunjavaju svoje potrebe za kalciferolom

For example, vitamin C⁸², vitamin B₆⁸³ and selenium⁸⁴ have lower serum concentration in the patients suffering from terminal kidney disease because some amount of selenium is removed in haemodialysis. Vitamin C and the active form of vitamin B₆ also have a high urinary loss if renal functions are impaired^{82,83}.

Diabetes is the next disease, which can cause a deficiency in some nutrients. In diabetic patients, there is increased clearance of vitamin B₁⁸⁵ and magnesium⁸⁶. Similarly, cancer patients with disintegrating tumour lose a high amount of blood, making them deficient in iron⁸⁷. Furthermore, older individuals can lack vitamin B₁ due to its decreased absorption^{88,89} and vitamin D due to the decreased ability of their skin to synthesize it as efficiently as the skin of young people⁹⁰.

Groups with certain physiological state

A major group of people with specific physiological states are pregnant women and infants. Pregnant women have a high demand for some vitamins and nutrients, if not replenished, they can easily have a deficiency of vitamin A⁹¹, vitamin B₉⁹², vitamin B₁₂⁹³, iron⁹⁴ and zinc⁹⁵. On the other hand, infants have small storage of some vitamins and nutrients, and due to their specific diet, they are at higher risk of having deficiency of vitamin C⁹⁶, vitamin B₁₂⁹³, vitamin E⁹⁷, vitamin A⁹⁸⁻¹⁰⁰, vitamin D¹⁰¹ and iron^{102,103}.

Another group of individuals is related to a widely spread social problem, alcoholism. The alcohol use disorder usually impedes the absorption of zinc¹⁰⁴, vitamin B₁¹⁰⁵, folate¹⁰⁶. Chronic alcoholism can also lead to vomiting, diarrhoea, and renal dysfunction, resulting in depletion of nutrients like magnesium¹⁰⁷ or folate¹⁰⁶. Finally, metabolites of alcohol can compete with active forms of some vitamins, like vitamin B₆, which makes it more susceptible to hydrolysis¹⁰⁸.

Vegetarians and vegans

It is impossible to ignore one more group, more precisely - two groups that have their own risks of micronutrient deficiencies - vegetarians and vegans¹⁰⁹. Lack of fish in the diet greatly increases the risk of vitamin D deficiency in vegans¹¹⁰. Vegetarians partially meet their calciferol needs with eggs¹¹¹. Although there is a risk of deficiency of vitamin D for people living in high latitudes with any diet¹¹².

konzumiranjem jaja¹¹¹. Takođe postoji rizik od nedostatka vitamina D kod ljudi koji žive na većim geografskim širinama bez obzira na ishranu¹¹².

Sa druge strane, nedostatak vitamina D značajno smanjuje apsorpciju kalcijuma, zbog čega vegani najverovatnije imaju manjak kalcijuma¹¹³. Štaviše, biljni derivati često sadrže fitinsku i oksalnu kiselinu, što sprečava apsorpciju kalcijuma, magnezijuma, cinka i drugih metala^{37,114,115}. Nasuprot tome, vegetarijanci imaju tendenciju da konzumiraju velike količine visokodostupnog kalcijuma¹¹⁶ i malo više vitamina D od vegana¹¹⁷. Vegetarijanci i vegani takođe su podložniji nedostatku selena^{118,119}.

Još jedan kritičan mikronutrijent za vegetarijance, a posebno za vegane je vitamin B₁₂. Ovaj vitamin se u biljkama ne akumulira u dovoljnim količinama. Stoga je jedini izvor za ljude hrana životinjskog porekla¹²⁰.

Postoje određene grupe ljudi sa određenim potrebama u ishrani, na primer dijabetičari i gojazni pacijenti zahtevaju znatno veće količine hroma i vanadijuma^{121,122}, a vegetarijanci i vegani imaju veću verovatnoću da imaju nedostatak ω -3 PUFAs¹²³ i joda^{124,125}, u odnosu na ljude na standardnom režimu ishrane. Međutim, nisu pronađeni značajni efekti ovih mikroelemenata na usnu duplju.

Slično tome, adekvatan unos mikroelemenata (cinka, bakara, vitamina C, vitamina A, vitamina E) ne samo da održava higijenu usne duplje, već održava i nivo antioksidansa, što smanjuje zapaljenski proces u usnoj duplji¹²⁶. Treba napomenuti to da ostatak mikronutrijenata ne treba zanemariti, jer svi oni imaju sistemski efekat, koji takođe na kraju utiče na usnu duplju. U članku smo razmotrili samo one mikroelemente koji imaju direktne efekte na usnu duplju i čiji su efekti dobro utvrđeni kliničkim studijama.

Vitamin D deficiency, on the other hand, significantly reduces calcium absorption, that's why vegans are likely to be calcium deficient¹¹³. Moreover, plant derivatives often contain phytic and oxalic acids, which impedes the absorption of calcium, magnesium, zinc and other metals^{37,114,115}. In contrast, vegetarians tend to consume large amounts of highly available calcium¹¹⁶ and a little more of vitamin D than vegans¹¹⁷. Vegetarians and vegans are also more prone to selenium deficiency^{118,119}.

One more critical micronutrient for vegetarians, and especially for vegans, is vitamin B₁₂. The vitamin is not accumulated in plants in enough amounts. Therefore, its only source for humans is animal-derived food¹²⁰.

There are certain groups of people with specific diet requirement. For instance, diabetic and obese patients require significantly higher amounts of chromium and vanadium^{121,122}, and vegetarians and vegans are more likely to be deficient in ω -3 PUFAs¹²³ and iodine^{124,125} than omnivores. However, the significant effects of these micronutrients on the oral cavity were not found.

Similarly, adequate intake of micronutrients (zinc, copper, vitamin C, vitamin A, vitamin E) not only sustain hygiene of the oral cavity but also maintain antioxidant level, which decreases inflammatory process in the oral cavity¹²⁶. It is to be noted that the rest of the micronutrients should not be ignored, since all of them have a systemic effect, which also eventually affects the oral cavity. The article has considered only those micronutrients which have direct effects on the oral cavity and whose effects have been well-established by clinical studies.

Zaključak

Zbog znatno većeg rizika od poremećaja u metabolizmu kalcijuma, usled nedostatka vitamina D i slabe apsorpcije kalcijuma u crevima, vegani bi trebalo da budu izuzetno oprezni u pogledu metabolizma minerala tvrdih zubnih tkiva. i nedostatak selena kod vegetarijanaca i vegana takođe povećava rizik od kvarenja zuba.

Deca, trudnice i dojilje takođe treba da budu svesni depresije antiinflamatornog i imunološkog odgovora mekih tkiva usne duplje, zato što su ove kategorije često u deficitu vitamina C, B₁₂, E, A, D i gvožđa.

Slično tome, ljudi koji konzumiraju alkohol trebalo bi da budu oprezni u pogledu statusa vitamina B₁, folata, cinka i magnezijuma i preduzmu odgovarajuće mere predostrožnosti, pre svega upotrebom suplemenata deficitarnih nutrijenta. Nedostatak vitamina B₉ i magnezijuma povećava rizik od parodontopatije a nedostatak cinka može prouzrokovati smanjenje osećaja ukusa, ulceracije, zaravnjenje filiformnih papila i kserostomiju.

Dalje, osobe sa hroničnim inflamatornim bolestima creva treba da budu svesne da su u deficitu sa cinkom, kalijumom, magnezijumom, vitaminima D, E, B₁₂, B₉, C i vitaminom B₁. Nedovoljna količina vitamina C, vitamina B₉, vitamina E, vitamina D i magnezijuma može dovesti do parodontalne bolesti, gingivitisa, ulceracija u usnoj duplji, pa čak i do depresije antiinflamatornog i imunološkog odgovora mekih tkiva usne duplje. S druge strane, angularni heilitis uzrokuje nedostatak vitamina B₁ i vitamina B₁₂, a rizik od oralnog karcinoma verovatno će biti povećan usled deficita vitamina B₉ i vitamina E. Dalje, kalijum je jedan od krivaca za nastanak karijesa, dok je cink krivac za zaravnjanje filiformnih papila, ulceraciju i kserostomiju.

Konačno, ljudi sa oboljenjem bubrega treba da vode računa o statusu vitamina C, vitamina B₆ i selena u cilju sprečavanja depresije antiinflamatornog i imunološkog odgovora mekih tkiva usne duplje, parodontalne bolesti i karijesa.

Dijabetičari se često mogu suočiti sa angularnim heilitisom, koji nastaje kao posledica deficit vitamina B₁. Još jedan čest problem kod dijabetičara je deficita magnezijuma, koji povećava rizik od pojave parodontopatije, naročito u ovoj populaciji.

Conclusion

Due to significantly higher risk of impaired calcium metabolism as a result of vitamin D deficiency, and poor absorption of calcium in the intestine, vegans should be extremely careful about mineral metabolism in hard tissues. Selenium deficiency also increases the risk of tooth decay in vegetarians and vegans.

Children, pregnant women and breastfeeding mothers should also be aware of depressed anti-inflammatory and immune response of oral soft tissues because they often lack vitamins C, B₁₂, E, A, D and iron.

Similarly, people who indulge in alcohol should be careful about their status of vitamin B₁, folate, zinc and magnesium, and take a preliminary precaution by taking their supplements. Lack of vitamin B₉ and magnesium increase risk of periodontitis, and zinc deficiency can cause a decrease in taste sensation, ulcers, flattened filiform papillae and xerostomia.

Furthermore, individuals with chronic inflammatory bowel diseases should be aware of developing zinc, potassium, magnesium, vitamin D, vitamin E, vitamin B₁₂, vitamin B₉, vitamin C and vitamin B₁ deficiency. Insufficient amount of vitamin C, vitamin B₉, vitamin E, vitamin D and magnesium can lead to periodontal disease, gingivitis, ulcer of the oral cavity and even depressed anti-inflammatory and immune response of oral soft tissues. On the other hand, angular cheilosis is caused by lack of vitamin B₁ and vitamin B₁₂, and oral cancer risk is likely to be increased in vitamin B₉ and vitamin E deficient state. Furthermore, potassium deficiency is one of the culprits for dental caries, while zinc deficiency is the culprit for flattened filiform papillae, ulcers, and xerostomia.

Finally, people with kidney diseases ought to take care of vitamin C, vitamin B₆ and selenium status for preventing depressed anti-inflammatory and immune response of oral soft tissues, periodontal disease and dental caries respectively.

Diabetic patients can often face with angular cheilosis due to vitamin B₁ deficiency. Another common problem among diabetic patients is magnesium deficiency, which increases periodontitis risks especially in this population.

Conflict of interest

Declarations of interest: none

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TERAPIJA REKURENTNIH ORALNIH ULCERACIJA KOD PACIJENATA SA HIV-om

MANAGEMENT OF RECURRENT APHTHOUS STOMATITIS IN HIV

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Sažetak

Uvod: Danas je infekcija virusom humane imunodeficiencije (HIV) česti zdravstveni problem. Ljudi sa HIV-om žive duže i potrebno im je zbrinjavanje oralnih manifestacija ove bolesti. To je i razlog zašto je rad sa pacijentima sa HIV infekcijom prisutan u svakodnevnoj stomatološkoj i medicinskoj praksi. Iako rekurentne oralne ulceracije (rekurentni aftozni stomatitis; RAS) povezane sa HIV-om predstavljaju mali procenat oralnih lezija, one su jedno od najbolnijih stanja usne duplje.

Cilj: rada je da se ukaže na terapijske mogućnosti RASa i unapređenje zdravlja kod osoba sa HIVom

Zaključak: Jednom kada se postavi dijagnoza RAS-a, izbor specifičnog načina lečenja individualan je i uvek treba uzimati u obzir potencijalne neželjene efekte primenjenih lekova. Važno je smanjiti bol i postići dugotrajnu remisiju.

Cljučne reči: HIV rekurentni aftozni stomatit, RAS, terapija, oralne ulceracije

Abstract

Introduction: Today, human immunodeficiency virus (HIV) infection is often health problem. People with HIV are living longer and more of them are seeking care for the oral complications of this disease. This is the reason why the management of HIV infection is regular in the dental and medical everyday practice. Although HIV-related recurrent aphthous stomatitis (RAS) constitute a small percentage of oral lesions they are one of the most painful conditions of the oral cavity.

The aim: is to point out the therapeutic possibilities and health improvement in people with HIV.

Conclusion: Once a diagnosis of RAS is reached, the choice of a specific treatment modality is individual and the potential side effects of drugs should always be taken into account. It is important to reduce pain and achieve a prolonged remission.

Key words: HIV, recurrent aphthous stomatitis, RAS, therapy, oral ulcers

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Uvod

Infekcija virusom humane imunodeficijencije (HIV) predstavlja globalni zdravstveni problem i broj obolelih od HIV-a raste¹. HIV infekcija utiče na više aspekata društva i menja zdravlje ljudi. Danas osobe sa HIV-om žive duže i sve se češće javljaju stomatologu radi lečenja oralnih manifestacija bolesti. Ovo i jeste razlog zbog koga se lečenje obolelih sa HIV infekcijom danas često u svakodnevnoj stomatološkoj i medicinskoj praksi².

Oralne manifestacije HIV-a dobro su poznate i više od 80% osoba zaraženih HIV-om ima simptome ili znakove koje stomatolog može uočiti u usnoj duplji. Usna duplja igra važnu ulogu u nadgledanju napredovanja HIV bolesti uočavanjem oralnih HIV manifestacija³. Najčešća HIV oportunistička oralna infekcija je oralna kandidijaza. Takođe primećuje se to da Kaposijev sarkom ima veliku prevalenciju u Africi i Latinskoj Americi, a histoplazmoza je česta kod osoba zaraženih HIV-om na Tajlandu. Oralne ulceracije povezane sa HIV-om, kao što su rekurentni aftozni stomatitis (RAS) afte, virusne i tuberkulozne infekcije, nespecifični i neoplastični ulkusi iako čine mali procenat oralnih lezija kod ovih pacijenata predstavljaju jedne od najboljih stanja usne duplje i smanjuju kvalitet života pacijenta. Od svih ulceracija, RAS su najčešće oralne ulceracije sa učestalošću od 1% u Brazilu do 14% u Južnoj Africi⁴. Osim toga, prevalencija ostalih specifičnih oralnih lezija poput kandidijaze, vlasaste leukoplakije i Kaposijevog sarkoma niža je kod pacijenata na antiretrovirusnoj terapiji i može sugerisati to da su neka od ovih oralnih stanja rezultat kasnog početka antiretrovirusne terapije i potrebna su dalja istraživanja u ovoj oblasti⁵.

Pregled

RAS se javlja kod 25% opšte populacije. Najčešće se javlja u toku puberteta, a učestalost i težina kliničke slike smanjuje se sa godinama. Klinička slika RAS-a podeljena je u tri osnovna stadijuma. Prodromalni stadijum razvija se u prvih 48 sati u vidu peckanja na mestu gde će se razviti ulceracija. U sledećoj fazi, razvija se papula praćena bolom, okružena reaktivnim eritematoznim haloom. U trećem ulcerativnom stadijumu razvija se jasno definisana ulceracija veličine 1 mm - 3 mm, praćena bolom. Ova faza traje nekoliko nedelja, kada započinju regeneracija epitela, prekrivanje ulceracije i smanjenje bola⁵.

Introduction

Human immunodeficiency virus (HIV) infection is an overall health problem. The number of persons living with HIV is growing¹. HIV infection influences multiple aspects of society and modulates health. Today, people with HIV are living longer and more of them are seeking care for the oral complications of this disease. This is the reason why the management of HIV infection is regular in the dental and medical everyday practice².

Oral HIV manifestations are well defined and more than 80% of HIV infected persons have symptoms or signs that are visible to dentists. The oral cavity plays an important role in supervising the progression of HIV disease through the occurrence of HIV manifestations³. The most common HIV opportunistic infection is oral candidiasis. It is also noticed that Kaposi's sarcoma has a high prevalence in Africa and Latin America and histoplasmosis is often in HIV infected persons in Thailand. HIV-related oral ulcers encounter a small percentage of oral lesions like recurrent aphthous stomatitis (RAS), viral, tuberculous, non-specific and neoplastic ulcers. They are one of the most painful conditions of the oral cavity and reduce the quality of patient's life. RAS are the majority of oral ulcerations with the frequency from 1% in Brazil to 14% in South Africa⁴. The prevalence of specific oral lesions like candidiasis, hairy leukoplakia and Kaposi's sarcoma is lower among patients on antiretroviral therapy and could suggest that some of this oral conditions are the result of late antiretroviral therapy initiation and should be further investigated⁵.

Review

RAS affects up to 25% of the general population. The onset is usually during adolescence and diminishes in frequency and severity with age. The clinical features of RAS are divided into three major stages. Prodromal stage develops in the first 48 hours with a tingling sensation at the site where the ulceration will develop. In the next stage a papule develops with increasing pain. The papule is surrounded by a reactive erythematous halo. During the third ulcerative stage, papule ulcerates and aching, defined, oval 1-3 mm ulcer develops. This stage lasts to several weeks when epithelial regeneration, coverage of the ulcer and lessening of pain begins⁵.

Najčešće korišćena *klasifikacija RAS-a* zasniva se na težini bolesti i povezanosti sa sistemskim faktorima. "Obične afte" nisu povezane sa sistemskim faktorima i javljaju se samo 2 do 4 puta godišnje. "Kompleksne afte" povezane su sa sistemskim faktorima, ili rekurentnim oralnim i genitalnim ulceracijama, ili je oboljenje konstantno aktivno sa novostvorenim lezijama koje se razvijaju kako stare lezije nestaju. Ove složene ulceracije u novijoj literaturi nazivaju se "lezije slične aftama". Najčešće bolesti povezane sa RAS-om su Behčetova bolest, Kronova bolest, ulcerozni kolitis, enteropatija osetljiva na gluten, HIV infekcija i ciklička neutropenija⁵.

Starija klasifikacija RAS-a zasiva se na kliničkom izgledu bolesti. Prema ovoj klasifikaciji RAS je podeljen u tri oblika: *minor*, *major* i *herpetiformni*. Danas postoji i poseban dodatni entitet – aftozne ulceracije povezane sa HIV-om (Tabela 1).

Minor afte (minor aftozne ulceracije) čine 75% do 85% svih aftoznih lezija. Manje su od 10 mm, obično zarastaju u roku od 14 dana bez ožiljaka i lokalizuju se na nekratiniziranoj mukozi (labijalna ili bukalna sluzokoža, pod usne duplje, ventralna strana jezika).

Major afte (*peradenitis mucosa necrotica recurrens*; PMNR; Suttonova bolest) čine 10% svih aftoznih lezija. Simptomi su mnogo bolniji. PMNR polako zarasta, može trajati i do nekoliko meseci i obično ostavlja ožiljak po zarastanju. Češće se javlja na usnama, mekom nepcu i sluzokoži, koja prekriva manje pljuvačne žlezde.

Herpetiformne afte retko se javljaju i čine do 10% svih aftoznih lezija. One se vide kao mnogobrojne (do 100) manje od 3 mm, zaobljene, bolne lezije koje su vrlo slične onima kod intraoralnog herpes simpleks virusa. Javljaju se na oralnoj sluzokoži, spajaju se i stvaraju mnogo veće ulceracije. Obično traju do mesec dana, a u nekim slučajevima mogu ostaviti ožiljak po zarastanju⁵.

HIV- povezane aftozne ulceracije

Kao i minor RAS, HIV aftozne lezije povezane sa HIV-om vide se kao manje ulceracije (po broju manjem od 5) lokalizovane na nekratinizovanoj mukozi. Često su šire od 10 mm i mogu trajati i do nekoliko meseci⁶. Uočeno je da samo 3% bolesnika zaraženih HIV-om imaju aftozne ulceracije i da ovi pacijenti ne pripadaju ni jednoj, određenoj etničkoj grupi, ni jednom, određenom polu. Ipak, kod njih broj CD4+ je ispod 100 ćelija/ml što može biti važno za diferencijalno dijagnostičko isključenje nekih specifičnih infekcija i maligniteta.

The most common used RAS classification is based on disease severity and association with systemic factors. "Simple aphthosis" is not associated with systemic factors and occurs only 2–4 times per year. "Complex aphthosis" is associated with systemic diseases, either recurrent oral and genital ulcers are present, or disease is continuously active with new lesions developing as older lesions heal. These complex ulcers are called "aphthous-like lesions." The most common diseases connected with RAS are Behcet disease, Crohn disease, ulcerative colitis, gluten-sensitive enteropathy, HIV infection and cyclic neutropenia⁵.

Former RAS classification is based on clinical appearance of the disease. According to this, RAS are divided in three forms: minor, major and herpetiform. Nowadays, there is a special additional entity – HIV associated aphthous ulcers (Table 1).

Minor aphthae (mild aphthous ulcers) make up 75-85% of all aphthous lesions. They are smaller than 10 mm, usually heal within 14 days without scar and are localized on the nonkeratinized mucosa (labial or buccal mucosa, floor of the mouth, ventral border of the tongue).

Major aphthae (*peradenitis mucosa necrotica recurrens*; PMNR; Sutton's disease) make up 10% of all aphthous lesions. The symptoms are more painful. PMNR tend to heal slowly and can last up to several months, usually leaving a scar. They have a predilection for the lips, soft palate and mucosa overlying the minor salivary glands.

Herpetiform aphthae are rare and make up to 10% of all aphthous lesions. They are multiple (up to 100) smaller than 3 mm, rounded, painful and very similar to lesions of intraoral herpes simplex. They occur throughout the oral mucosa, fuse and produce much larger ulcers. Usually they last up to 1 month and in some cases may leave a scar⁵.

HIV- associated aphthous ulcers

Like RAS minor, HIV-associated aphthous ulcers are five or fewer in number and localized on nonkeratinized mucosa. They are often wider than 10 mm and can persist to several months⁶. It was noticed that only 3% HIV-infected patients have aphthous ulcers and they do not fall into any ethnic group or gender. Nevertheless, these patients have CD4 + counts below 100 cells/ml that can be important to exclude some specific infections and malignancy.

Tabela 1. Poređenje kliničkih oblika RAS
Table 1. Comparison of clinical features of RAS

Lezija	Veličina	Broj	Trajanje	Vrsta sluzokože
Lesion	Size	Number	Duration	Type of mucosa
Minor	< 10 mm	1-5	7-14 dana/days	Nekeratinizirana Nonkeratinized
Major	> 10 mm	1-10	Nedelje do meseci Weeks to months	Nekeratinizirana Nonkeratinized
Herpetiformne Herpetiform	< 10 mm	> 10	7-14 dana/days	Nekeratinizirana Nonkeratinized
HIV-povezane HIV-associated	> 10 mm	1-5	Nedelje do meseci Weeks to months	Nekeratinizirana Nonkeratinized

Aftozne lezije povezane sa HIV-om klinički su slične major aftama, ali su trajnije i otporniji na lečenje čak i tetraciklinom i kortikosteroidima. Postoje neka razmatranja toga da su major afte povezane sa HIV-om zapravo minor afte koje se javljaju kod HIV pozitivnih pacijenata. Takođe, duboke ulceracije kod HIV pozitivnih pacijenata nazvane su NOS (ne definisane ulceracije), a u slučaju ekspozicije kostiju NUS (nekrotizirajući ulcerozni stomatitis). U većini slučajeva, NOS ulceracije na mekim tkivima predstavljaju NUS bez zahvatanja kosti ili obrnuto.

Smatra se da mnoge ulceracije kod HIV pozitivnih pacijenata predstavljaju infekciju virusom herpes simpleks (HSV) i kao takve uspešno se leče talidomidom. Potvrđeno je da sistemska terapija talidomidom ima najbolju efikasnost u RAS terapiji HIV seropozitivnih pacijenata i smernice za propisivanje ovog leka leka detaljno su dokumentovane u podacima iz literature. Ipak, treba istaći da je talidomid kontraindikovano kod pacijenata sa poliradikulopatijom ili encefalopatijom budući da može zakomplikovati kliničko stanje pacijenta.

Etiologija RAS i HIV

RAS je veoma čest poremećaj oralne sluzokože i može biti uzrokovan raznim etiološkim faktorima. Iz ovih razloga, histopatološkim pregledom postavlja se definitivna dijagnoza. Trajanje, učestalost i mesto javljanja ulceracija obično su modifikovano delovanjem sistemskih faktora. Kod HIV pozitivnih pacijenata može se javiti širok dijapazon oralnih ulceracija, a njihova precizna etiologija i uloga virusa obično ostaju nejasni.

HIV-associated aphthous ulcers are clinically similar to major RAS, but are more persistent and resistant to treatment even with tetracycline and steroids. There are some considerations that HIV-associated major aphthous ulcers are conventional RAS just present in HIV-positive patients. Also, deep ulcerations in HIV-positive patients are named NOS (not otherwise specified ulcers), and in case of bone exposure NUS (necrotizing ulcerative stomatitis). The most of the cases of NOS ulcers in the soft tissues represent NUS without involving bone, or vice versa.

It is considered that many ulcers in HIV patients represent herpes simplex virus (HSV) infection and such lesions are successfully treated with thalidomide. It is confirmed that systemic thalidomide therapy has the best efficacy in the RAS of HIV seropositive patients therapy and guidelines for prescribing such medication are well documented in the literature data. However, thalidomide is contraindicated in patients with polyradiculopathy or encephalopathy because it may complicate the clinical condition of the patient.

RAS aetiology and HIV

RAS is a very common disorder of the oral mucosa and can be caused by multifarious etiological factors. For these reasons, histopathological examination warrants a definitive diagnosis. Usually, duration, frequency and site of ulcers are specified by the underlying systemic condition. In HIV-positive patients wide spectrum of oral ulcerations may be present and their precise aetiology and the role of viruses usually remain unclear.

U svakodnevnoj praksi, kada su ulceracije kod RAS velike i kada zarastaju polako nakon primenjene rutinske terapije, lekari bi trebalo da uzmu u obzir testiranje pacijenta na HIV i pored činjenice da samo mali broj pacijenata sa HIV bolešću ima RAS⁸.

Imuna patogeneza i etiologija RAS-a tek trebaju biti potpuno razjašnjeni. Pretpostavlja se da su predisponirajući faktori za nastanak RAS-a trauma, stres, hormonska neravnoteža i preosetljivost na hranu. Takođe, poznato je da je kod RAS-a infiltracija epitela T-limfocitima zapravo odgovor na neki neidentifikovani antigen povezan sa keratinocitima, i da je smrt keratinocita posredovana diferencijacijom citotoksičnih T-ćelija i proizvodnjom tumor nekrosis faktora- α (TNF α)⁹.

Kod bolesnika sa HIV-om koji imaju mali broj CD4 T-limfocita i tešku kliničku sliku HIV-a obično se razvijaju duboke, bolne, nekrotične ulceracije zbog izraženog poremećaja imunološke ravnoteže i lokalnog sloma imunološke regulacije. Ulceracije su obično prisutne na sluzokoži i ždreću i izazivaju tešku disfagiju i disartriju⁶.

Terapija RAS-a

Lečenje RAS-a zavisi od broja lezija, veličine, trajanja i učestalosti recidiva. Svaka specifična vrsta lečenja zasniva se na potrebama pacijenta i mora uzeti u obzir korist i potencijalne neželjene efekte lekova¹⁰. Prvi korak u terapiji RAS-a je detaljno uzimanje anamneze vezane za simptome i istoriju bolesti. Treba uraditi detaljne analize krvi kako bi se isključio nedostatak gvožđa ili vitamina B₁₂. Jednom kada se postavi definitivna dijagnoza RAS-a pacijent treba da dobije uputstva o stanju i očekivanom ishodu iz svakog od različitih ponuđenih načina lečenja¹¹.

Dijetalne i opšte mere

Pacijenti često navode da je određena hrana odgovorna za nastanak RAS-a i preporučuje se njeno izbegavanje. Obično se pacijentima savetuje da izbegavaju tvrdu hranu, orašaste plodove, kiselu hranu ili pića, slane obroke, alkoholna i gazirana pića. Takođe treba izbegavati sredstva za čišćenje zuba koja sadrže natrijum-lauril-sulfat¹¹.

In everyday practice when RAS ulcers are large and heal slowly even after applied routine therapy, clinicians should consider HIV testing even small number of patients with HIV disease has RAS⁸.

The immune pathogenesis and aetiology of RAS has yet to be fully elucidated. It is suggested that the predisposing RAS factors are trauma, stress, hormonal imbalance and food hypersensitivity. It is also known that in RAS, the infiltration of the epithelium by T lymphocytes is in response to some unidentified keratinocyte-associated antigen when keratinocyte death is mediated by the differentiation of cytotoxic T cells and involves the production of tumour necrosis factor- α (TNF α) by these leucocytes⁹.

In in HIV patients with low CD4 T-lymphocyte counts and severe HIV disease deep, painful, necrotic ulcers usually develop due to immune imbalance and the local breakdown in immunoregulation. Ulcers are usually present on the buccal and pharyngeal mucosae and cause profound dysphagia and dysarthria⁶.

Treatment of RAS

Treatment of RAS depends on the number of lesions, size, duration and frequency of recurrences. Every specific treatment modality is based on the patient's needs and must take into account drug's potential side effects and benefits¹⁰. The first step in RAS therapy is in-depth patient interview about symptoms and disease history. Blood tests should be performed in order to rule out iron or vitamin B₁₂ deficiency. Once a diagnosis of RAS is established as part of informed consent, the patient should receive instruction about the condition and the expected outcome from each of the various treatment plans offered¹¹.

Dietary and general measures

Food that has often been reported by patients to be responsible for the causation of RAS should be avoided. Usually, patients are instructed to avoid hard food, nuts, acidic foods or drinks, salty meals, alcoholic and carbonated beverages. Also, teeth cleaning products containing sodium lauryl sulphate should be avoided¹¹.

Lokalna terapija

Lokalni anestetici mogu ublažiti simptome i smanjiti trajanje RAS-a. Obično se lokalno primenjuju: lidokain kao gel (Xylocaine 2% gel, Lidocaine 2% gel) ili sprej (Xylocaine sprej), polidokanol kao pasta (Solcoseryl zubna pasta), i benzokain kao pastile (Dolo-Dobendan pastile). Lokalni anestetici se mogu primeniti direktno na leziju u obliku rastvora (2% rastvor Xylocaina), kombinovanih preparata (sprej Acoïn pumpice) ili gotovih sredstava za ispiranje usta (Ezafluor)¹¹.

Antiseptički i antiinflamatorni lekovi mogu da smanje trajanje RAS-a. Sredstva za ispiranje usta koje sadrže hlorheksidin (Chlorhexidine gluconate sol. 2%) smanjuju učestalost, trajanje i težinu RAS-a. Zubne paste i vodice za ispiranje usta sa triklosanom (Rutisept extra 0,1%) i dekspantenolom (Panthenol sprej, Bepanthen sol.) predstavljaju novu lokalnu antiinflamatornu i analgetsku terapijsku opciju¹¹.

Lokalno primenjeni tetraciklin smanjuje trajanje i bolnost RAS-a. Korišćenjem tetraciklin-hidrohlorida u obliku praha može se izbeći problem stabilnosti vodenog rastvora tetraciklin-hidrohlorida. Male kapsule napunjene tetraciklin-hidrohloridom (250 mg) mogu se uzimati sa 5 ml vode kao sredstvo za ispiranje usta. U trudnoći treba izbegavati tetraciklin, a 5-aminosalicilna kiselina može se lokalno koristiti tri puta dnevno¹¹.

U slučajevima sa nedovoljnim uspehom lokalnih anestetika i antiinflamatornih lekova, obično se koriste lokalni kortikosteroidi. Oni smanjuju zapaljensku reakciju i smanjuju trajanje RAS-a. Triamcinolon-acetonid u orabazi (Kenalog) ili pronizon u pasti (Dontisolon D) mogu se koristiti jednom ili dva puta dnevno, kao opcija lečenja. Kombinacija lokalnog anestetika tokom dana i triamcinolonske paste noću, takođe se može koristiti, jer mnogi literaturni podaci ističu njihovu efikasnost. Dugotrajna upotreba lokalnih kortikosteroida ne preporučuje se zbog mogućeg razvitka lokalnih gljivičnih infekcija. U slučaju bolnih i veoma dubokih ulceracija, obično se preporučuje intralezijsko davanje kortikosteroida (Triamcinolon 10 mg/ml u dozi od 0,1 ml do 0,5 ml po leziji)^{12,13}.

Topical therapy

Local anaesthetics can relieve symptoms and decrease the duration of the RAS. Usually are locally applied: lidocaine as a gel (Xylocaine 2% gel, Lidocaine 2% gel) or a spray (Xylocaine spray), polidocanol as a paste (Solcoseryl dental paste), and benzocaine as lozenges (Dolo-Dobendan lozenges). Local anaesthetics can be applied directly on the lesions in a form of a solution (Xylocaine 2% solution), a combination preparations (Acoïn pump spray) or a ready-made mouthwashes (Ezafluor)¹¹.

Antiseptic and anti-inflammatory therapeutics can decrease the duration of the RAS. Chlorhexidine-containing mouthwashes (Chlorhexidine gluconate sol. 2%) cut down the incidence, duration and the severity of the RAS. Toothpastes and mouthwashes with triclosan (Rutisept extra 0.1%) and dexpanthenol (Panthenol spray, Bepanthen sol.) are the new local anti-inflammatory and analgesic treatment option¹¹.

Locally applied tetracycline decreases the duration and soreness of the RAS. Tetracycline hydrochloride in a form of a powder avoids the stability problem of tetracycline hydrochloride watery solution. Small capsules filled with tetracycline hydrochloride (250 mg) can be taken with 5 ml water as a mouthwash. In pregnancy, tetracycline should be avoided and 5-aminosalicylic acid locally used thrice daily¹¹.

In cases with inadequate success of local anaesthetics and anti-inflammatory agents combination local steroids are usually used. They reduce the inflammatory reaction and decrease the duration of RAS. Triamcinolone acetonide in orabase (Kenalog) or prednisolone in a paste (Dontisolon D) can be used once or twice daily as a treatment option. The combination of a local anaesthetic during daytime and triamcinolone paste at night can also be used as many literature data emphasize its efficiency. Long-term use of local steroids is not suggested because of local fungal infections. In case of painful very deep ulcerations the use of intralesional injection of steroids (Triamcinolon 10 mg/ml in a dose of 0.1–0.5 ml per lesion) is usually recommended^{12,13}.

Sistemska terapija

Holhicicin je predstavljen kao nova terapijska opcija zbog svoje sposobnosti da inhibira hemotaktičku aktivnost neutrofila. Obično se nakon njegove primene smanjuje broj i trajanje ulceracija. Preporučuje se primena holcicina (1 do 2 mg / dan oralno) u trajanju najmanje 4 nedelje do 6 nedelja, a recidivi RAS-a uobičajeni su nakon prestanka terapije. U teškim slučajevima RAS-a koji su rezistentni na monoterapiju holhicicinom, preporučuje se kombinacija pentoksifilina, pronizona, imunosupresiva ili interferona alfa. Holhicicin se ne sme koristiti tokom trudnoće i preporučuje se primena kontraceptivnih sredstava kod žena u trajanju od 3 meseca, a kod muškaraca i do 6 meseci nakon prestanka terapije ovim lekom¹².

Sistemska kortikosteroidi često se koriste u kombinaciji sa drugim imunosupresivnim lekovima. Pronizon (10–30 mg / dan) se propisuje u slučajevima dubokih bolnih ulceracija u istoj dozi i trajanju kao i kod HIV negativnih bolesnika sa RAS-om. Kortikosteroidi se mogu koristiti tokom trudnoće, u periodu do jednog meseca¹².

Dapsone (100–150 mg/dan) inhibira povećanu hemotaktičku aktivnost neutrofila. Nažalost, često se javljaju brzi recidivi nakon prekida terapije. Terapiju treba sprovoditi veoma oprezno, jer se mogu javiti hemoliza, methemoglobinemija i agranulocitoza kao ozbiljne nuspojave. Iz ovih razloga preporučuje se povremeno davanje i askorbinske kiseline¹⁴.

Thalidomid se koristi kao sredstvo za ispitivanje lečenja RAS-a povezanog sa HIV-om, uprkos njegovoj teratogenosti. Propisane doze talidomida su široke: od niskih (50 mg/dan) do visokih (200 mg/dan). Nažalost, kao i kod primene dapsona, recidiv se javlja oko 3 nedelje nakon prestanka terapije. Takođe, njegova primena ima brojne očekivane nuspojave poput privremenih cerebralnih simptoma (glavobolja, letargija, kserostomija, zatvor). Zbog mogućih teških oštećenja ploda ne može se koristiti tokom trudnoće i neophodna je primena kontraceptivnih sredstava za vreme lečenja ovim lekom¹⁵.

Pokazalo se da je *levamisol* efikasan (150 mg/dan, tri uzastopna dana) protiv RAS-a, iako njegova upotreba mora biti veoma pažljiva zbog rizika od agranulocitoze pa se preporučuje pažljivo nadgledanje pacijenta¹⁵.

Systemic therapy

Colchicine is introduced as a new therapeutic option because of the neutrophil's chemotactic activity inhibition. Usually, a decreased number and duration of ulcers is present after its administration. At least 4–6 weeks (1 to 2 mg/day orally) of Colchicine application is recommended and recurrence of RAS is common following cessation of therapy. In severe RAS cases, resistant to monotherapy with colchicine, combination with pentoxifylline, prednisolone, immunosuppressants or interferon alpha can be applied. Colchicine should not be used during pregnancy. A contraceptive method should be applied in women for 3 months and in men up to 6 months after cessation of therapy¹².

Systemic corticosteroids are often used in combination with other immunosuppressive drugs. Prednisolone (10–30 mg/day) is prescribed in cases of deep painful ulcers with the same doses and duration as in HIV-negative patients with RAS. Corticosteroids can be used during pregnancy and for a period up to 1 month¹².

Dapsone (100–150 mg/day) inhibits the enlarged neutrophil chemotactic activity. Unfortunately, rapid relapse often occurs after discontinuation of therapy. Its application must be very careful because haemolysis, methaemoglobinemia and agranulocytosis are its serious side-effects. For these reasons an intermittent administration of ascorbic acid is advisable¹⁴.

Thalidomide is used as an investigational agent for the treatment of RAS associated with HIV despite its teratogenicity. The prescribed thalidomide doses are wide: from low (50 mg/day) to high (200mg/d). Unfortunately, like in dapsone application the recurrence occurs in about 3 weeks after cessation of therapy. It has numerous expected side-effects like temporary cerebral symptoms (headache, lethargy, xerostomia, constipation). Due to severe congenital defects it cannot be used during pregnancy and adequate contraception is necessary¹⁵.

Levamisol is shown to be effective (150 mg/day three successive days) against RAS although its usage must be very vigilant due to the risk of agranulocytosis and close patient monitoring is therefore recommended¹⁵.

Mogu se koristiti *antimetaboliti*, poput azatioprina i metotreksata. Azatioprin (1 do 2 mg/kg/dan) smanjuje učestalost i ozbiljnost RAS-a, kontraindikovano je tokom trudnoće i dojenja zbog mogućih nuspojava, poput neplodnosti i oštećenja jetre, može ometati rast i ne preporučuje se deci. Za vreme primene ovog leka, neophodno je svaka 3 meseca kontrolisati krvnu sliku i funkciju jetre. U teškim slučajevima RAS-a može se pažljivo koristiti i metotreksat (7,5 do 20 mg/nedeljno). Dugotrajna terapija ovim lekom zahteva praćenje krvne slike i funkcije jetre svakog meseca, jer može doći do teške depresije koštane srži i poremećaja funkcije jetre¹⁶.

Imunomodulatori poput ciklosporina A (3 do 6 mg/kg/dan) inhibiraju aktivaciju T-ćelija. Efikasni su u oko 50% pacijenata sa RAS-om i mogu se koristiti kao monoterapija ili u kombinaciji sa kortikosteroidima. Ne sme se naglo prestati sa njihovom primenom jer može doći do ponovne pojave RAS-a. Ne mogu se koristiti tokom trudnoće i dojenja i kod pacijenata sa bubrežnom insuficijencijom¹⁷.

Alkilirajuća sredstva poput hlorambucila i ciklofosfamida mogu se koristiti u slučajevima teškog RAS-a. Hlorambucil (2-8 mg/dan) inhibira funkciju B- i T-ćelija i utiče na značajno smanjenje ulceracija, a u kliničkoj praksi je potvrđeno potpuno odsustvo lezija nakon njegove primene¹⁷.

Interferon alfa (Roferon A) je veoma uspešan u lečenju RAS-a, a potpuna remisija ulkusa obično se postiže nakon primene velikih doza leka. Niske doze preporučuju se samo kao terapija za održavanje kada se lečenje visokim dozama pokazalo uspešno u periodu od mesec dana do 4 meseca. Paracetamol (500 mg, oralno, 1 sat pre i posle injekcije) može se dodatno koristiti jer smanjuje sporedne efekte terapije koji se javljaju u vidu simptoma sličnih gripu na početku terapije i zavise od doze primenjenog leka. Nažalost, u mnogim slučajevima dolazi do brzog recidiva RAS-a nakon prekida terapije ovim lekom¹⁸.

Fizikalna terapija. U mnogim slučajevima pacijent sa HIV-om zahteva složenu interdisciplinarnu terapiju i sistemski pristup lečenju bolesti. Obično je pored standardne anti-HIV terapije, potrebna dodatna terapija kako bi se eliminisale ulceracije. Terapija laserima male snage (LLLT) može se primeniti zbog njenih specijalnih efekata poput biostimulativnog, analgetskog i anti-inflamatornog dejstva, što izaziva dodatno smanjenje bola. Dobro je poznato da LLLT poboljšava oralno zdravlje,

Anti-metabolites like azathioprine and methotrexate can be used. Azathioprine (1 to 2 mg/kg/day) reduces the incidence and severity of RAS. It is contraindicated during pregnancy and lactation due to its possible side-effects like infertility and liver damage. It may interfere with growth and is not recommended for children. Blood picture every month and liver function every 3 months should be carefully monitored. In severe RAS methotrexate (7.5 to 20 mg/week) can be efficiently but carefully used. Long-term therapy requires monitoring of blood picture and liver function every month, because severe bone marrow depression and liver function abnormalities may occur¹⁶.

Immunomodulators like Cyclosporine A (3 to 6 mg/kg/day) inhibit T-cell activation. They are effective in about 50% of patients with RAS and can be used as a monotherapy or in combination with steroids. Rapid dose reduction is forbidden because it can lead to rebound phenomenon. They cannot be used during pregnancy, nursing and renal insufficiency¹⁷.

Alkylating agents like chlorambucil and cyclophosphamide can be used in cases of severe RAS. Chlorambucil (2-8 mg/day) inhibits B- and T-cell function and shows marked improvement of ulcerations. Clinical practice has confirmed complete absence of lesions after chlorambucil administration¹⁷.

Interferon alpha (Roferon A) is very successful in the treatment of RAS. Usually, complete remission of ulcers is achieved after administration of high doses. Low doses are recommended as a maintenance therapy when treatment with high doses is successful in the first 1 to 4 months. Paracetamol (500 mg orally 1 h before and after the injection) can be additionally used as it decreases the initial dose-dependent flu-like symptoms as a side-effect. Unfortunately, in many cases there is a rapid RAS recurrence following discontinuation of therapy¹⁸.

Physical therapy. In many cases HIV patient requires complex multispecializing therapy and systemic approach to treatment of the disease. Usually, an additional therapy is necessary to solve the problem of ulcers. The low-intensity laser therapy (LLLT) can be applied because of its special effects like biostimulation, analgesia, and reduction of inflammation which leads to reduction in pain after laser treatment. It is well known that LLLT improves oral health allowing the feeding and giving the time required for the patient's body to have a positive response to the medication¹⁹.

obezbeđujući nesmetanu ishranu pacijenta što omogućava organizmu da pozitivno reaguje na lekove¹⁹. Upotreba LLLT-a kod RAS-a važna je alternativna terapija kod HIV pozitivnih pacijenta koja izaziva regresiju lezija i poboljšava kvalitet života pacijenata²⁰.

Zaključak

Infekcija virusom humane imunodeficiencije (HIV) veliki je globalni zdravstveni problem, a oralne ulceracije povezane sa HIV-om predstavljaju rani nalaz bolesti. Ove ulceracije smanjuju kvalitet života pacijenta i dobar su pokazatelj napredovanja bolesti i imunosupresije. Neophodno je bolje informisati stomatologe o oralnim manifestacijama i lečenju ove bolesti.

Lečenje RAS-a kod pacijenata zaraženih HIV-om zavisi od težine bolesti i učestalosti recidiva. Važno je smanjiti bol i postići dugotrajnu remisiju. Izbor načina lečenja individualan je, a uvek je potrebno uzeti u obzir i potencijalne neželjene efekte lekova.

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The use of LLLT in RAS is an important alternative therapy in HIV patient causing the regression of lesions and improvement of the quality of life of this patients²⁰.

Conclusion

Human immunodeficiency virus (HIV) infection is a major global health problem and HIV-related oral ulcers are an early finding of the disease. They reduce the quality of patient's life and are useful markers of disease progression and immunosuppression and dentists should be better informed about the oral manifestations and treatment of this disease.

Treatment of RAS in HIV infected patients depends on the severity of the disease and the frequency of recurrences. It is important to reduce pain and achieve prolonged remission. The choice of a specific treatment modality is individual and the potential side effects of drugs should always be taken into account.

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AVULZIJA STALNIH ZUBA KOD DECE I ODRASLIH - TERAPIJSKE MOGUĆNOSTI ZA DUŽI OPSTANAK PERMANENT TOOTH AVULSION IN CHILDREN AND ADULTS – THERAPEUTIC OPTIONS FOR LONGER SURVIVAL

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Sažetak

Uvod: Avulzije stalnih zuba (traumatska ekstrakcija, izbijanje zuba) predstavljaju jedne od najtežih povreda stalnih zuba i mogu se javiti kao samostalne povrede ili udružene sa ostalim povredama zuba ili povredama regije lica i vilica. Avulzije zuba definišu se kao izbijanje zuba iz alveole, uz potpuno kidanje periodontalnih vlakana, pri čemu jedan deo njih ostaje vezan za cement korena zuba, a drugi za alveolarnu kost, kompromitujući zubnu pulpu, cement korena i alveolarnu kost. Visoka zastupljenost i brojne posledice na stomatognatni sistem, koje za sobom ostavljaju, čine da se avulzije stalnih zuba mogu smatrati povredama od značaja za javno zdravlje.

Cilj rada: je da ukaže na terapijske mogućnosti avulzije stalnih zuba, koje mogu obezbediti njihov duži opstanak u usnoj duplji.

Zaključak: Strategija lečenja avulziranih stalnih zuba uvek je bazirana na ograničavanju infekcije korenskog kanala i periradikularne upale, prebacujući ravnotežu od nepovoljnog zarastanja (resorpcija zamene) prema povoljnom (periodontalnom) zarastanju. Uspeh terapije i periodontalno zarastanje zavise od trajanja i uslova ekstraoralnog čuvanja zuba, stepena oštećenja periodontalnog ligamenta i stanja pulpe.

Ključne reči: avulzija, stalni zubi, replantacija, terapija

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Abstract

Introduction: Permanent tooth avulsions (traumatic extraction; total luxation) are one of the most severe permanent tooth injuries and can occur as single injuries or associated with other dental injuries or injuries to the face and jaws region. They are defined as the luxation of teeth from the alveoli with complete rupture of periodontal fibres, or with one part attached to the root cementum and the other to the alveolar bone, thus compromising the dental pulp, root cementum, and alveolar bone. The high prevalence and numerous negative consequences on the stomatognathic systems they have suggest permanent tooth avulsions should be regarded as an important public health problem.

The aim: is to point out the therapeutic possibilities of permanent tooth avulsion that can ensure their longer survival in the oral cavity.

Conclusion: The treatment strategy for avulsed permanent teeth is always based on limiting root canal infection and periradicular inflammation, shifting the balance from unfavourable (replacement resorption) to favourable (periodontal) healing. The success of therapy and periodontal healing depend on the duration and conditions of extraoral tooth preservation, the degree of damage to the periodontal ligament, and the condition of the pulp.

Key words: avulsion; permanent teeth; replantation; therapy

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Uvod

Povrede stalnih zuba zauzimaju značajno mesto u oralnoj patologiji savremenog čoveka. Procena je da se učestalost povreda zuba u dečjem uzrastu kreće u rasponu od 2,4% do 34%, a da u odrasloj populaciji svaka četvrta odrasla osoba, tokom svog životnog veka, doživi neku vrstu povrede zuba¹. Istraživanja sprovedena širom sveta ukazuju na to da 0,5%-16% svih povreda stalnih zuba čine avulzije^{2,3}. U Srbiji avulzije zuba čine 5% svih povreda zuba⁴.

Avulzije stalnih zuba (traumatska ekstrakcija; izbijanje zuba) predstavljaju jedne od najtežih povreda stalnih zuba, i mogu se javiti kao samostalne povrede ili udružene sa ostalim povredama zuba ili povredama regije lica i vilica. Avulzije stalnih zuba definišu se kao izbijanje zuba iz alveole, uz potpuno kidanje periodontalnih vlakana, pri čemu jedan deo njih ostaje vezan za cement korena zuba, a drugi za alveolarnu kost, kompromitujući tako zubnu pulpu, cement korena i alveolarnu kost⁵. Epidemiološke studije ukazuju na to da su najčešće avulzirani zubi gornji centralni sekutići⁶, i da je uglavnom izbijen jedan zub, a ređe više stalnih zuba. Iako se mogu javiti u bilo kojoj životnoj dobi, avulzije stalnih zuba se, zbog visoke rezilijencije potpornog aparata mladih stalnih zuba i nezavršene mineralizacije okolne alveolarne kosti, u najvećem broju slučajeva javljaju u periodu između 7. i 14 godine života⁶. Visoka zastupljenost i brojne negativne posledice koje za sobom ostavljaju, čine da se avulzije stalnih zuba mogu smatrati povredama od značaja za javno zdravlje.

Zarastanje periodontalnog tkiva

Brz i adekvatan tretman, koji ima za cilj očuvanje avulziranog zuba i okolne alveolarne kosti od izuzetnog je značaja⁷. Terapija izbora u zbrinjavanju izbijenih zuba je replantacija, i sprovodi se sa ciljem obezbeđivanja zarastanja periodontalnog tkiva uz potpunu regeneraciju periodoncijuma. Revaskularizacija pulpnog tkiva počinje 4 dana od povrede⁸, i u koronarnom delu pulpnog tkiva dolazi do neoangiogeneze, proliferacijom mezenhimalnih ćelija. Nadalje, 7 dana posle replantacije avulziranog stalnog zuba dolazi do srastanja pokidanih gingivalnih vlakana periodoncijuma čime se smanjuje mogućnost prodora mikroorganizama kroz gingivalni džep. Utvrđeno je da revaskularizacija pulpnog tkiva napreduje brzinom od 0,5 mm dnevno i da je za kompletnu revaskularizaciju stalnih sekutića potrebno 30 do 40 dana⁹, pod uslovom da nije došlo do infekcije.

Introduction

Injury to permanent dentition occupies a significant place in the oral pathology of the modern man. It is estimated that the incidence of dental injuries in children ranges from 2.4 to 34% and that in the adult population, every fourth adult experiences some kind of dental injury during their lifetime¹. Researches conducted worldwide indicate that 0.5-16% of all permanent tooth injuries are avulsions^{2,3}. In Serbia, dental avulsions account for 5% of all dental injuries⁴.

Permanent tooth avulsions (traumatic extraction; total luxation) are one of the most severe permanent tooth injuries and can occur as single injuries or associated with other dental injuries or injuries to the face and jaws region (Figure 1). They are defined as the luxation of teeth from the alveoli with complete rupture of periodontal fibres, or with one part attached to the root cementum and the other to the alveolar bone, thus compromising the dental pulp, root cementum, and alveolar bone⁵. Epidemiological studies indicate that the most commonly avulsed teeth are upper central incisors⁶, usually one or, less often, several permanent teeth. Although they may occur at any age, permanent tooth avulsions mostly occur between the ages of 7 and 14 due to the high resilience of the supporting apparatus of immature permanent teeth and incomplete mineralization of the surrounding alveolar bone⁶. The high prevalence and numerous negative consequences they have suggest permanent tooth avulsions should be regarded as an important public health problem.

Periodontal Tissue Healing

Prompt and adequate treatment, which aims to preserve the avulsed tooth and the surrounding alveolar bone, is crucial⁷. Replantation is the therapy of choice in the management of avulsed teeth, and it is carried out to ensure the healing of periodontal tissue with complete regeneration of the periodontium. The revascularization of the pulp tissue begins 4 days after the injury⁸, and the proliferation of mesenchymal cells results in neoangiogenesis, which occurs in the coronal part of the pulp tissue. Furthermore, 7 days after the replantation of the avulsed permanent tooth, the ruptured gingival fibres of the periodontium coalesce, thereby reducing the possibility of microorganisms penetrating through the gingival pocket. It was found that

Međutim, u kliničkim uslovima ovo uglavnom nije moguće očekivati, te se pozitivnim ishodom može smatrati i zarastanje periodontalnog ligamenta uz reparatorne procese koji dovode do površinske resorpcije korena. Eksterna inflamatorna resorpcija korena i zarastanje periodontalnog tkiva uz zamensku resorpciju korena predstavljaju nepovoljan ishod replantacije izbijenog stalnog zuba.

Prilikom avulzije zuba dolazi do prekida neurovaskularnog snopa u predelu vrha korena zuba i rupture pulpe, što za posledicu može imati nekrozu pulpnog tkiva. Nekrotična pulpa podložna je bakterijskoj kontaminaciji. Ako ne dodje do revaskularizacije ili se ne sprovede adekvatna endodontska terapija, kanal korena postaje inficiran. Kombinovana mikrobiološka flora u korenskom kanalu oštetiće cement na spoljnoj površini korena, dovodeći do pojave eksterne inflamatorne resorpcije koja može biti vrlo agresivna. Eksterna inflamatorna resorpcija posledica je prodora bakterijskih metabolita iz inficiranog pulpnog tkiva, kroz dentinske kanaliće, do eksponirane površine korena. Kiseli bakterijski metaboliiti dovode do porasta kiselosti što predstavlja stimulans za početak osteoklastne aktivnosti. Resorptivni procesi, u početku dešavaju se na okolnom koštanom tkivu, jer je cement korena otporniji na inflamatorne agense. Cement i predentin smatraju se prvom linijom odbrane od resorpcije. Utvrđeno je to da osteoklasti ne resorbuju nemineralizovani koštani matriks. Spoljašnji sloj cementa prekriven je slojem cementoblasta formirajući zonu nemineralizovanog cementoida, dok je dentin prekriven predentinom, sa sličnom organskom strukturom. Eksterna resorpcija korena dogodiće se u slučaju oštećenja predentina i precementa kada inflamatorni agensi deluju na nezaštićenu površinu korena¹⁰. Eksterna resorpcija nastaviće se sve dok se mikrobnii agensi ne uklone iz korenskog kanala i okoline korena, i može imati superakutni tok uslovljavajući brzi gubitak zuba¹¹. Andreasen i sar.¹² utvrdili su to da progresija resorpcije korena zuba zavisi od uzrasta pacijenta. Ovi autori su utvrdili da je stopa resorpcije korena zuba značajno veća kod pacijenata koji su u trenutku povrede imali između 8 i 16 godina u odnosu na pacijente koji su u trenutku povrede imali između 17 i 39 godina.

Ako se periodontalna vlakna, koja su ostala vezana za površinu korena ne isuše, posledice avulzije zuba obično su minimalne^{13,14}.

the revascularization of the pulp tissue progresses at a rate of 0.5 mm per day and that complete revascularization of permanent incisors takes about 30 to 40 days⁹, provided that no infection has occurred.

However, this is generally impossible to expect in clinical conditions. Therefore, the healing of the periodontal ligament with reparative processes that lead to superficial root resorption may be considered a positive outcome. External inflammatory resorption of the root and healing of the periodontal tissue with replacement root resorption represent an unfavourable outcome of the replantation of the avulsed permanent tooth.

At the time of tooth avulsion, the neurovascular bundle is interrupted at the level of the tooth root tip, and the pulp ruptures, which can result in pulp tissue necrosis. Necrotic pulp is susceptible to bacterial contamination. Unless revascularization occurs or adequate endodontic therapy is performed, the root canal becomes infected. The combined microbiological flora in the root canal will damage the cementum on the outer surface of the root, leading to external inflammatory resorption, which can be rather aggressive. External inflammatory resorption is a consequence of the penetration of bacterial metabolites from the infected pulp tissue, through dentinal tubules, to the exposed root surface. Acidic bacterial metabolites lead to an increase in acidity which is a stimulus for the onset of osteoclast activity. Resorptive processes initially occur on the surrounding bone tissue, given that the root cementum is more resistant to inflammatory agents. The cementum and predentin are considered the first line of defence against resorption. Osteoclasts were found not to resorb unmineralized bone matrix. The outer layer of the cementum is covered with the cementoblast layer forming a zone of unmineralized cementoid, while the dentin is covered with predentin, with a similar organic structure. External root resorption will occur in cases of predentin and precementum damage when inflammatory agents act on the unprotected surface of the root¹⁰. External resorption will continue until microbial agents are removed from the root canal and the root environment, and may have a superacute course causing rapid tooth loss¹¹. Andreasen et al.¹² concluded that the progression of tooth root resorption depended on the age of the patient. These authors found that the rate of tooth root resorption was significantly higher in patients aged 8 to 16 compared to patients aged 17 to 39 at the time of injury.

Hidrirane ćelije periodontalnog ligamenta delimično će održati svoju vitalnost i omogućiti će zarastanje ligamenta bez razvoja veće inflamacije. Inflamacija se može razviti na ograničenim delovima korena ali će zarastanje korena biti moguće deponicijom novog cementa. U slučaju prekomernog sušenja periodontalnih vlakana pre replantacije, oštećene ćelije će izazivati difuzni inflamatorni odgovor na površini korena. Tada, za razliku od delimično oštećenog korena, koji biva pokriven cementoblastima, nema ovakvog zarastanja. Postoji velika površina korena koju cementoblasti ne mogu prekriti u kratkom periodu, tako da se kost direktno vezuje za površinu korena. Koren se postepeno zamenjuje košću, što je poznato kao zamenska resorpcija korena ili ankiloza^{15,16}. Ankiloza može imati uticaj na rast alveolarnog grebena i može oslabiti položaj neoštećenog susednog zuba¹⁷. Ankilotični zub ima karakterističan perkutorni zvuk, izmenjenu boju krunice i vremenom se nalazi u infraokluziji (Slika 1). S obzirom na to da se povrede dešavaju najčešće u prednjem, estetskom segmentu gornje vilice, potrebno je naći dobro rešenje za ublažavanje ovakvih posledica.

If the periodontal fibres that remain attached to the root surface do not dry out, the consequences of tooth avulsion are usually minimal^{13,14}. Hydrated cells of the periodontal ligament will partially maintain their vitality and allow the ligament to heal without the development of greater inflammation. Inflammation can develop on limited parts of the root, but root healing will be possible with the deposition of new cementum. In the case of excessive drying of periodontal fibres before replantation, the damaged cells will provoke a diffuse inflammatory response on the root surface. Then, unlike the partially damaged root that will be covered with cementoblasts, there is no such healing. There is a large root area that cementoblasts cannot cover in a short time, thus the bone binds directly to the root surface. The root is gradually replaced by bone, which is known as replacement root resorption or ankylosis^{15,16}. Ankylosis can affect the alveolar ridge growth and can weaken the position of an intact adjacent tooth¹⁷. The ankylosed tooth has a characteristic percussion sound, a changed colour of the crown, and eventually becomes infraoccluded (Figure 2). Given that injuries most often occur in the anterior, aesthetic segment of the maxilla, it is necessary to find a good solution to mitigate such consequences.



Slika 1. Ankilotičan avulzirani zub 11 u infraokluziji kod devojčice stare 12 godina. Replantacija avulziranog zuba izvršena 17 sati nakon povrede. Avulzirani zub endodontski tretiran

Figure 1. Ankylotic avulsive tooth 11 in infracclusion in a 12-year-old girl. Replantation of the avulsed tooth was performed 17 hours after the injury. Avulsated tooth endodontically treated



Slika 2. (A) Avulzija zuba 12,11,21 udružena sa frakturom alveolarnog nastavka i nosnih struktura; (B) Izgled posle repozicije koštanih struktura i avulzije stalnih zuba, imobilizacija zuba izvršena rigidnom vezom; (C) Izgled pacijenta godinu dana posle povrede.

Figure 2. (A) Tooth avulsion 12, 11, 21 associated with fracture of alveolar process and nasal structures; (B) Appearance of the patient one year after the therapy (replantation and immobilization of avulsed teeth)

Strategija lečenja avulziranih zuba

Strategija lečenja avulziranih stalnih zuba uvek je bazirana na ograničavanju infekcije korenskog kanala i periradikularne upale, prebacujući ravnotežu od nepovoljnog zarastanja (resorpcija zamene) prema povoljnom (periodontalnom) zarastanju.

Redosled zbrinjavanja avulzija stalnih zuba preporučen je od Međunarodnog udruženja za dentalnu traumatologiju 2007. godine¹⁸, a dopunjen je 2012. godine¹⁹, pa zatim i 2020 godine²⁰.

Opšte je prihvaćeno to da uspeh terapije i periodontalno zarastanje zavise od trajanja i uslova ekstraoralnog čuvanja zuba, stepena oštećenja periodontalnog ligamenta i stanja pulpe^{21,22}. Starost pacijenta, kao i način i dužina splintiranja imaju uticaja na stepen i način preživljavanja avulziranih zuba u vilicama.

Najbolja terapija avulziranih zuba je neposredna replantacija na mestu povrede, koja ima za cilj da spreči sušenje periodontalnih vlakana na površini korena zuba, čme se povećava šansa za preživljavanje replantiranog zuba i smanjuje rizik od nastanka komplikacija u vidu eksterne resorpcije i zamenske resorpcije.

Treatment Strategy for Avulsed Teeth

The treatment strategy for avulsed teeth is always based on limiting the root canal infection and periradicular inflammation, shifting the balance from unfavourable (replacement resorption) to favourable (periodontal) healing.

The order of the management procedures for permanent tooth avulsions was recommended by the International Association of Dental Traumatology in 2007, amended first in 2012¹⁹, and then again in 2020²⁰.

It is generally accepted that the success of therapy and periodontal healing depend on the duration and conditions of extraoral preservation of teeth, the degree of damage to the periodontal ligament, and the condition of the pulp^{21,22}. The age of the patient, as well as the manner and duration of splinting, affect the degree and manner of the survival of avulsed teeth in the jaws.

The best therapy for avulsed teeth is immediate replantation at the injury site, which aims to prevent drying of periodontal fibres on the surface of the tooth root, thereby increasing the chances for survival of the reimplanted tooth and decreasing the risk of complications such as external resorption and replacement resorption.

Neposrednom replantacijom smatra se tretman izveden u prvih dvadeset minuta od trenutka povrede. Visok procenat preživljavanja imaju i zubi koji su replantirani u prvih 30 minuta od povrede¹⁵. Međutim, vrlo često ovakav tretman nije moguće izvesti, pa se u tom slučaju primenjuje odložena replantacija tj. replantacija zuba u periodu dužem od sat vremena od momenta povrede. Prema nekim autorima, vreme koje prođe od trenutka povrede do momenta javljanja lekaru, u proseku iznosi između jednog sata i 4 sata²³. Za to vreme, za ishod terapije od najvećeg je značaja prezervacija ćelija periodontalnog ligamenta, jer vitalne ćelije omogućavaju restituciju, dok nekrotične ćelije uzrokuju inflamaciju sa sledstvenom resorpcijom okolnih tkiva.

Izbor odgovarajućeg medijuma za transport avulziranog zuba, od mesta povrede do ustanove gde će biti ukazana pomoć i način čuvanja zuba jednako su značajni kao i vreme proteklo od povrede do zbrinjavanja. Idealan medijum za transport i čuvanje avulziranog zuba je onaj koji ima sposobnost održavanja vitalnosti ćelija periodontalnog ligamenta (PDL) i pulpe, koji poseduje klonogenske sposobnosti, deluje antioksidativno, ne sadrži mikroorganizme, ima kompatibilnu fiziološku pH i osmolalnost, visoku dostupnost i nisku cenu. Postoje mnogi pripremljeni rastvori za očuvanje vitalnosti ćelija pulpe i PDL, a jedan do njih je i Henkov rastvor u kome ćelije mogu održati vitalnost i preko 96 sati²⁴. Ovaj rastvor preporučilo je Međunarodno udruženje za dentalnu traumatologiju 2007 godine¹⁸. Od tada, pojavljuje se veći broj predloga za čuvanje avulziranih zuba, kao što su pljuvačka, voda, led, fiziološki rastvor, Viaspan[®], minimalni esencijalni medijum (MEM), propolis, ekstrakt zelenog čaja, crnog dudu, kokosova voda, sportski napitci i sredstva za oralnu rehidraciju^{25,26}. Kako bi održali normalne uslove za očuvanje vitalnosti zuba, ovi medijumi moraju imati isti osmolaritet, pH i ćelijske nutrijente. Testirane su i druge vrste rastvora, kao što su sojino mleko, mleko u prahu, enfamil i tečnost za kontaktna sočiva, ali bez zadovoljavajućih rezultata.

Kada postoji prekid kontinuiteta neurovaskularnog snopa, sve metabolite (kalcijum-fosfat, kalijum) i glukozu treba dopremiti ćelijama. U slučaju odložene replantacije, u cilju povećanja stope preživljavanja avulziranih zuba preporučuju se određeni pre-replantacijski postupci.

The term immediate replantation refers to the treatment performed within the first 20 minutes after the injury. Teeth replanted within the first 30 minutes after the injury also have a high survival rate¹⁵. However, such a treatment is very often impossible. Therefore, in that case, delayed replantation is used instead, i.e. tooth replantation within more than an hour after the injury. According to some authors, the time that elapses between the moment of injury and the moment of receiving medical help is on average between 1 and 4 hours²³. During this time, the preservation of the cells of the periodontal ligament is of the utmost importance for the outcome of therapy, given that vital cells enable restitution, whereas necrotic cells cause inflammation with consequent resorption of surrounding tissues.

The choice of the appropriate medium for the transport of avulsed tooth, from the site of injury to the facility where medical assistance will be provided, and the manner in which the tooth is stored are just as important as the time elapsed from the injury to received medical care. The ideal medium for transporting and storing the avulsed tooth is the one that is capable of maintaining the vitality of periodontal ligament (PDL) and pulp cells, has clonogenic abilities, acts as an antioxidant, does not contain microorganisms, has compatible physiological pH and osmolality, high availability and low price. There are various ready-made solutions for preserving the vitality of pulp and PDL cells, one of them being Hanks' solution in which cells can maintain vitality for over 96 hours²⁴. This solution was recommended by the International Association of Dental Traumatology in 2007¹⁸. Since then, numerous suggestions for the preservation of avulsed teeth have emerged - saliva, water, ice, saline, Viaspan[®], Minimal Essential Medium (MEM), propolis, green tea extract, black mulberry extract, coconut water, energy drinks, and oral rehydration agents^{25,26}. To maintain normal conditions for tooth vitality, these media must have the same osmolarity, pH, and cellular nutrients. Other types of solutions, such as soy milk, milk powder, Enfamil, and contact lens fluid, have also been tested but without satisfactory results.

When there is a break in the continuity of the neurovascular bundle, all metabolites (calcium phosphate, potassium) and glucose should be delivered to the cells. In the case of delayed replantation, certain pre-replantation procedures are recommended to increase the survival rate of avulsed teeth.

U pogledu sistemske primene antibiotika, prvi izbor trebalo bi da bude odgovarajuća doza tetraciklina, koji su osim antimikrobnih osobina, pokazali i anti-resorptivni učinak, kao i inhibitorni efekat na osteoklaste i kolagenazu. Međutim, kako je sistemska upotreba tetraciklina kod dece do 12. godine života u mnogim zemljama zabranjena, sistemski treba ordinirati penicilinske preparate ili makrolide. Lokalna primena kortiko preparata takođe smanjuje koštanu resorpciju. Imidijetna primena paste za tretman kanala korena zuba koje sadrže kombinaciju kortikosteroida i tetraciklina ima povoljan efekat na periradikularno tkivo, zbog kontrolisanog oslobađanja medikamenata kroz dentinske kanaliće prema periodoncijumu.

U pogledu splintiranja avulziranih zuba, preporuka je da se splintiranje vrši fleksibilnim splintom, a da trajanje splintiranja ne prelazi 2 nedelje¹⁹.

Tretman zuba sa nezavršenim rastom korena

Kod zuba sa nezavršenim rastom korena, kada se na rendgen snimku uočava da je apikalni otvor veći od 1.1 mm i kada je zub van alveole bio manje od 60 minuta, postoji mogućnost restitucije ćelija pulpe i periodontalnog ligamenta. Pre-replantacijske procedure nisu potrebne, jer bi produžile vreme boravka zuba van alveole i dovele do oštećenja periodontalnog ligamenta čiji se ostaci nalaze na korenu avulziranog zuba. Neki autori, pre replantacije predlažu potapanje zuba u rastvor sa tetraciklinom trajanju od 5 minuta, radi dezinfekcije pulpe, stimulisanja procesa revaskularizacije pulpnog tkiva i oporavka periodoncijuma^{27,28}.

Splint se postavlja u periodu od 7 do 10 dana, i poželjno je da bude jednostavan za fiziološko i mehaničko čišćenje. Pod ovim okolnostima potrebno je oko mesec dana za revaskularizaciju koja se dešava u oko 50% slučajeva²⁹. Kontrolne preglede zuba treba uraditi jednom mesečno. U slučaju nekroze pulpe, odmah treba endodontski lečiti zub. Punjenje kalcijum-hidroksidom ili u kombinaciji sa mineral-trioksid agregatom trebalo bi da stvori apikalnu barijeru i spreči resorpciju korena. Ako dođe do nekontrolisane inflamacije, usled sušenja periodontalnih vlakana ili zbog infekcije pulpe, eksterna resorpcija i gubitak zuba, obično se odigravaju brže i agresivnije nego kod zuba sa završenim rastom korena.

Regarding the systemic administration of antibiotics, the first choice should be an appropriate dose of tetracyclines, which, in addition to antimicrobial properties, have also shown an antiresorptive effect, and an inhibitory effect on osteoclasts and collagenase. However, since the systemic use of tetracycline in children under the age of 12 is prohibited in many countries, penicillin preparations or macrolides should be administered systemically. Topical application of corticosteroids also reduces bone resorption. The immediate application of the tooth root canal treatment paste containing a combination of corticosteroids and tetracycline has a beneficial effect on the periradicular tissue due to the controlled release of drugs through the dentinal tubules towards the periodontium.

Regarding splinting of avulsed teeth, it should be done with a flexible splint, and the duration of splinting should not exceed 2 weeks¹⁹.

Treatment of Teeth with Incomplete Root Development

In teeth with incomplete root development, when the X-ray shows that the apical opening is greater than 1.1 mm, and when the tooth was outside the alveolus for less than 60 minutes, there is a possibility of restitution of pulp and periodontal ligament cells. Pre-replantation procedures are not necessary as they would prolong the time the tooth spends outside the alveolus and lead to damage to the periodontal ligament, whose residuals are found on the root of the avulsed tooth. Some authors suggest immersing the tooth in a tetracycline solution for 5 minutes prior to replantation to disinfect the pulp, stimulate the process of the revascularization of the pulp tissue, and recover the periodontium^{27,28}.

The splint is placed for a period of 7-10 days, and physiological and mechanical cleaning should be simple. Under these circumstances, revascularization takes about a month to occur, and it is reported in about 50% of cases²⁹. Dental check-ups should be done once a month. In case of pulp necrosis, the tooth should be treated endodontically. Filling with calcium hydroxide or in combination with mineral trioxide aggregate should create an apical barrier and prevent root resorption. If there is uncontrolled inflammation as a result of drying of periodontal fibres or due to pulp infection

Razlog tome je to što kod mladih pacijenata, prilikom oštećenja cementa, široki dentinski kanalići dopuštaju slobodno kretanje iritansa ka spoljnoj površini korena i dovode do brže eksterne resorpcije.

Treba izbegavati rigidno šiniranje. Duži period nošenja splinta preporučuje se jedino kada je avulzija zuba sa nezavršenim rastom korena udružena sa frakturom alveolarnog nastavka.

U slučaju kada je kod zuba sa nezavršenim rastom korena od trenutka povrede prošlo više od jednog sata, postoje različiti stavovi po pitanju replantacije. Pojedini stomatolozi, zbog mogućih komplikacija, ne predlažu replantaciju avulziranog zuba, već ortodontski tretman³⁰. Drugi, kao prelazno rešenje koje bi sprečilo resorpciju alveolarnog grebena, nastalog usled vađenja zuba, predlažu dekoronaciju³¹. Na ovaj način preventira se deformitet dentoalveolarnog segmenta do perioda povoljnog za implantaciju³². Međutim, prema aktuelnom vodiču za tretman avulziranih zuba sa nezavršenim rastom korena¹⁹, čak iako je od trenutka povrede prošlo jedan sat ili više sati, replantaciju treba razmotriti kao terapiju izbora, koja se sprovodi sa ciljem privremenog očuvanja konture i visine alveolarnog grebena radi kasnije protetske terapije^{1,4,30-32}. Međutim, ishod odložene replantacije u ovom slučaju najčešće je loš.

Endodontski tretman zuba sa nezavršenim rastom korena treba izbegavati, osim u slučaju kada se klinički i radiografski dijagnostikuje nekroza pulpe¹⁹.

Tretman zuba sa završenim rastom korena

Kompletno zarastanje periodontalnog ligamenta, kod zuba sa završenim rastom korena, sigurno je samo u slučaju ako je zub replantiran u prvih pet minuta od trenutka povrede³³. U svakom slučaju, treba insistirati na replantaciji u prvih 15 do 20 minuta.

Kod zuba sa završenim rastom korena, revaskularizacija pulpe nije moguća, tako da je endodontski tretman neizbežan. U zavisnosti od načina čuvanja, načina nastanka povrede i vremena proteklog od nastanka povrede, predloženo je više terapijskih mogućnosti, kako bi se održala vitalnost okolnog tkiva, odložila ankiloza i resorpcija. Ako je replantacija urađena u prvih 20 minuta, poželjno je koren zuba obraditi u istoj poseti lekaru i napuniti pastom koja sadrži kortikosteroide i tetracikline. Punjenje se kasnije menja, a zub puni kalcijum-hidroksidom.

external resorption and tooth loss usually occur faster and more aggressively than in teeth with completed root growth. The reason is that in young patients, when the cementum is damaged, wide dentinal tubules allow free movement of irritants towards the outer surface of the root and lead to faster external resorption.

Rigid splinting should be avoided. A longer period of wearing a splint is recommended only when the avulsion of the tooth with incomplete root growth is associated with a fracture of the alveolar process.

Regarding teeth with incomplete root development, in case that more than one hour has passed since the moment of injury, attitudes concerning replantation are different. Due to possible complications, some dentists do not suggest replantation of the avulsed tooth, but orthodontic treatment³⁰. Others suggest decoronation as a temporary solution that would prevent the resorption of the alveolar ridge, caused by tooth extraction³¹. In this way, the deformity of the dentoalveolar segment is prevented until a period favourable for implantation³². However, according to current guidelines for the treatment of avulsed teeth with incomplete root development¹⁹, even if one or more hours have passed since the injury, replantation should be taken into consideration as the therapy of choice to temporarily preserve the contour and height of the alveolar ridge for later prosthetic therapy^{1,4,30-32}. Nevertheless, the outcome of delayed replantation in such cases is usually poor.

Endodontic treatment of teeth with incomplete root development should be avoided, except when pulp necrosis is clinically and radiographically diagnosed¹⁹.

Treatment of Teeth with Completed Root Development

Complete healing of the periodontal ligament in teeth with completed root development is safe only if the tooth is replanted in the first five minutes from the moment of injury³³. Anyway, it should be insisted on the replantation in the first 15-20 minutes.

In teeth with completed root development, pulp revascularization is not possible. Therefore, endodontic treatment is inevitable. Depending on the method of preservation, type of injury, and the time elapsed since the injury, several therapeutic

U slučaju odložene replantacije, kada je ekstraalveolarno vreme duže od 60 minuta, ćelije periodontalnog ligamenta definitivno su izgubile vitalnost. Uklanjanjem ovih ostataka, smanjuje se mogućnost inflamacije. Može se primeniti kiretaža oštrom kiretom, skalrom ili potapanje u limunsku kiselinu i natrijum-hipohlorit. Posle ispiranja zuba sterilnim fiziološkim rastvorom, poželino je zub staviti u dvoprocentni rastvor natrijum-fluorida na 5 minuta. Fluoridi dovode do konverzije hidroksiapatita sa oštećene površine korena u fluorapatit, koji se taloži na površinu korena i ima zaštitnu ulogu.

Za stimulaciju zarastanja cementa i periodontalnog ligamenta lokalna aplikacija proteina glednog matriksa (Emdogain, Biora, Malme, Švedska) na koren avulziranog zuba i unutar alveole, može biti od koristi u slučaju replantacije zuba u periodu do 60 minuta od nastanka povrede, dok je kasnija upotreba sa ograničenim uspehom³⁴.

Lokalna upotreba baznog fibroblastnog faktora rasta bFGF dovodi do stvaranja novih ćelija periodontalnog ligamenta i kolagenih vlakana koja se direktno vezuju za cement i kost, smanjujući tako ankilozu i resorpciju korena zuba kod kojih je urađena odložena replantacija³⁵⁻³⁷.

Kako bi se izbeglo širenje infekcije iz korenskog kanala kod odložene replantacije, poželino je endodontski tretman odraditi neposredno i van alveole: koren prvo napuniti antibiotskom pastom sa dodatim kortikosteroidima, a kasnije kalcijum-hidroksidom, definitivnim punjenjem. Glavni efekat kalcijum-hidroksida je antibakterijsko svojstvo, a osim toga kalcijum-hidroksid pokazuje i povoljni uticaj na mestu resorpcije ier čini sredinu više alkalnom i promovira stvaranje čvrstog tkiva³⁸. Međutim, ne treba ga ostavljati u kanalu korena na period duži od 3 meseca, ier može dovesti do nekroze ćelijske populacije koja teži da zaceli mesto povrede na površini korena.

Zaključak

Strategija lečenja avulziranih stalnih zuba uvek je bazirana na ograničavanju infekcije korenskog kanala i periradikularne upale, prebacujući ravnotežu od nepovoljnog zarastanja (resorpcija zamene) prema povoljnom (periodontalnom) zarastanju. Uspeh terapije i periodontalno zarastanje zavise od trajanja i uslova ekstraoralnog čuvanja zuba, stepena oštećenja periodontalnog ligamenta i stanja pulpe.

options have been proposed to maintain the vitality of the surrounding tissue, delay ankylosis and resorption. If the replantation is done within the first 20 minutes, the tooth root should be processed at the same time and filled with corticosteroid and tetracycline paste. The filling is changed later, and the tooth is filled with calcium hydroxide.

Regarding delayed replantation, i.e. when the extra-alveolar time is longer than 60 minutes, the periodontal ligament cells have unquestionably lost their vitality. By removing these residues, the possibility of inflammation is reduced. Curettage with a sharp curette or scaler or immersion in citric acid and sodium hypochlorite can be used. After rinsing the tooth with a sterile physiological solution, it is necessary to put the tooth in 2% sodium fluoride solution for 5 minutes. Fluorides lead to the conversion of hydroxyapatite from the damaged root surface to fluorapatite, which is deposited on the root surface and has a protective role.

To stimulate the healing of the cementum and periodontal ligament, the local application of enamel matrix protein (Emdogain, Biora, Malmo, Sweden) to the root of the avulsed tooth and inside the alveolus may be useful in the cases of tooth replantation within 60 minutes from injury, whereas later use has limited success³⁴.

Topical use of the basic fibroblast growth factor (bFGF) leads to the formation of new periodontal ligament cells and collagen fibres that bind directly to the cementum and bone, thus reducing ankylosis and the resorption of tooth roots in which delayed replantation has been performed³⁵⁻³⁷.

To avoid the spread of infection from the root canal during delayed replantation, it is desirable to perform endodontic treatment immediately and outside the alveoli. The root is first filled with antibiotic paste with added corticosteroids, and then with calcium hydroxide, as a final filling. The main effect of calcium hydroxide is its antibacterial feature. Furthermore, calcium hydroxide has a favourable effect at the resorption site given that it makes the environment more alkaline and promotes the formation of solid tissue³⁸. However, it should not be left in the root canal for longer than 3 months since it can lead to necrosis of the cells that tend to heal the site of injury on the root surface.

Conclusion

The treatment strategy for avulsed permanent teeth is always based on limiting root canal infection and periradicular inflammation, shifting the balance from unfavourable

Starost pacijenta, udruženost povreda i način i dužina splintiranja od esencijalnog su značaja za stepen i način preživljavanja avulziranih zuba u vilicama.

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(replacement resorption) to favourable (periodontal) healing.

The success of therapy and periodontal healing depend on the duration and conditions of extraoral tooth preservation, the degree of damage to the periodontal ligament, and the condition of the pulp. The age of the patient, concomitant injuries and the manner and duration of splinting are essential to the degree and manner of survival of avulsed teeth in the jaws.

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ACKNOWLEDGEMENTS

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2. Corporate author: Federation Dentaire Internationale. Technical Report No.28. Guidelines for antibiotic prophylaxis of infective endocarditis for dental patients with cardiovascular disease. *Int Dent J* 1987;37:235.

3. No author given: Coffee drinking and cancer of the pancreas (editorial). *BMJ* 1981;283:628

4. Volume with supplement: Magni R, Rossoni G, Berti R, BN52021 protect guinea pig from heart anaphylaxis. *Pharmacol Res Commun* 1988;20 Suppl 5:75-8.

Books or other monographs:

5. Personal author(s): Tullman JJ, Redding SW. Systemic Disease in Dental Treatment. St. Louis: The CV Mosby Company; 1983:1-5.

6. Chapter in a book: Rees TD. Dental management of the medically compromised patient. In: McDonald RE, Hurt WC, Gilmore HW, Middleton RA, eds. *Current Therapy in Dentistry*, vol. 7. St. Louis: The CV Mosby Company; 1980:3-7.

7. Dissertations and thesis: Teerakapong A. Langerhans Cells in human periodontally healthy and diseased gingiva. (Thesis). Houston, TX: University of Texas; 1987.92 p.

Other published material:

8. Newspaper article: Shaffer RA. Advances in chemistry are starting to unlock mysteries of the brain. *The Washington Post* 1989 Aug 7; Sect.A:2 (col. 5).

References - electronic quotations:

9. Online journals without volume and page information. Berlin JA, Antman EM. Advantages and limitations of metaanalytic regressions of clinical trials data. *Online J Curr Clin Trials* (serial online). June 4; doc 134. Accessed July 20, 2000.

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11. World Wide Web.Centers for Disease Control and Prevention. Preventing emerging infectious diseases: Addressing the problem of antimicrobial resistance. Available at: <http://www.cdc.gov/ncidod/emergplan/antiresist/>. Accessed November 5, 2001.

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