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ORIGINALNI RAD
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EFEKTI RAZLIČITIH ANTIBIOTSKIH TERAPIJA AKUTNOG RINOSINUZITISA

EFFECTS OF DIFFERENT ANTIBIOTICS IN THE TREATMENT OF ACUTE RHINOSINUSITIS

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Sažetak

Uvod: *Sinusitisi su upale paranazalnih sinusa i mogu biti infektivne, alergijske ili autoimune prirode. Akutni rinisinuzitis najčešće je virusnog porekla i javlja se u okviru infekcije gornjih disajnih puteva. Ako je bakterijskog porekla, najčešći uzročnici su bakterije Streptococcus, Pneumococus i Haemophilus. Neke upale mogu početi kao virusne, a da se kod 0,5% – 2% njih razvije tzv. bakterijska superinfekcija, tj. naknadna kolonizacija bakterijama. Sinusitisi uzrokovani virusima traju 7 – 10 dana, dok bakterijski mogu trajati duže.*
Cilj rada: *Cilj ove studije bio je da se uporede tri terapijska protokola u lečenju akutnog bakterijskog rinosinuzitisa.*
Materijal i metode: *Prospektivna klinička studija sprovedena na Klinici za bolesti uva, nosa i grla Kliničkog centra Niš od oktobra 2019. do januara 2020. godine, u koju su uključeni pacijenti sa akutnim bakterijskim rinosinuzitisom, kod kojih smo upoređivali efikasnost i bezbednost levofloxacina u trajanju 5 dana, levofloxacina u trajanju 10 dana sa efikasnošću tretmana amoxicilin-klavolunatom. Uključeno je 62 pacijenta sa kliničkim i radiološkim dokumentovanim simptomima.*
Rezultati: *Potvrda bakterijske etiologije ne radi se rutinski u kliničkoj praksi, pošto zahteva punkciju sinusa ili endoskopski pregled srednjeg nosnog hodnika. Kao posledica toga, izbor antibiotske terapije je empirijski. U našem istraživanju, koristili smo levofloxacin u trajanju od 5 dana (500 mg jednom dnevno), levofloxacin u trajanju od 10 dana (500 mg jednom dnevno) i amoksicilin-klavulonat u trajanju od 10 dana (500 mg – 125 mg tri puta dnevno) i dobijeni rezultati pokazali su to da ne postoje statistički značajne razlike u pogledu izbora antibiotika i dužine primene terapije.*
Zaključak: *Nalazi ove studije sugerišu to da kratki kurs tretmana antibioticima ima sličnu efikasnost u odnosu na duži kurs lečenja bolesnika s akutnim, nekomplikovanim bakterijskim sinusitisom, onda kada je tretman indikovan.*

Ključne reči: *akutni rinosinuzitis, antibiotik, terapija*

Abstract

Introduction: *Sinusitis is an inflammation of the paranasal sinuses and it can be infectious, allergic or autoimmune. Acute rhinosinusitis commonly has viral origin and occurs as part of the upper respiratory tract infections. The most common pathogens are Streptococcus, Pneumococcus and Haemophilus influenzae. Some inflammations may start as viral, but develop into bacterial superinfection, i.e., subsequent colonization of the bacteria in 0.5-2% of cases. Viral sinusitis lasts for 7–10 days, whereas bacterial may take longer.*
The aim: *The aim of this study was to compare three therapeutic protocols for the treatment of acute bacterial rhinosinusitis.*
Materials and Methods: *A prospective clinical study was conducted at the Ear, Nose and Throat Clinic, Clinical Center Nis from October 2019 to January 2020, and it involved patients with acute bacterial rhinosinusitis in whom we compared the efficiency and safety of levofloxacin administration for five and 10 days with the efficiency of amoxicillin clavulanate treatment. The study included 62 patients with documented clinical and radiological symptoms.*
Results: *Confirmation of bacterial etiology is not routinely performed in clinical practice since it requires antral puncture or endoscopic examination of the middle nasal meatus. Consequently, the choice of antibiotic therapy is empiric. In our study, we used levofloxacin for five (500 mg once a day) and 10 days (500 mg once a day) and amoxicillin-clavulanatefor 10 days (500 mg–125 mg three times a day), and the results showed no statistically significant difference in regard to the choice of antibiotics and the duration of therapy.*
Conclusion: *The findings of this study suggest that a short course of antibiotic treatment has similar efficiency compared to a longer course of treatment of patients with uncomplicated acute bacterial sinusitis when treatment is indicated.*

Key words: *acute rhinosinusitis, antibiotics, therapy*

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Uvod

Sinusitisi su upale paranazalnih sinusa i mogu biti infektivne, alergijske ili autoimune prirode[1-16]. Najčešće se javljaju istovremeno sa upalama sluzokože nosne šupljine, te je adekvatniji naziv rinosinusitis[1]. Po trajanju mogu biti akutni (do 3 nedelje), subakutni (od 3 nedelje do 12 nedelja) i hronični (od 12 nedelja, pa sve do više meseci ili godina)[2].

Prema tome koliko je paranazalnih šupljina i koju je paranazalnu šupljinu zapaljenje zahvatilo, upale delimo na monosinuzitise (sinusitis maxillaris, sinusitis ethmoidalis, sinusitis frontalis i sinusitis sphenoidalis), polisinuzitise (kada su zahvaćeni sinusi sa jedne strane glave) i pansinuzitise (kada su zahvaćene sve paranazalne šupljine)[3,4].

Akutne upale paranazalnih šupljina najčešće prate akutne upale nosa. Akutne kataralne upale obično se ne dijagnostikuju i prođu nezapaženo i/ili su praćene kijavicom. U ovim slučajevima, pored jake kijavice, bolesnici se žale i na glavobolju[5]. Gnojne upale nadovezuju se na akutna kataralna stanja ili, pak, od početka postaju gnojna, ako za to postoje izvesni preduslovi kao, npr. masovna infekcija, loša ventilacija paranazalnih šupljina, oslabljene imunobiološke snage organizma, oslabljena lokalna reakcija sluzokože sinusa, itd.[6].

Akutni rinisinuzitis najčešće je virusnog porekla i javlja se u okviru infekcije gornjih disajnih puteva. Ako je bakterijskog porekla, najčešći uzročnici su bakterije Streptococcus, Pneumococcus i Haemophilus. Neke upale mogu početi kao virusne, a da se kod 0,5% – 2% njih desi tzv. bakterijska superinfekcija, tj. naknadna kolonizacija bakterijama. Sinusitisi uzrokovani virusima traju od 7 do 10 dana, dok bakterijski mogu trajati duže[7,8].

Posebnu vrstu sinusitisa predstavljaju oni uzrokovani gljivicama. Po pravilu, javljaju se kod osoba sa bolestima i stanjima koja uzrokuju smanjeni imunitet, kao što su dijabetes i AIDS ili nakon transplantacija tkiva i organa i kod osoba na terapiji imuno-supresivnim lekovima i mogu biti opasni po život zbog mogućeg brzog širenja infekcije i/ili mikotične sepse[4,5].

Cilj rada

Cilj ove studije bio je da se uporede tri terapijska protokola u lečenju akutnog bakterijskog rinosinuzitisa.

Introduction

Sinusitis represents an inflammation of the paranasal sinuses and it can be infectious, allergic and autoimmune in nature[1-16]. They most often occur simultaneously with the inflammation of the mucous membrane of the nasal cavity, therefore, rhinosinusitis is a more appropriatename[1]. According to their duration, they can be acute - lasting up to three weeks, subacute - lasting three to 12 weeks and chronic - lasting more than 12 weeks up to several months or years[2].

Depending on the number of paranasal cavities and which paranasal cavity was infected, inflammations are classified into monosinusitis (sinusitis maxillaris, sinusitis ethmoidalis, sinusitis frontalis and sinusitis sphenoidalis), polysinusistis (the sinuses on one side of the head are infected) and pansinusitis (all paranasal cavities are infected)[3,4].

Acute inflammation of the paranasal cavities is most often accompanied by acute inflammation of the nose. Acute catarrhal inflammations are usually not diagnosed and go unnoticed commonly accompanied by sneezing. In such cases, patients also complain of headaches in addition to sneezing[5]. Purulent inflammations develop after acute catarrhal inflammations or they are purulent from the onset if certain preconditions are met, such as mass infection, poor ventilation of paranasal cavities, weakened immunobiological strength of the body, weakened local reaction of the sinus mucosa, etc[6].

Acute rhinosinusitis is most often of viral origin and it occurs as part of upper respiratory tract infection. If it is of bacterial origin, the most common causes are Streptococcus, Pneumococcus and Haemophilus influenzae. Some inflammations may start as viral with the so-called bacterial superinfection, i.e. subsequent bacterial colonization developing in 0.5–2% of cases. Sinusitis caused by viruses last for seven to 10 days whereas bacterial sinusitis can last longer[7,8].

A special type is sinusitis caused by fungi. As a rule, these occur in people with diseases and conditions related to reduced immunity, such as diabetes, AIDS, tissue and organ transplantation, treatment with immuno-suppressive drugs and they can be life-threatening due to the rapid spread of the infection and/or mycotic sepsis[4,5].

Materijali i metode

Prospektivna klinička studija sprovedena je na Kinici za bolesti uva, grla i nosa Univerzitetskog kliničkog centra Niš od oktobra 2019. do januara 2020. godine, u koju su uključeni pacijenti sa akutnim bakterijskim rinosinuzitisom, kod kojih smo upoređivali efikasnost i bezbednost levofloxacina (500 mg jednom dnevno u trajanju od 5 dana ili 10 dana aplikovanja levofloxacina od 500 mg jednom dnevno) sa efikasnošću tretmana amoxicilin-klavulonata (500 mg – 125 mg tri puta dnevno tokom 10 dana). Uključeno je 62 pacijenta sa kliničkim i radiološkim dokumentovanim simptomima, od kojih su 20 bili lečeni levofloxacinom u trajanju 5 dana, 20 levofloxacinom u trajanju od 10 dana i 22 amoxicilinom i klavulonatom u trajanju od 10 dana.

Kriterijumi za uključenje u studiju bili su: starost od 18 godina, klinička dijagnoza akutnog bakterijskog rinosinusitisa (ABR) – prisustvo purulentne sekrecije iz nosa, facijalni bol i/ili pritisak prisutni više od 7 dana i manje od 28 dana. Svi pacijenti pregledani su prvog dana, od trećeg do petog dana, od osmog do petnaestog dana i na kraju studije, dvadeset osmog dana.

Merenje ishoda: 1. Efikasnost je merena prema kliničkom uspehu baziranom na pregledu pacijenta u momentu kontrole.

Izlečenje je definisano kao rezolucija znakova i simptoma ABR do nivoa koji je postojao pre pojave akutne bolesti i bez potrebe za novom terapijom antibioticima.

Neuspeh terapije definisan je kao prisustvo jednog simptoma ili znaka ili više simptoma ili znakova i/ili potrebom za dodatnom antimikrobnom terapijom ili promenom antimikrobne terapije.

2. Sigurnost je analizirana kod svih ispitanika koji su uzeli jednu dozu leka iz studije. Registrovani su svi prijavljeni neželjeni efekti.

Rezultati

Između oktobra 2019. i januara 2020. godine kod 62 pacijenta dijagnostikovan je akutni rinosinuzitis.

U ispitivanoj grupi bilo je 30 (48,39%) osoba muškog pola i 32 (51,61%) osobe ženskog pola ($p>0,05$) što znači da nije bilo statistički značajne razlike (Tabela 1).

Urađena analiza simptoma, koji su bili prisutni kod pacijenata tokom ispitivanja, pokazala je značajno češće pojavu kašalja (58 ispitanika; 93,55%), sekrecije iz nosa (53 ispitanika; 85,48%) i zapušenog nosa (50 ispitanika; 80,64%), a najmanje zastupljeni

Aim of the study

The aim of this study was to compare three therapeutic protocols in the treatment of acute bacterial rhinosinusitis.

Material and Methods

A prospective clinical study was conducted at the Ear, Nose and Throat Clinic of the Clinical Center Niš from October 2019 to January 2020. The study included patients with acute bacterial rhinosinusitis in whom we compared the efficiency and safety of levofloxacin (500 mg once a day for five days or 500 mg a day once a day for 10 days) with the efficiency of amoxicillin - clavulanate treatment (500 mg – 125 mg three times a day for 10 days). The study included 62 patients with clinically and radiologically documented symptoms who were treated with levofloxacin for five days (20 patients), levofloxacin for 10 days (20 patients), and amoxicillin and clavulanate for 10 days (22 patients).

The inclusion criteria were the following: age over 18 years, clinical diagnosis of ABR (acute bacterial rhinosinusitis), presence of purulent nasal secretions, facial pain and/or pressure for more than seven and less than 28 days. All patients were examined on day one, days three to five, days eight to 15 and at the end of the study on day 28.

Measurement of outcomes: 1. Efficiency was measured according to clinical success based on patient examination at the time of check-up.

Successful treatment was defined as the resolution of ABR signs and symptoms to the level before the acute disease onset and without the need for a new antibiotic therapy.

Failure of the treatment was defined as the presence of one or more symptoms or signs and/or the need for additional antimicrobial therapy or change in antimicrobial therapy.

2. Safety was analyzed in all subjects who took one dose of the medication listed in the study. All reported side effects have been documented.

Results

From October 2019 to January 2020, 62 patients were diagnosed with acute rhinosinusitis.

The examined group included 30 males (48.39%) and 32 (51.61%) females. No statistically significant difference was observed in this regard ($p>0.05$) (Table 1).

Tabela 1. Distribucija po polu
Table 1. Distribution according to gender

	Distribucija po polu / Distribution according to gender	
Muški / Male	30	48.39%
Ženski / Female	32	51.61%
Ukupno / Total	62	100%

Vrednosti su prikazane kao broj (%)
*Hi-kvadrat test. +Nije statistički značajan
Values in numbers (%)
*Chi-square test.+No statistical significance

Tabela 2. Ukupan broj pacijenata sa navedenim tegobama
Table 2. Total number of patients with the listed complaints

	Ukupan broj pacijenata sa navedenim tegobama / Total number of patients with the listed symptoms	
Opšta slabost / Generalized weakness	7	11.29%
Jaka glavobolja / Severe headache	24	38.71%
Jak bol u sinusima / Severe sinus pain	20	32.26%
Zapušen nos / Nasal congestion	50	80.64% *
Bol u uhu / Ear pain	13	20.97%
Iskašljavanje / Expectoration	21	33.87%
Visoka temperatura / High fever	9	14.51%
Vrtoglavica / Dizziness	15	24.19%
Sekrecija iz nosa / Nasal discharge	53	85.48% *
Bol u grlu / Sore throat	18	29.03%
Kašalj / Coughing	58	93.55% *

Vrednosti su prikazane kao broj (%)
*Hi-kvadrat test+Statistički značajan
Values in numbers (%)
*Chi-square test +Statistically significant

simptomi bili su opšta slabost (7 ispitanika; 11,29%) i visoka temperatura (9 ispitanika; 14,51%) ($p < 0,05$) (Tabela 2).

Dužina trajanja simptoma pre javljanja lekaru pokazala je da se 29 (46,77%) pacijenata javilo lekaru u periodu kraćem od 7 dana od pojave simptoma, a 20 (32,26%) pacijenata u periodu 7 dana nakon pojave simptoma, dok preostalih 13 (20,97%) pacijenata kao odgovor nisu dali ni jedno ni drugo ($p = 0,045$), što predstavlja statistički značajnu razliku (Tabela 3).

Od faktora rizika za nastanak oboljenja najčešće su prisutne pušačke navike, kod 41 (66,13%) pacijenta, devijacija septuma, kod 39 (62,90%) pacijenata, a najređe nosna polipoza, kod 6 (9,68%) pacijenata ($p < 0,05$), što je statistički značajno (Tabela 4).

The analysis of symptoms present in patientson examination showed a significantly more frequent occurrence of coughing - 58 patients (93.55%), nasal discharge - 53 patients (85.48%) and nasal congestion - 50 patients (80.64%) and the least common symptoms were generalized weakness - 7 patients (11.29%) and high fever - 9 patients (14.51%), ($p<0.05$) (Table 2).

Duration of symptoms before reporting to the doctor showed that 29 patients (46.77%) reported to the doctor in less than seven days after the onset of symptoms, 20 patients (32.26%) reported after seven days from the onset and the remaining 13 patients (20.97%) did not provide an answer. A p value of 0.045 points to a statistically significantdifference (Table 3) .

Pošto su pacijenti pokazivali slične simptome, nasumičnim odabirom pacijente smo podelili u tri grupe. Ispitanici iz prve grupe koristili su levofloxacin 5 dana (500 mg jednom dnevno), druge grupe levofloxacin 10 dana (500 mg jednom dnevno), a treće amoxicilin-klavulonat 10 dana (500 mg – 125 mg tri puta dnevno) ($p > 0,05$), što ne pokazuje statističku značajnost (Tabela 5).

Among the risk factors for the development of the disease, smoking habits are most often present in 41 patients (66.13%), deviated septum in 39 (62.90%) patients and least often present were nasal polyps in 6 (9.68%) patients. The findings have statistical significance ($p<0.05$) (Table 4).

Tabela 3. Dužina trajanja simptoma
Table 3. Duration of symptoms

	Dužina trajanja simptoma / Duration of symptoms				
			X	SD	CV
Kraće od 7 dana / Less than seven days	29	46.77%	5.27	0.69	0.13
Duže od 7 dana / More than seven days	20	32.26%	9.15	0.85	0.09
Drugo / For a long time	13	20.97%	14.46	1.45	0.10
Ukupno / Total	62	100%			

Vrednosti su prikazane kao broj (%)
*Hi-kvadrat test+Statistički značajan
Values in numbers (%)
*Chi-square test+Statistically significant

Tabela 4. Ukupan broj pacijenata sa pridruženim oboljenjima i faktorima rizika
Table 4. Total number of patients with associated diseases and risk factors

	Pridružena oboljenja i faktori rizika / Associated diseases and risk factors	
DM	12	19.35%
Nosna polipoza / Nasal polyps	6	9.68%
Devijacija septoma / Deviated septum	39	62.90% *
HOBP / COPD	32	51.61%
Pušacke navike / Smoking	41	66.13% *
Hronični alergijski rinitis / Chronic allergic rhinitis	15	24.19%
Alergija na penicilin / Penicillin allergy	14	22.58%

Vrednosti su prikazane kao broj (%)
*Hi-kvadrat test+Statistički značajan
Values in numbers (%)
*Chi-square test.+Statistically significant

Tabela 5. Antibiotici
Table 5. Antibiotics

	Broj pacijanata / Number of patients	
Levofloxacin u trajanju od 5 dana / Levofloxacin 5 days	20	32.26%
Levofloxacin u trajanju od 10 dana / Levofloxacin 10 days	20	32.26%
Amoksicilin-klavulonat u trajanju 10 dana / Amoxicillin-clavulanate 10 days	22	35.48%
Ukupno / Total	62	100%

Vrednosti su prikazane kao broj (%)
*Hi-kvadrat test+Statistički nije značajan
Values in numbers (%)
*Chi-square test+No statistical significance

Tabela 6. Klinička uspešnost
Table 6. Clinical success

	Levofloxacin u trajanju od 5 dana / levofloxacin 5 days	Levofloxacin u trajanju od 10 dana / levofloxacin 10 days	Amoksicilin-klavulonat u trajanju od 10 dana / amoxicillin-clavulanate 10 days
Na kraju lečenja / End of treatment	18/20 90%	19/20 95%	20/22 90.91%
Na kraju studije / End of study	15/20 75%	16/20 80%	17/22 77.27%

Vrednosti su prikazane kao broj/ukupan broj (%)
*Hi-kvadrat test+Nije statistički značajan
Values in numbers (%)
*Chi-square test+No statistical significance

Na kraju lečenja levofloxacinom u trajanju od 5 dana 18/20 (90%) pacijenata pokazalo je kliničku uspešnost, lečenja levofloxacinom u trajanju od 10 dana kliničku uspešnost pokazalo je 19/20 (95%) pacijenata, lečenja amoksicilin-klavulonatom u trajanju od 10 dana kliničku uspešnost pokazalo je 20/22 (90,91%) pacijenta. Na kraju studije, prilikom lečenja levofloxacinom u trajanju od 5 dana kliničku uspešnost pokazalo je 15/20 (75%) pacijenata, lečenja levofloxacinom u trajanju od 10 dana kliničku uspešnost pokazalo je 16/20 (80%) pacijenata, lečenja amoksicilin-klavulonatom u trajanju od 10 dana kliničku uspešnost pokazalo je 17/22 (77,2%) pacijenta ($p > 0,05$), što znači da nema statistički značajne razlike između grupa (Tabela 6).

Pojava neželjenih efekata kod pacijenata lečenih levofloxacinom tokom 5 dana bila je prisutna kod 6/20 (30%) pacijenta, kod pacijenata lečenih levofloxacinom tokom 10 dana bila je prisutna kod 8/20 (40%) pacijenata, a kod pacijenata lečenih amoxicilin-klavulonatom kod 11/22 (50%)

Since the patients had similar symptoms, we randomly divided the patients into three groups. The first group used levofloxacin for five days (500 mg once a day), the second group used levofloxacin for 10 days (500 mg once daily)and the third group was administered amoxicillin-clavulanate for 10 days (500 mg – 125 mg three times a day). ($p>0.05$) which shows no statistical significance (Table 5).

At the end of a 5-day levofloxacin treatment, clinical success was recorded in 18/20 (90%) patients. Clinical success was achieved in 19/20 (95%) patients treated with levofloxacin for 10 days and in 20/22 (90.915) patients treated with amoxicillin-clavulanate for 10 days. At the end of the study, clinical success was achieved in 15/20 (75%) patients treated with levofloxacin for five days, 16/20 (80%) patients treated with levofloxacin for 10 days, and 17/22 (77.2%) patients treated with amoxicillin-clavulanate for 10 days. The p-value was $p>0.05$ which means that there was no statistically significant difference between the groups (Table 6).

pacijenta (p < 0,05), što je statistički značajno. Prekid tretmana lečenih levofloxacinom u trajanju od 5 dana bio je sproveden kod jednog pacijenta od 20 (5%) pacijenta, levofloxacinom u trajanju od 10 dana kod jednog pacijenta od 20 (5%) pacijenata, a amoksicilin-klavulonatom kod 2/22 (9,09%) pacijenta (p < 0,05), što je statistički značajna razlika. Najčešće prisutni simptomi bili su dijareja, kod 3 pacijenta od 20 (15%) pacijenata i nauzeja, kod jednog pacijenta od 20 (5%) pacijenata lečenih levofloxacinom tokom 5 dana, dijareja kod 4 pacijenta od 20 (20%) pacijenata i nauzeja kod dva pacijenta od 20 (10%) pacijenta lečenih levofloxacinom tokom 10 dana, dijareja kod 7 pacijenata od 22 (31,82%) pacijenta i nauzeja kod 3/22 (13,63%) pacijenta lečenih amoxicilin-klavulonatom (p < 0,05), što je statistički značajno (Tabela 7).

Side effects in the group treated with levofloxacin for 5 days were recorded in 6/20 (30%) patients. The group treated with levofloxacin for 10 days had 8/20 (40%) patients with side effects and the group treated with amoxicillin-clavulanate had 11/22 (50%) patients with side effects, the p-value was p<0.05 which is statistically significant. With regard to discontinuation of treatment, the group treated with levofloxacin for five days had 1/20 (5%) patient; the group treated with levofloxacin for 10 days had 1/20 (5%) patient and the amoxicillin-clavulanate had 2/22 (9.09%) patients. For this criterion, p<0.05 which points to a statistically significant difference. The most common adverse effects were diarrhea in 3/20 (15%) patients and nausea in 1/20 (5%) patient treated with levofloxacin for five days; diarrhea in 4/20 (20%) patients and nausea in 2/20 (10%) patients treated with levofloxacin for 10 days; and diarrhea in 7/22 (31.82%) and nausea in 3/22 (13.63%) patients treated with amoxicillin-clavulanate. Here, p<0.05, which is statistically significant (Table 7).

Tabela 7. Analiza sigurnosti leka
Table 7. Drug safety analysis

Tretman / Treatment	Najmanje 1 neželjeni efekat vezan za tretman / Minimum one side effect related to treatment	Prekid tretmana / Discontinuation of treatment	Neželjeni efekti /Side effects	
			Dijareja / Diarrhea	Nauzeja / Nausea
Levofloxacin u trajanju od 5 dana / Levofloxacin 5 days	6/20 (30%)	1/20 (5%)	3/20 (15%)	1/20 (5%)
Levofloxacin u trajanju od 10 dana / Levofloxacin 10 days	8/20 (40%)	1/20 (5%)	4/20 (20%)	2/20 (10%)
Amoxicillin-clavulanate	11/22 (50%)	2/22 (9.09%)	7/22 (31.82%)	3/22 (13.63%)

Vrednosti su prikazane kao broj/ukupan broj (%)
*Hi-kvadrat test+Statistički značajan
Values in numbers/total numbers (%)
*Chi-square test+Statistically significant

Diskusija

Rinosinusitis (RS) spada među najčešća stanja u medicini, od kojeg oboli oko 15% odraslih godišnje. Prethodne studije pokazuju da je visoka stopa propisivanje antibiotika radi lečenja RS u preko 80% slučajeva akutnog RS i preko 50% slučajeva hroničnog RS[2,3]. Dobijeni rezultati pokazali su to da nema statistički značajne razlike od oboljevanja od RS u pogledu pola u ispitivanoj grupi (Tabela 1). U Americi, pokazana je veća učestalost kod žena, što se može tumačiti i efektima klime i podneblja.

Simptomi sinusitisa su bol iznad zahvaćenog sinusa u vidu probadanja, koji se pojačava pri saginjanju i kašlju, osećaj pritiska ili punoće u predelu sinusa, glavobolja, zapušenost nosa, bol u uhu, pojačana sekrecija iz nosa kako spreda, tako i slivanjem u grlo, koja može da varira od vodenaste pa do gnojne, slabost, malaksalost, povišena telesna temperatura, napetost i edem lokalno. Nekad se mogu javiti i krvarenje iz nosa i bol lociran u nekim specifičnim delovima glave, u zavisnosti od zahvaćenog sinusa – bol u zubima i prednjoj strani obraza, kod maksilarnog sinusa, u očima, slepoočnici i temenu, kod etmoidalnog i sfenoidalnog sinusa[9]. Dobijeni rezultati pokazali su to da su u ispitivanoj grupi najčešći simptomi bili kašalj, sekrecija iz nosa i zapušen nos (Tabela 2), što se slaže sa podacima iz literature[8,9,10,11]. U pogledu perioda javljanja lekaru, većina obolelih zatražila je lekarsku pomoć u periodu kraćem od 7 dana od pojave simptoma (Tabela 3).

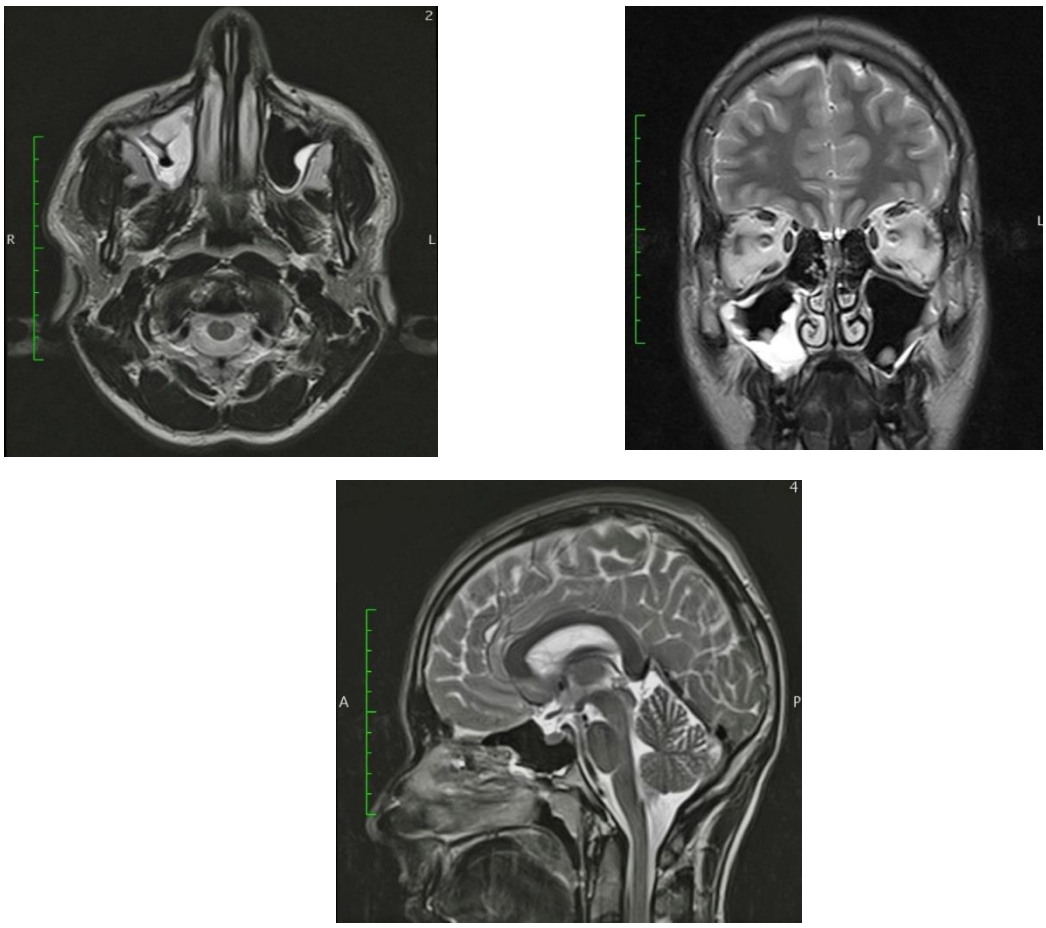
Uzročnici u sinus, u daleko najvećem broju slučajeva, dospevaju preko nosa, a samo retko nekim drugim putem, kao što je preko krvi ili direktnim unošenjem, npr. preko povrede[7,9,12,13]. Takođe, upala maksilarnog sinusa može poticati od zapaljenskog procesa na korenu zuba, ako koren štrči u sinusnu šupljinu ili je proces na korenu uznapredovao ili je zapušten. Neka stanja, kao što su anatomski deformiteti, alergija, zamor i prethodna infekcija sinusa mogu uticati na češću pojavu bakterijske superinfekcije, zbog narušavanja normalne fiziologije sinusa[12]. Sinusitis mogu uzrokovati i hemijski iritansi, kao što su duvanski dim, isparenja hlora i drugih hemijski agresivnih susptanci, koje srećemo u industriji ili domaćinstvu. Dobijeni rezultati pokazali su to da su u ispitivanoj grupi najčešća pridružena oboljenja i simptomi devijacija septuma, pušačke navike i HOBP, što je u saglasnosti sa podacima iz literature[4,6,10] (Tabela 4).

Discussion

Rhinosinusitis (RS) is one of themost common medical conditions affecting 15% of adults each year. Previous studies have shown a high rate of prescribing antibiotics to treat RS, namely, over 80% in cases of acute RS and over 50% in chronic RS cases[2,3]. The obtained results showed that there was no statistically significant difference in the incidence of RS with regard to gender in the study groups (Table 1). In USA, a higher incidence has been recorded among women, which can be explained by the effects of climate and region.

Sinusitis symptoms include a stabbing pain above the affected sinus, which increases upon bending and coughing, a feeling of pressure or fullness in the sinus area, headache, nasal congestion, ear pain, increased secretion from the nose both to the frontal area and in the throat with the secretion varying from watery to purulent. The symptoms also include weakness, fatigue, fever, tension and local edema. Depending on the affected sinus, bleeding from the nose and pain located in some specific parts of the head can sometimes occur - pain in the teeth and front of the cheeks with maxillary sinus; pain in the eyes, temples and the top of the head with ethmoidal and sphenoid sinuses[9]. The obtained results showed that the most common symptoms were coughing, nasal secretion and nasal congestion (Table 2), which is in line with literature data[8,9,10,11]. With regard to the period of reporting to the doctor, the majority of patients sought medical help within the period of time less than seven days from the onset of symptoms (Table 3).

In most cases, causative agents reach the sinus through the nose, rarely in some other way, such as through blood or by direct intake, e.g., through injury[7,9,12,13]. Also, inflammation of the maxillary sinus can occur from the inflammatory process at the root of the tooth if the root protrudes into the sinus cavity or if the process at the root is advanced or neglected. Some conditions, such as anatomical deformities, allergies, fatigue, previous sinus infection may lead to more frequent bacterial superinfections due to disruption of normal sinus physiology[12]. Sinusitis can also be caused by chemical irritants, such as tobacco smoke, chlorine fumes and fumes from other chemically aggressive industrial or household substances. The obtained results showed that the most common associated diseases and symptoms in the tested groups were septal deviation, smoking and COPD, which is in accordance with the literature data[4,6,10] (Table 4).



Slika 1,2,3. Triplanarni prikaz akutnog zapaljenja maksilarnog i sfenoidnog sinusa
Figure 1,2,3. Triplanar presentation of acute inflammation of the maxillary and sphenoid sinuses

Važno je zapamtiti da „abnormalni" radiološki nalazi, koji uključuju sinuse, ne potvrđuju nužno dijagnozu akutnog rinosinusitisa, jer 42% normalnih osoba može pokazati neki oblik abnormalnog zadebljanja sluzokože sinusa na CT-u[11]. Podjednako važno, snimanje ne može razlikovati virusni i bakterijski rinosinusitis, tako da se u smernicama za lečenje akutnog bakterijskog rinosinusitisa ističe to da nije potrebno pre davanja terapije raditi radiološku dijagnostiku, nego tek u slučaju neuspeha terapije i preteće komplikacije. Preporuka je da se radi kompjuterizovana tomografija paranazalnih sinusa.

Terapijske smernice uglavnom podržavaju 10 – 14 dana antibiotskog režima kod pacijenata sa akutnim bakterijskim sinusitisom[5,6,7,15,16]. Međutim, nivo dokaza za takvu preporuku prilično je slab. Takođe, duže lečenje antibioticima može imati nedostake u poređenju sa kraćim vremenom korišćenja antibiotika, koje može biti jednako uspešno, kao što su povećanje bakterijske rezistencije, veća toksičnost i veća cena lečenja.

It is important to remember that "abnormal" radiological findings which include the sinuses do not necessarily confirm the diagnosis of acute rhinitis because 42% of otherwise healthy people can show some form of abnormal thickening of the sinus mucosa on CT scan[11]. Of equal importance is the fact that imaging cannot distinguish between the viral and bacterial rhinosinusitis so the guidelines for the treatment of acute bacterial sinusitis emphasize that it is not necessary to do radiological diagnostics before administering treatment but only in case of treatment failure and threatening complications. The recommendation is to perform computed tomography of the paranasal sinuses.

Therapeutic guidelines generally support 10 – 14 days of antibiotic treatment in patients with acute bacterial sinusitis[5,6,7,15,16]. However, the amount of evidence for such a recommendation is rather small. In addition, longer antibiotic treatment may have disadvantages compared to shorter antibiotic administration, which can be just as successful.

Potvrda bakterijske etiologije ne radi se rutinski u kliničkoj praksi, pošto zahteva punkciju sinusa ili endoskopski pregled srednjeg nosnog hodnika. Kao posledica toga, izbor antibiotske terapije je empirijski, u većini slučajeva, među antibioticima potencijalno efektivnim prema najčešćim izazivačima infekcije gornjeg respiratornog trakta, a prema smernicama za lečenje akutnog bakterijskog rinosinuzitisa[5,6,7].

Smernice preporučuju da se odraslima sa blagom formom bolesti, koji nisu lečeni prethodno antibioticima, kao preporuka inicijalnog tretmana, ordinira: amoxicillin/clavulanate, amoxicillin (1,5 g/dnevno – 3,5 g/dnevno), cefpodoxime proxetil ili cefuroxime. Odraslima sa blagom formom bolesti, koji su u prethodnom periodu od 4 nedelje do 6 nedelja lečeni antibioticima i kod odraslih sa srednje teškom formom bolesti preporuka je da se ordinira: amoxicillin/clavulanate, amoxicillin (3 g – 3,5 g), cefpodoxime proxetil ili cefixime. Kod odraslih sa srednje teškom formom bolesti, koji su lečeni antibioticima u prethodnom periodu od 4 nedelje do 6 nedelja preporučeni antibiotici za lečenje su: amoxicillin/clavulanate, levofloxacin, moxifloxacin, ili doxycyclin[1-16]. U našem istraživanju koristili smo levofloxacin u trajanju od 5 dana (500 mg jednom dnevno), levofloxacin u trajanju od 10 dana (500 mg jednom dnevno) i amoksicilin-klavulonat u trajanju od 10 dana (500 mg – 125 mg tri puta dnevno), a dobijeni rezultati pokazali su to da ne postoje statistički značajne razlike u pogledu izbora antibiotika i dužine primene terapije. Dobijeni rezultati su u skladu sa podacima iz literature[1,3,4,15] (Tabela 6). Muhamad i sar. saopštavaju slične rezultate u studiji, koja upoređuje ove dve grupe antibiotika[15]. Burić i sar. ispituju i promenu bakterijske flore kod postojanja oroantralne fistule i bakterijskog sinuzitisa, što ukazuje na širi značaj ispitivanja upotrebe antibiotske terapije kod bolesnika sa sinuzitisom[12]. Tokom istraživanja zapaženo je to da je pojava neželjenih efekata nešto češća kod pacijenata koji su koristili amoksicilin-klavulonat i da je kod njih primećena veća neuspešnost terapije u odnosu na pacijente koji su koristili levofloxacin (Tabela 7).

The disadvantages include increased bacterial resistance, higher toxicity, higher treatment cost. The confirmation of bacterial etiology is not routinely done in clinical practice as it requires antral puncture or endoscopic examination of the middle nasal meatus. Consequently, the choice of antibiotic treatment is in most cases empirical and includes antibiotics potentially effective against the most common causes of upper respiratory tract infections and according to the guidelines for the treatment of acute bacterial rhinosinusitis[5,6,7].

The guidelines recommend:Adults with mild disease who have not received antibiotics: Amoxicillin/clavulanate, amoxicillin (1.5–3.5 g/day), cefpodoxime proxetil, or cefuroxime is recommended as initial therapy. Adults with mild disease who have had antibiotics in the previous 4–6 weeks and adults with moderate disease: Amoxicillin/clavulanate, amoxicillin (3–3.5 g), cefpodoxime proxetil, or cefixime is recommended. Adults with moderate disease who have received antibiotics in the previous 4–6 weeks: Amoxicillin/clavulanate, levofloxacin, moxifloxacin, or doxycycline is recommended. In our study, we used levofloxacin for five days (500 mg once a day), levofloxacin for 10 days (500 mg once a day) and amoxicillin-clavulanate for 10 days (500 mg–125 mg three times a day). The obtained results showed that there are no statistically significant differences regarding the choice of antibiotic and the length of treatment. Our results are in accordance with the literature data[1,3,4,15] (Table 6). Muhamad et al. reported similar results in a study comparing these two groups of antibiotics[15]. Buric et al. also examined the change in bacterial flora in the presence of oroantral fistula and bacterial sinusitis, which points toa wider importance of testing the use of antibiotic treatment in patients with sinusitis[12]. During the study, it was noticed that the occurrence of side effects is somewhat more common in patients who used amoxicillin-clavulanate and that failure of treatment was also more common in this group compared to patients who used levofloxacin (Table 7).

Zaključak

Nalazi ove studije sugerišu na to da kratki kurs tretmana antibioticima ima sličnu efikasnost u odnosu na duži kurs lečenja bolesnika sa akutnim, nekomplikovanim bakterijskim sinusitisom, onda kada je tretman indikovan. Ipak, treba podvući značaj lekarske procene, tako da antimikrobna terapija ne treba neprimereno da se ograniči kod pacijenta koji nije adekvatno reagovao na propisanu terapiju.

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Conclusion

The findings of this study suggest that a short antibiotic treatment has similar efficiency compared to a longer course in patients with acute uncomplicated bacterial sinusitis when this treatment is indicated. However, the importance of medical assessment should be underlined so that antimicrobial therapy should not be inadequately limited in patients who have not had a proper response to prescribed therapy.

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MEDICINSKI ZNAČAJ PROTOZOA USNE DUPLJE U STOMATOLOŠKOJ PRAKSI

ORAL CAVITY PROTOZOA RELEVANT IN THE PRACTICE OF DENTISTRY

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Sažetak

Uvod: *Usna duplja čoveka je mesto za kolonizaciju najraznovrsnijih mikroorganizama u organizmu ljudi. Brojni faktori mogu uticati na homeostazu oralnog mikrobioma. Parodontalne bolesti nastaju usled poremećene homeostaze oralnog mikrobioma i odbrane domaćina, kada dolazi do inflamatorne reakcije, koja zahvata tkivo parodoncijuma. Uticaj parazita na patofiziologiju parodoncijuma još uvek nije dovoljno proučen, pa bi sadašnja i naredna naučna istraživanja trebalo da daju brojne odgovore.*
Cilj rada: *U svetlu sadašnjih saznanja vezanih za patogenezu, dijagnostiku i epidemiologiju infekcija oralne duplje uzrokovanih vrstama protozoa Entamoeba gingivalis i Trichomonas, cilj rada je da se kroz pregled literature ukaže na značaj protozoa u stomatološkoj praksi, kao i na moguće manifestacije parazitskih infekcija od značaja za javno zdravlje, koje se mogu ispoljiti i u usnoj duplji.*
Zaključak: *Stomatolozi imaju bitnu ulogu u dijagnozi oralnih oboljenja uzrokovanih protozoama usne duplje, kao i protozoa bitnih za javno zdravlje, koje daju sistemske infekcije, a patološke promene mogu se ispoljiti i u usnoj duplji. Njihovo dijagnostikovanje je svakako veliki izazov i zahteva multidisciplinarni pristup, u cilju što brže dijagnoze i adekvatnog lečenja.*

Ključne reči: *usna duplja, protozoe, parodontalne bolesti, lajšanijaza, toksoplazmoza*

Abstract

Introduction: *Oral cavity is the colonization site of most diverse microorganisms. The homeostasis of oral microbioma is affected by numerous factors. Periodontal diseases occur as a consequence of disturbed oral microbioma homeostasis, when an inflammatory reaction occurs in the periodontal tissue. The impact of parasites on periodontal pathophysiology has not been sufficiently studied, and present and future research should hopefully answer quite a few questions concerning the issue.*
Aim of the paper: *In the light of the present knowledge of the pathogenesis, diagnosis and epidemiology of oral cavity infections caused by Entamoeba gingivalis and Trichomonas tenax, the aim of the paper was review of literature which could to point to the importance of protozoa in the practice of dentistry and to possible oral cavity manifestations of parasitic infections relevant for public health.*
Conclusion: *Dentists have an essential role in the diagnosis of oral diseases caused by oral cavity protozoa, and protozoa relevant for public health that produce systemic infections, the pathological changes of which may manifest in the oral cavity. Their identification represents a challenge and requires multidisciplinary approach for a timely diagnosis and adequate management.*

Key words: *oral cavity, protozoa, periodontal diseases, leishmaniasis, toxoplasmosis*

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Uvod

Usna duplja čoveka je mesto za kolonizaciju najraznovrsnijih mikroorganizama u organizmu ljudi. Ova kolonizacija može uključivati različite endogene i egzogene vrste, koje formiraju oralni biofilm na površinama sluzokože usne duplje i zuba. Vrste su strukturno i funkcionalno organizovane u polimikrobne zajednice sa složenim međusobnim odnosima između određene oralne mikrobiote i organizma domaćina. Mnogi biotički i abiotički faktori mogu promeniti labilnu homeostazu oralnog mikrobioma[1,2,3]. Termin mikrobiom koristi se za označavanje ekološke zajednice komensalnih, simbiotskih i patogenih mikroorganizama. Oralni mikrobiom / oralna mikrobiota / oralna mikroflora predstavljaju mikroorganizme, koji se nalaze u ljudskoj usnoj duplji, koji čine bakterije, gljive, eukariote i virusi[4,5].

Parodontalne bolesti (gingivitis i parodontopatija) su rezultat poremećaja homeostaze oralnog mikrobioma i domaćina koje karakteriše inflamatorna reakcija koja zahvata tkivo parodoncijuma[6]. Nova klasifikacija parodontopatija obuhvata tri forme: (1) parodontitis, (2) nekrotizirajući parodontitis, (3) parodontitis kao direktna manifestacija sistemskih bolesti. Na osnovu opisa (lokalizovanog ili generalizovanog), težine i složenosti lečenja utvrđena su tri stadijuma: početni parodontitis (I stadijum), umereni parodontitis (II stadijum), teški parodontitis sa potencijalom za dodatni gubitak zuba (III stadijum) i uznapredovali parodontitis sa ekstenzivnim gubitkom zuba i potencijalom gubitka denticije (IV stadijum). Prema ovoj klasifikaciji, parodontitis može imati tri nivoa progresije (A - spora, B - umerena i C - brza) [7]. Višedimenzionalni sistem faza i stepena je osmišljen kako bi se opisale različite manifestacije parodontitisa u pojedinačnim slučajevima. Faze opisuju težinu i obim bolesti, stepeni opisuju verovatnu stopu progresije[7]. Kliničke karakteristike parodontalnih bolesti su: recesija desni, destrukcija alveolarne kosti, gubitak parodontalnih ligamenata povezanih sa pojavom parodontalnih džepova i naslagama zubnog kamenca[8]. Parodontalne bolesti promovišu uspostavljanje mikrookruženja koje omogućava rast anaerobnih mikroorganizama[9], migraciju mikroorganizama u tkiva, narušava imunski odgovor, izazivajući resorpciju parodoncijuma[10,11].

Introduction

Oral cavity is the colonization site of most diverse microbiomes in the human organism. Various endogenous and exogenous species may be involved, forming an oral biofilm on the mucosal surfaces of the oral cavity and teeth. The species are structurally and functionally organized in polymicrobial communities, with complex relationships existing between oral microbiota and the organism of the host. Many biotic and abiotic factors are capable of changing the unstable balance of oral microbiome[1,2,3]. The term microbiome is used to denote an ecological community of commensal, symbiotic and pathogenic microorganisms. Oral microbiome/oral microbiota/oral microflora consists of microorganisms that reside in the human oral cavity and comprises bacteria, fungi, eukaryotes and viruses[4,5].

Periodontal diseases (gingivitis and periodontitis) represent the result of disturbed host oral microbiome homeostasis, characterized by an inflammatory reaction involving the periodontal tissue[6]. The new classification of periodontitis includes the three following forms: (1) periodontitis, (2) necrotizing periodontitis, (3) periodontitis as a direct manifestation of systemic diseases. Based on the extent of the disease (localized or generalized), severity, and complexity of management,the three stadiumsare defined as follows: early periodontitis (I stadium); moderate periodontitis (II stadium); severe periodontitis, with the potential for added loss of teeth (III stadium); and advanced periodontitis, with extensive loss of teeth and potential loss of dentition (IV stadium). According to this classification, periodontitis is characterized by three levels of progression (A - slow, B - moderate and C - rapid)[7]. A multidimensional system of stages and grades has been devised to further describe the different manifestations of periodontitis in individual cases. Stages describe the severity and the extent of the disease, grades describe the likely rate of progression[7]. Clinical characteristics of periodontal diseases involve gingival recession, destruction of the alveolar bone, and loss of periodontal ligaments associated with the development of periodontal pockets and with dental plaque depositions[8]. Periodontal diseases favor the creation of an anaerobic microenvironment, which further enables the growth of anaerobic microorganisms[9], migration of microorganisms into tissues, and disrupts the immune response causing periodontal resorption[10,11].

Utvrđeni su i neki faktori rizika domaćina za nastanak parodontalnih bolesti, kao što su pušenje i *Diabetes mellitus*[12-14], ali i druge bolesti i stanja (dati u pregledu literature)[15-17].

Dok je patološka uloga nekih specifičnih bakterijskih sojeva tokom parodontalnih bolesti dobro dokumentovana, uticaj parazita na patofiziologiju parodoncijuma još uvek nema čvrste dokaze[18].

Parazit je patogeni organizam koji živi na račun domaćina i usled patogenog dejstva dovodi do razvoja bolesti kod domaćina. Patogenost je sposobnost parazita da prodre u organizam domaćina, održi se, razmnožava, oštećuje tkiva i remeti funkcije organizma i, u manjoj ili većoj meri aktivira imunski sistem domaćina. Proučavanjem medicinski značajnih protozoa, helminata i artropoda bavi se zooparazitologija (pripadnici carstva protisti i carstva animalia)[19]. Paraziti imaju složene životne cikluse, prolaze kroz nekoliko faza razvoja u životnom ciklusu i pri tom dolazi do morfoloških, strukturnih, biohemijskih i antigenskih promena samog parazita, što dovodi i do različitih kliničkih manifestacija i posledica po samog domaćina. U toku životnog ciklusa paraziti mogu imati i više domaćina, a mnoge parazitske infekcije prenose se sa životinja na ljude (zoonoze)[19]. Humane parazitske infekcije su brojne i mogu biti bez ikakvih kliničkih manifestacija, mogu biti blagog toka, čak bezazlene, ali isto tako mogu da dovedu i do fatalnog ishoda. Iako su najčešće prisutne u siromašnim sredinama, od parazitoza nisu pošteđeni ni ljudi u ekonomski razvijenim zemljama[19].

Parazitološka dijagnostika podrazumeva korišćenje konvencionalnih dijagnostičkih mikroskopskih metoda (nativni i trajno obojeni preparati), koje se zasnivaju na analizi morfoloških i morfometrijskih karakteristika parazita. Na osnovu ovih parametara teško je izvršiti preciznu dijagnostiku do nivoa vrste. Osetljivost trofozoita u spoljašnjoj sredini i neophodnost brzog dostavljanja uzorka, priprema preparata i brza identifikacija parazita često nisu u rutinskom radu ispoštovane pa je broj pozitivnih nalaza na protozoe iz usne duplje mali. Metode kultivacije ne koriste se u rutinskom radu i rezervisane su za referentne i naučnoistraživačke laboratorije. Novi alati molekularne biologije i genomske analize omogućile su detekciju i identifikaciju već poznatih, ali i „novih“ mikrobiota u mnogo većem broju, ali još uvek nisu deo rutinskog rada, već se koriste u naučno istrživačkom radu[19].

Host-related risk factors for periodontal diseases, such as *diabetes mellitus* and smoking[12–14] have also been established, along with other diseases and conditions included in the reference numbers[15–17].

While the pathological role of some specific bacterial species in periodontal diseases has been well documented, the impact of parasites on the pathophysiology of the periodontium has not been firmly established[18]. A parasite is a pathogenic organism living at the expense of its host and often produces a disease in the host organism. Pathogenicity is the parasite's ability to infest the host, and to survive, replicate, damage the tissues and disturb the functions in the host organism, activating to a lesser or greater extent the immune system of the host. Zooparasitology studies medically relevant protozoa, helminths and arthropods (members of the kingdom Protista and kingdom Animalia)[19]. Parasites have complex life cycles, with several different developmental stages;during the development,they undergomorphological, structural, biochemical and antigenic changes, which produces different clinical manifestations and consequences in their hosts. During their life cycle, parasites can infest different hosts, and many parasitic infections are transmitted from animals to human beings (zoonoses)[19]. Human parasitic infections are numerous. They may progress without any clinical manifestations, or they are associated with a mild clinical course, but they may produce a fatal outcome as well. Although they are present mostly in poor social environments, the people living in well developed countries are not spared either[19].

Parasitology diagnosis involves using conventional diagnostic microscopy methods (native and permanently stained preparations) based on the morphological and morphometric parasite characteristics. Based on these parameters it is difficult to precisely diagnose the parasite to the level of species. Trophozoite sensitivity in open air is often overlooked, and the necessity for rapid sample delivery, sample preparation and immediate parasite identification are not always well observed and performed in routine work; the number of positive findings of protozoa in the oral cavity is thus rather low. The methods of cultivation are not used in routine work - these are reserved for reference and research laboratories. The new tools of molecular biology and genomic analysis have made possible the detection and identification of even greater numbers of already known and „new“ microbiota, but are still not used routinely; they are used mostly in research work[19].

Cilj rada je da se kroz pregled literature ukaže na medicinski značaj protozoa, kao uzročnika infekcije oralne duplje u svetlu sadašnjih saznanja, vezanih za patogenezu, dijagnostiku i epidemiologiju vrsta *Entamoeba gingivalis* i *Trichomonas tenax*, kao i na moguće simptome i znake parazitskih infekcija uzrokovanih protozoama *Leishmania sp. i Toxoplasma gondii*, koje se mogu ispoljiti i u usnoj duplji i predstavljati veliku nepoznanicu i dijagnostičku dilemu u ordinaciji lekara stomatologa.

Entamoeba gingivalis

Entamoeba gingivalis (Gros, 1849; Brumpt, 1913.) je protozoa, komensal usne duplje ljudi, koja postoji samo u vegetativnoj formi (trofozoit – aktivni stadijum sposoban za metaboličke procese, deobu i kretanje). Trofozoiti *Entamoeba gingivalis (E. gingivalis)* ne preživljavaju izvan tela domaćina. Ova vrsta taksonomski pripada razredu Lobosea, familiji Entamoebidae, rodu Entamoeba gde pripada i patogena vrsta *E. haestolyticae* uzročnik amebijaze[19,20].

Trofozoit *E. gingivalis* je morfološki sličan trofozoitu *E. histolytica*, patogenoj protozoi digestivnog trakta. Neophodno je praviti razliku između njih, budući da se obe vrste mogu naći u uzorcima sputuma (*E. histolytica* ako je prisutna u plućnim apscesima u slučajevima invazivne, sistemske amebijaze). Veličina trofozoita kreće se od 5 μm do 30 μm, mada je uobičajena veličina od 10 μm do 20 μm. Trofozoit se diferencira na spoljašnju, providnu ektoplazmu i unutrašnju zrnastu endoplazmu. U periodu mirovanja, ektoplazma je jedva vidljiva, ali tokom perioda kretanja izgleda kao debeo sloj, koji čini oko polovine zapremine aktivno pokretne amebe[19]. Endoplazma je zrnasta, sadrži vakuole i obično je prepuna plutajućih čestica hrane. Vakuole sadrže zaobljena, tamno obojena tela, poreklom uglavnom iz jedara degenerisanih epitelnih ćelija, limfocita i povremeno leukocita, bakterija i bez prisustva eritrocita. *E. gingivalis* je „čistač“ dezintegrisanih ćelija i bakterije nisu veliki izvor ishrane za njih. U endoplazmi se nalazi jedno malo, sferično jedro (nucleus), gotovo neupadljivo. Unutar jedra je prisutan centralni ili ekscentrični kariozom iz kojeg se fibrile zrakasto protežu do perifernog prstena. Umereno debela nuklearna membrana sadrži nepravilno raspoređen hromatin. Parazit se kreće formiranjem ektoplazmatskih pseudopodija i reprodukuje se binarnom fisijom[19].

The aim of the paper was to point out the medical significance of protozoa as the causes of oral cavity infections in the light of current knowledge of pathogenesis, diagnosis and epidemiology of the species *Entamoeba gingivalis* and *Trichomonas tenax*, as well as the possible symptoms and signs of parasitic infections caused by the protozoa *Leishmania sp.* and *Toxoplasma gondii* that may manifest in the oral cavity, presenting practising dentists with considerable diagnostic dilemmas.

Entamoeba gingivalis

Entamoeba gingivalis (Gros, 1849; Brumpt 1913) is a protozoan and a commensal in human oral cavity, existing only in its vegetative form (trophozoite is an active parasite stage, with metabolic processes, division and motility). *E. gingivalis* trophozoites cannot survive outside the host organism. Taxonomically, this species belongs to the class Lobosea, family Entamoebidae, genus Entamoeba, where also belongs the pathogenic species *E. haestolyticae*, the cause of amebiasis[19,20].

E. gingivalis trophozoite is morphologically similar to *E. haestolytica* trophozoite, a pathogenic protozoan of the digestive tract. It is necessary to differentiate between the two, since both species can be found in sputum specimens (*E. haestolytica* is encountered in the sputum if it is present in a pulmonary abscesses in the cases of invasive, systemic amebiasis). The size of trophozoites ranges from 5 μm to 30 μm, although it usually measures 10–20 μm. A trophozoite can be differentiated into outer, transparent cytoplasm, and inner, granular endoplasm. In the period of dormancy, the ectoplasm is barely visible, but in the period of motility it appears as a thick layer making up around half of the volume of an actively moving ameba[19]. The endoplasm is granular, contains vacuoles and is usually filled with floating food particles. The vacuoles contain round, dark stained bodies, originating mostly from the nuclei of degenerated epithelial cells, lymphocytes and at times leukocytes, bacteria, without the presence of erythrocytes. *E. gingivalis* is the „cleaner“ of disintegrated cells and bacteria do not constitute a large food source for them. In the endoplasm, there is a small, spheric, almost completely inconspicuous nucleus. Within the nucleus, there is a central or eccentric karyosome, from which fibrils radiate towards the peripheral ring. Moderately thick nuclear membrane contains irregularly distributed chromatin. The parasite moves by forming ectoplasmic pseudopodia and replicates by binary fission[19].

E. gingivalis može biti faktor rizika povezan sa oralnim oboljenjima, ali se još uvek ne zna njena uloga u patogenezi ovih poremećaja[21]. Loša oralna higijena, gingivitis, parodontopatija i koegzistirajuće sistemske bolesti mogu dovesti do porasta populacije ove protozoe u usnoj duplji[12-17]. Najčešća lokacija su parodontalni džepovi (anaerobni uslovi pogoduju kolonizaciji), potom sluzokoža gingive, sluzokoža palatinskih krajnika i mekog nepca[22]. Dugotrajna ekstenzivna oralna upala može povećati rizik od kardio-vaskularnih bolesti[23,24], reumatoidnog artritisa[25] i oralnog karcinoma[26].

Ukupna prevalencija *E. gingivalis* procenjena je na 37% (95% CI 29–46%), a najveća prevalencija *E. gingivalis* utvrđena u Jordanu (87%) (95% CI 81–92%), dok je najniža u Portugaliji sa 3% (95% CI 0–10%)[17]. Istraživanje Eke i sar. je pružili su dokaze o visokoj prevalenciji parodontopatije kod odrasle populacije starije od 30 godina u SAD (42,2%, a 7,8% sa težim oblicima parodontopatije). Rezultati istraživanja su pokazali da je povećana prevalencija umerenog tipa parodontopatije zavisna od godina života (stariji muškarci), etičke i manjinske pripadnosti, ekonomskog statusa (siromašnija populacija) i oralne higijene[27]. Slična situacija je i zemljama zapadne Evrope[28]. U cilju smanjenja prevalencije parodontopatije među populacijom starosti 45-74 godine u USA je i zakonom obavezujući skrining oralnog zdravlja kod starijih osoba. U sklopu inicijative Zdravi ljudi 2020. oralno zdravlje je jedan od indikatora za praćenje zdravlja nacije[29].

Primenom tehnika molekularne biologije identifikovani su različiti subtipovi u usnoj duplji. Kod osoba sa zdravim parodoncijumom *E. gingivalis* subtip 1 (ST1) se javlja u 48,6%, a *E. gingivalis* ST2 - varijanta kamaktli (89% identična *E. gingivalis* ST1) u 29,5%. Prisustvo *E. gingivalis* ST1 prijavljeno je u 57,8% kod osoba sa parodontalnom bolešću, dok je *E. gingivalis* ST2 – kamaktli varijanta prisutna je u 50,0%[30]. Rezultati Garcia i sar. pokazuju ga je ST1 *E. gingivalis* utvrđen kod 47,5% pacijenata na ortodontskom lečenju, dok je 73,8% imalo *E. gingivalis* ST2 – varijanta kamaktli što ukazuje na njihove genetske razlike i razlike u patogenosti[31].

Takođe, nedavno objavljeni rezultati pokazuju da *E. gingivalis* napada upaljenu i oštećenu oralnu sluzokožu, inhibira proli-feraciju ćelija, bez mogućnosti regeneracije oštećenog tkiva. Aktivacijom interleukina 8 dolazi do povećane migracije neutrofila, monocita i T limfocita, oslobađanje histamina iz bazofila, što još više pojačava upalni process[32].

E. gingivalis can be a risk factor associated with oral diseases, but its exact role in the pathogenesis of these disorders is still unknown[21]. Poor oral hygiene, gingivitis, periodontitis and coexisting systemic diseases may induce the growth of this protozoan's population in the oral cavity[12–17]. The most common localization are periodontal pockets (this anaerobic environment favors colonization), then gingival mucosa, mucosa of the palatine tonsils and soft palate[22]. A long-lasting, extensive oral inflammation may increase the risk for cardiovascular diseases[23,24], rheumatoid arthritis[25], and oral cavity carcinoma[26].

The overall prevalence of *E. gingivalis* has been estimated at 37% (95% CI 29–46%), with the highest prevalence rate reported in Jordan (87%) (95% CI 81–92%) and the lowest in Portugal (3%) (95% CI 0–10%)[21]. The study by Eke et al. presented evidence for a high prevalence rate of periodontitis in adults aged above 30 years in the USA (42.2%, and 7.8% with more severe forms of periodontitis). The results of the study suggested that the increased prevalence of moderate-type periodontopathy was dependent on the age (older males), ethnicity and minority status, socioeconomic status (poor population groups) and oral hygiene[27]. The situation is similar in Western European countries[28]. Oral health screening has been even regulated by law in the USA for older population groups (from 45–74 years of age), in an attempt at reducing the prevalence of periodontitis in these individuals. In the Healthy People 2020 initiative, oral health is one of the indicants in overall national health surveillance[29].

Utilizing the techniques of molecular biology, different subtypes have been identified in the oral cavity. In individuals with a healthy periodontium, *E. gingivalis* subtype 1 (ST1) occurs in 48.6%, and *E. gingivalis* ST2 - Kamaktli variant (89% identical to E. gingivalis ST1) in 29.5%. *E. gingivalis* ST1 presence was reported in 57.8% of individuals with periodontal disease, while *E. gingivalis* ST2 -Kamaktli variant, was present in 50.0%.30 The results by Garcia et al. showed that *E. gingivalis* ST1 was established in 47.5% of patients on orthodontic treatment, while 73.8% had *E. gingivalis* ST2 - Kamaktli variant, which indicated their genetic and differences in pathogenicity[31].

Further, some recently published data indicate that *E. gingivalis* attacks inflamed and damaged oral mucosa and inhibits cell proliferation, without any possibility for the damaged tissue to regenerate.

Oštećeno tkivo pogoduje daljem razvoju protozoa u usnoj duplji. Parodontopatija dovodi do ireverzibilnog oštećenja epitela i gubitka koštanog tkiva alveolarnog nastavka, što rezultira gubitkom zuba ili totalnom bezubošću. U slučaju komplikacija parodontopatije (parodontalni apsces, nekroza tkiva parodonta) javljaju se intezivni bolovi i neprijatan zadah. Kliničkim pregledom uočava se krvarenje, otok gingive i povećana pokretljivost zuba[33,34].

Studija Bao[32] i autora pokazala je virulentni potencijal *E. gingivalis*. Navedeni autori smatraju da se ovaj kolonizator oralne sluzokože ne može smatrati oportunističkim mikroorganizmom. Umesto toga, *E. gingivalis* treba posmatrati kao moćnog mikrobnog pokretača destruktivnih oblika parodontopatije čija je uloga uglavnom bila potcenjena. Zato bi stomatolozi trebalo da se postaraju da parodontalni džepovi i tkivo budu očišćeni od ove protozoe[32].

E. gingivalis se prenosi direktnim, odnosno, oralnim putem (ljubljenjem, korišćenjem zajedničkog pribora za održavanje oralne higijene i pribora za jelo, ali i putem kontaminiralne vode i hrane (indirektnim putem). Prevencija uključuje izbegavanje direktnih i indirektnih puteva prenošenja: korišćenje sopstvenog pribora za ličnu higijenu i pribora za jelo predhodno dobro opranog, kao i izbegavanje ljubljenja ako postoji rizik da osoba može biti nosilac *E. gingivalis*[22].

Trichomonas tenax

Trichomonas tenax (T. tenax) pripada grupi kosmopolitskih, anaerobnih Protista – flagelata koji izazivaju oralnu trihomonijazu. *T. tenax*, kao i njegova srodna vrsta, *Trichomonas vaginalis* (uzročnik genitalne trihomonijaze), svrstan je u kolo Parabasalia, razred Zoomastigophora, porodicu Trichomonadidae, rod Trichomonas[35]. Javlja se u obliku trofozoita ovalnog ili okruglog oblika i nema formu ciste. Približne je dužine od oko 15μm, ima 4 slobodne flagele na prednjem širem kraju koje polaze iz blefaroplasta. Peta flagela je povezana sa površinom ćelije formirajući talasastu (undulentnu) membranu. Paralelno sa ovom membranom nalazi se hromatofilna nit *(costa)* i aksostil koji daje čvrstinu parazitu. Ima jedno jedro sa endozomom koje je raspoređeno u prednjoj zoni, blizu tačke umetanja flagela. Trofozoit je vegetativni oblik koji se hrani putem fagocitoze i pinocitoze od ostataka hrane i bakterijama iz usne duplje; razmnožava se i predstavlja infektivnu formu parazita (nema formu ciste). Reprodukcija je uzdužnom binarnom podelom, bez polne reprodukcije[35].

Increased neutrophil, monocyte and T lymphocyte migration and histamine release from basophils occur via interleukin-8 activation, which further intensifies the process of inflammation[32]. The presence of damaged tissue favors continued development of protozoa in the oral cavity. Periodontitis induces irreversible damage to the epithelium and bone tissue loss in the alveolar processus, which results in tooth loss or total edentulousness. In case of periodontal disease complications (periodontal abscess, periodontal tissue necrosis), strong pains and halitosis could occur as well. Clinical examination typically reveals bleeding, swollen gums and increased teeth movement[33,34].

The study by Boa et al. demonstrated the virulent potential of *E. gingivalis*. These authors believed that this oral mucosa colonizer could not be considered an opportunistic microorganism. Instead, *E. gingivalis* should be thought of as a potent microbial inducer of destructive periodontitis forms, the role of which was mostly underrated. Practising dentists should therefore take care that inflamed periodontal pockets and tissue should be made and stay clean of this protozoan[32].

E. gingivalisis transmitted by direct, i.e. oral route (by kissing, using the same toothbrush, eating tools and kitchenware), but also by contaminated water and food (indirect route). The prevention involves avoidance of direct and indirect transmission routes: using one's own personal hygiene tools and eating tools, well washed before use, and avoidance of kissing if there is a risk of *E. gingivalis* carrier status[22].

Trichomonas tenax

Trichomonastenax(T. tenax) belongs to the group of cosmopolitan, anaerobic flagellate protists which cause oral trichomoniasis. *T. tenax*, as well as its kin species *Trichomonas vaginalis* (the cause of genital trichomoniasis) is classified in the phylum Parabasalia, classis Zoomastigophora, family Trichomonadida, and genus Trichomonas[35]. It occurs in the trophozoite form of oval or round shape and does not have a cyst form. It measures about 15 μm in length. It has four free flagella on its anterior, wider end, originating in the blepharoplast. The fifth flagellum is connected to the cell surface, forming a wavy, undulant membrane. In parallel to this membrane, there is a chromatophilic thread (costa) and axostil, giving firmness to the parasite. There is one nucleus, with an endosome, situated in the anterior zone, close to the point of flagella insertion.

Prvobitno je identifikovan kao bezopasni komensal koji živi u ljudskoj usnoj duplji i distribuira se između zuba, desni, jezika i pljuvačke ljudi sa lošom oralnom higijenom[36,37], a zatim kao parazit nađen u parodontalnim džepovima[38].

Konvencionalna detekcija i identifikacija *T. tenax* se najčešće vrši metodom svetlosne mikroskopije i kultavacije[39,40], pa zavisno od korišćene metode (najčešće mikroskopija) i geografskog područja ispitivanja, prevalencija *T. tenax* je u rasponu od 0 do 94,1%[18]. Sem u usnoj duplji, *T. tenax* nađen je u pljuvačnim žlezdama, limfnim nodusima i u respiratornom traktu[41-45]. Trihomonada je otkrivena i u usnoj duplji pacijenata sa oslabljenim imunitetom usled urođenih sistemskih bolesti, kao i na hroničnoj imunosupresivnoj terapiji, što ne isključuje njena oportunistička svojstva[1,46]. Primenom molekularnih metoda dijagnostike, utvrđeno je da je *T. tenax* značajno zastupljeniji kod pacijenata sa Daunovim sindromom koji imaju parodontalne lezije, u poređenju sa kontrolnom grupom pacijenata, sa neznatnom razlikom u indeksu plaka između dve grupe[47].

Na patogeni potencijal *T. tenax* ukazala su istraživanja koja su utvrdila proteolitička, a posebno kolagenolitička svojstva ove flagelate kod ljudi sa patološkim promenama u usnoj duplji[48]. Rezultati studija objavljenih poslednjih šezdeset godina o etiopatogenezi T. tenax još uvek nisu dovoljni da potvrde ulogu ove flagelate u nastanku bolesti, iako je utvrđeno: 1) da se *T. tenax* češće otkriva u oralnom biofilmu sa mesta sa parodonto-patijom nego na zdravim mestima; 2) da je sposoban da proizvede različite enzime koji bi mogli da učestvuju u parodontalnoj razgradnji i da ima sposobnost da se prilepi na epitelne ćelije (njegov lizirani oblik bi mogao da izazove sintezu IL-8); 3) da detaljnije analize prisustva flagelate u usnoj duplji nisu sprovedene nakon nehirurškog lečenja parodontopatije[49].

Pacijenti sa dijagnozom infekcije koju izaziva *T. tenax* najčešće imaju suva usta, sindrom pečenja u ustima, spontani bol i bol tokom gutanja, a intraoralnim pregledom mogu se uočiti parodontalni džepovi, glositis i hronična parodontopatija[49].

Nedavni rezultati sistematskog pregleda literature i meta analize pokazali su globalnu objedinjenu prevalenciju od 17% (95% CI 14–22%) infekcije uzrokovane *T. tenax*. Najveća prevalencija je procenjena na 56% (42–69%) u Čileu, dok je najniža prevalencija u Keniji sa 3% (1–6%). Analiza je pokazala da je infekcija najčešća u starosnoj grupi od 46 do 55 godina sa 15% (0-100%).

The trophozoite is a vegetative form feeding by phagocytosis and pinocytosis on food debris and bacteria present in the oral cavity; it replicates and represents the infective parasite form (without any cyst form). The reproduction occurs by longitudinal binary division, without any sex reproduction[35].

The parasite has been originally identified as a harmless commensal living in the human oral cavity distributed between the teeth, on the gums, tongue and in the saliva of individuals with poor oral hygiene[36,37], and then has been found as a parasite in periodontal pockets[38].

Conventional detection and identification of *T. tenax* is most commonly performed using the method of light microscopy and cultivation[39,40]. Depending on the methodology used (usually microscopy) and geographic area, the prevalence of *T. tenax* ranges from 0% to 94.1%[18]. In addition to the oral cavity, *T. tenax* has been found in salivary glands, lymph nodes and respiratory tract[41-45]. The trichomonad has also been detected in the oral cavity of patients with a weak immunity due to congenital systemic diseases, as well as in those on chronic immunosuppressive therapy, which does not exclude its opportunistic characteristics[1,46]. Using the molecular diagnostic methods, it has been established that compared to controls, *T. tenax* is significantly more prevalent in patients with Down syndrome who have periodontal lesions, with a negligent difference in the plaque index between the groups[47].

The pathogenic potential of *T. tenax* has been stressed in the studies which have established proteolytic, and especially collagenolytic potentials of this flagellate in people with oral cavity pathologies[48]. The results of the studies of etiopathogenesis of *T. tenax* published in the last sixty years are still insufficient to confirm the role of this flagellate in the development of disease, although the following has been established: 1) *T. tenaxis* more frequently identified in the oral biofilm from the sites affected by periodontitis than from healthy localizations; 2) *T. tenax* has the ability to attach to epithelial cells (its lysed form could induce IL-8 synthesis); 3) more detailed analyses of the flagellate presence in the oral cavity have not been done after a non-surgical treatment of periodontitis[49].

Patients with the diagnosis of an infection caused by *T. tenax* usually have dry mouth, burning mouth syndrome, experience spontaneous pain and pain when swallowing, and an intraoral inspection may reveal the presence of periodontal pockets, glossitis and chronic periodontitis[50].

Ukupna prevalencija zavisno od primenjenih dijagnostičkih procedura identifikacije parazita (mikroskopija, kultivacija, molekularne metode) bila je 21% (12–32%), 19% (8–35%) i 17% (12–23%). Analiza podgrupa je pokazala prevalenciju *T. tenax* kod pacijenata sa kandidozom [22% (3–52%)], gingivitisom [21% (9–36%)] i parodontopatijom [27% (10–48%)[51].

Visoka heterogenost parodontalne prevalencije *T. tenax* može biti u korelaciji sa neusaglašenim skriningom populacije u pogledu uzrasta, pola, postojanja neke sistemske bolesti i metodama koje se koriste za parazitološku dijagnozu. Molekularne dijagnostičke tehnike za otkrivanje i identifikaciju vrsta roda Trichomonas, kao što su amplifikacija i sekvencioniranje genoma, pouzdan su alat za brzu i specifičnu karakterizaciju trihomonada[1]. Svakako, eksperimentalni modeli na životinjama, korišćenjem relevantnih fiziopatoloških modela parodontopatije, neophodni su da bi se ispitala sposobnost *T. tenax* da izazove i/ili pogorša bolest, kao i standardizovane eksperimentalno dizajnirane epidemiološke studije[18].

Kolonizacija usne duplje *T. tenax* se češće javlja kod starijih osoba i retko kod dece (kao i *E. gingivalis*). Put prenosa je pljuvačka i infekcija se može desiti direktno, poljupcem, ili indirektno, kontaktom preko pribora za jelo, ličnu higijenu sl., odnosno s bilo čim što može imati tragove zaražene pljuvačke[1]. *T. tenax* se lako prenosi između članova porodice[52], a novi podaci ukazuju na mogućnost međusobne razmene trihomonada između različitih vrsta domaćina[1]. Molekularnim tehnikama *T. tenax* je dijagnostikovana u usnoj duplji pasa, mačaka i u mandibularnoj žlezdi psa.1 Činjenica da je *T. tenax* pronađen kod životinja i njihovih vlasnika može ukazivati na porodični ili kućni karakter infekcije ovom vrstom i ukazuje na mogućnost prenošenja oralne trihomonijaze sa čoveka na domaće životinje i obrnuto; stoga se trihomonijaza usne duplje može smatrati antropozoonozom ili zooantroponozom[1].

Još jedan važan faktor koji utiče na infekciju oralne duplje je trajanje pranja zuba[53]. Pranje zuba kraće od 1 minuta, kao i suviše retko pranje, negativno utiču na stanje usne duplje i podstiču pojavu protozoa. S druge strane, negativno utiče i nepravilna upotreba dodatnih mehaničkih sredstava za oralnu higijenu, kao što su konac za zube ili čačkalice. Protisti se češće javljaju kod ljudi koji koriste mehanička sredstva. Ovo je verovatno zbog pogrešnog rukovanja ovim uređajima, koji mogu oštetiti tkivo desni i stoga izazvati upalu[53].

Recent results of a systematic literature review and meta-analysis have revealed global overall prevalence of 17% (95% CI 14–22%) of *T. tenax* infection. The highest prevalence rate was estimated to be 56% (42–69%) in Chile, while the lowest prevalence was reported in Kenya, with only 3% (1–6%). The analysis demonstrated that the infection was most common in those aged 46–55 years, with 15% (0–100%). The overall prevalence, depending on the applied diagnostic procedures for parasite identification (microscopy, cultivation, molecular methods), was 21% (12–32%), 19% (8–35%) and 17% (12–23%), respectively. The subgroup analysis dealt as well with the prevalence of *T. tenax* in patients with candidiasis [(22% (3–52%)], gingivitis [21% (9–36%)] and periodontitis [27% (10–48%)][51].

A high degree of heterogeneity of periodontal *T. tenax* prevalence could be related to unbalanced screening practices as to the factors of age, gender, presence of some systemic disease and methods utilized for parasitology diagnosis. Molecular diagnostic techniques devised to detect and identify the species of genus Trichomonas (such as genomic amplification and sequencing), represent a reliable tool for rapid and specific characterization of trichomonads[1]. Obviously, experimental animal models utilizing relevant physiopathologic models of periodontitis are necessary to assess the ability of *T. tenax* to cause and/or aggravate a disease, as well as standardized experimentally designed epidemiological studies[18].

Oral cavity colonization with *T. tenax* is more common in older individuals and is rare in children (similar to *E. gingivalis*). The transmission route is saliva and infections occur directly, by kissing, or indirectly, by a contact with eating tools, personal hygiene items, and similar, i.e. with anything that has come into contact with infected saliva[1]. *T. tenax* is easily transmitted between family members[52], and some recent data suggest the possibility of exchange of trichomonads between different host species1. Using molecular techniques, *T. tenax* has been diagnosed in the oral cavity of dogs and cats, and in the mandibular gland in dogs1. The fact that *T. tenax* has been identified in animals and their owners may indicate the possibility of a familial or household character of the infection with this species and suggests the possibility of transmission of oral trichomoniasis from humans to domestic animals and vice versa; oral trichomoniasis can therefore be considered an anthropozoonosis or zooanthroponosis[1].

Ostale protozoa: *Leishmania spp., Toxoplasma gondii*

Leishmania spp.

Vrste roda Leishmania su obligatni intracelularni paraziti tkiva sisara koje pripadaju potkraljevstvu Protozoa, kolu Sarcomastigophora, razredu Zoomastigophora (kao i rod Trichomonas, odnosno vrsta *T. tenax*). Uzročnici su oboljenja lajšmanioza koje je rasprostranjeno širom sveta, sem u Australiji i na Antarktiku. Lajšmanijaza je endemska parazitoza u mnogim zemljama, a najviše u zemljama u razvoju. Svetska zdravstvena organizacija je uvrstila lajšmanijazu na listu zanemarenih tropskih bolesti koje treba eliminisati do 2030[54].

Transmisija vrsta ovoga roda je najčešće zoonotska. Lajšmanije prenose ženke hematofagnih insekata (kolokvijalno peščane muve, eng. *Sand flies*) iz roda Phlebotomus i/ili Lutzomyia (vrste rasprostranjene u Americi) sa domaćih i divljih životinja (rezervoari parazita). Za vreme krvnog obroka insekta dolazi do ingestije amastigota (infektivni oblik za insekta) iz zaraženih domaćina. U crevima insekta (prelazni domaćin - vektor) amastigoti prelaze u promastigotni oblik koji je pokretan. Promastigoti se umnožavaju prostom binarnom fisijom u digestivnom traktu insekta i potom prelaze u metaciklične promastigote (infektivni oblici za čoveka) kada vrše invaziju bukalne šupljine insekta. Krvnim obrokom, ubodom preko kože, insekt unosi žrtvi (sisaru) infektivni oblik parazita koji vrši invaziju citoplazme mononuklearnih fagocita i prelazi u formu amastigota (Lajšman Donovan telo, eng. *Leishman Donovan body*) efikasno izbegavajući imunski odgovor nosioca. Nakon niza deoba i stvaranja velikog broja amastigota dolazi do pucanja zaražene ćelije. Osobođeni paraziti (amastigoti) vrše najezdu novih fagocita preko kojih se, zavisno od vrste parazita i imunskog statusa domaćina, infekcija širi (jetra, slezina, kostna srž, limfni nodusi, koža, creva i td.). Amastigoti koji se nađu u krvotoku nakon liziranja napadnute ćelije, ali i prepune parazitirane ćelije, budu ingestirani od strane insekta prilikom novog uboda[19].

Humana lajšmanioza je u prvom redu zoonoza, ali se može sa obolelog čoveka preneti na drugog čoveka (interhumani prenos) transfuzijom krvi, korišćenjem zajedničkih igala, sporadično seksualnim putem i transplancentarnim putem (kongenitalna lajšmanioza)[19].

Vrste roda Leishmania su morfološki istovetne, što ponekad pravi zabune u taksonomiji.

Another important factor of impact on oral cavity infection is the duration of teeth brushing[53]. Teeth brushing shorter than a minute, as well as very rare teeth brushing, has an unfavorable impact on the oral cavity health and may favor protozoan colonization. On the other hand, improper use of additional mechanical devices for oral hygiene, such as dental flosses or toothpicks, may also have a negative impact. Protists more commonly occur in people who tend to use these mechanical devices. This is probably the consequence of improper use of the devices, which may inflict damage to the gums and thus induce inflammation[53].

Other protozoans: *Leishmania spp., Toxoplasma gondii*

***Leishmania** spp.*

The species of the genus Leishmania are obligate intracellular parasites of mammalian tissues that belong to the subregnum Protozoa, phylum Sarcomastigophora, classis Zoomastigophora (as well as the genus Trichomonas, i.e. *T. tenax* species). They cause leismaniosis, a globally present disease (with the exception of Australia and Antarctica). Leishmaniasis is an endemic parasitosis in many countries, mostly affecting the developing countries. The World Health Organization classified leishmaniasis among the neglected tropical diseases that should be eliminated until 2030[54].

Transmission of the species of this genus is usually zoonotic. Leishmanias are transmitted by the bite of female hematophagous insects (colloquially called *sand flies*) from the genu s Phlebotomus and/or Lutzomyia (the species living in America) from domestic or wild animals (parasite reservoirs). During their blood meal, insects ingest amastigotes (an infective form for insects) from infected hosts. In the insect bowel (an intermediary host–vector) amastigotes transform to promastigotes (a mobile stage). Promastigotes replicate by simple binary fission in the insect digestive tract and then transform into metacyclicpromastigotes (a form infective to humans), when they invade the insect buccal cavity. By a blood meal, i.e. via a bite on the skin, the insect introduces the infectious parasite form into the victim (a mammal), which futher invades the cytoplasm of mononuclear phagocytes and transforms into the amastigote form (Leishman-Donovan body), efficiently evading the host immune response. After a sequence of divisions and creation of a large number of amastigotes, the

Poslednjih nekoliko godina zahvaljujući primeni metoda molekularne biologije izvršena je nova klasifikacija. Tako, subgenus Leishmania čine pet kompleksa u kojima se nalaze brojne vrste. Leishmania donovani kompleks obuhvata vrste: *L. donovani, L. infantum, L. chagasi, L. archibaldi*. Iste vrste lajšmanija mogu usloviti različite kliničke oblike lajšmanijaze, i obrnuto. Izdvojena su četiri klinička entiteta lajšmanijaze.1) visceralna lajšmanijaza (VL), 2) kožna lajšmanijaza (KL), 3) kožno-sluzokožna lajšmanijaza (KSL), 4) difuzna kožna lajšmanioza (DKL)[19].

Visceralna lajšmanijaza (kala-azar, Dum-dum groznica) je sistemsko oboljenje koje se karakteriše visokom temperaturom, hepatosplenomegalijom, limfoadenopatijom, anemijom, leukopenijom, trombo-citopenijom, značajnim gubitkom telesne težine i slabljenjem organizma. U nelečenih osoba, stopa smrtnosti je gotovo 100% u periodu od dve godine. Infekciju izazivaju vrste *L. donovani* kompleksa, i to: *L. donovani* je uzročnik indijske VL; *L. infantum* je uzročnik mediteranske VL; *L. chagasi* je uzročnik južnoameričke VL i *L. archibaldi* je uzročnik sudanske VL[19].

Kod mediteranskog tipa kala-azara (Mediteran, Jugoistočna Evropa, ali i Kina, Srednja Azija, Centralna i Južna Amerika), glavni rezervoar infekcije je pas. Lanac infekcije je na relaciji pas-insekt-pas, ali i na relaciji pas-insekt-čovek. Najčešće oboljevaju deca (otuda i naziv), ali nisu pošteđeni ni odrasli. Prvi autohtoni slučajevi VL u Srbiji su zabeleženi 1945. godine u Nišu i Dobričkom okrugu. U naredne tri godine na teritoriji južne, istočne i zapadne Srbije registrovano je preko 350 slučajeva lajšmanijaze, a tokom 1949. godine nekoliko obolelih u neposrednoj okolini Beograda (Srbija). U navedenom periodu, kala–azar je bio endemičan u svim republikama nekadašnje Jugoslavije, sem na teritoriji nekadašnje Hrvatske i nekadašnje Slovenije[55]. Glavni rezervoar parazita, prema sprovedenim istraživanjima, je pas, a vektori flebotomusi[56]. U prvoj dekadi ovog veka zabeležena su 22 slučaja VL u Srbiji i 1 slučaj koinfekcije HIV/lajšmanijaza koji je zabeležen u jugoistočnoj Srbiji (grad Niš)[57,58]. Jedna od glavnih pretnji u kontroli VL je interakcija s HIV infekcijom. Naime, VL se pojavila kao važna oportunistička infekcija (posle toksoplazmoze i kriptosporidioze) povezana sa HIV-om. U endemskim područjima visceralne lajšmanioze mnogi ljudi imaju asimptomatsku infekciju i istovremenu infekciju HIV-om (koinfekcija) što povećava rizik za razvoj aktivne VL između 100 i 2320 puta!

infected cell bursts. The released parasites (amastigotes) infect new phagocytes through which, depending on the parasite species and immune status of the host, the infection spreads further (to the liver, spleen, bone marrow, lymph nodes, skin, intestines, etc.). Amastigotes present in the bloodstream after the lysis of an infected cell (or a parasite-filled infested cell), are ingested by an insect during a new bite[19].

Human leishmaniasis is primarily a zoonosis, but can be transmitted from an infected individual to others (interhuman transmission) by blood transfusion, by sharing needles, sporadically even by sexual route and transplacentally (congenital leishmaniasis)[19].

The species of the Leishmania genus are morphologically identical, which sometimes creates confusion in their taxonomy. In recent years, owing to the molecular biology methods, a new classification has been made. The subgenus Leishmaniais thus composed of five complexes with numerous species. The Leishmaniadonovani complex involves the following species: *L. donovani*, *L. infantum*, *L. chagasi*, and *L. archibaldi*. The same leishmania species can cause different clinical forms of leishmaniasis, and vice versa. Four clinical entities of leishmaniasis are recognized: 1) visceral leishmaniasis (VL); 2) cutaneous leishmaniasis (CL); 3) mucocutaneous leishmaniasis (MCL); and 4) diffuse cutaneous leishmaniasis (DCL)[19].

Visceral leishmaniasis (kala-azar, Dum-dum fever) is a systemic disease characterized by high temperature, hepatosplenomegaly, lymphadenopathy, anemia, leukopenia, thrombocytopenia, and significant loss of body weight. In untreated individuals, the mortality rate is almost 100% in the period of two years. The infection is caused by the following species from the Leishmaniadonovani complex: *L. donovani*, as the cause of Indian VL; *L. infantum*, as the cause of Mediterranean VL; *L. chagasi*, as the cause of South American VL; and *L. archibaldi*, as the cause of Sudan VL[19].

In the Mediterranean type of kala-azar (Mediterranean region, South Eastern Europe, but also China, Middle Asia, Central and South America) the principal infection reservoir is the dog. The infection chain is dog-insect-dog, but also dog-insect-human. Children are most commonly affected, but adults are not spared either. The first autochthonous (native) cases of VL in Serbia were recorded in 1945 in Niš and in Dobrič County. In the next three years there were over 350 reported cases of leishmaniasis in the territories of South, Eastern and Western Serbia, and in 1949, there were several infections in the vicinity of Belgrade as well.

U Južnoj i Jugoistočnoj Evropi oko 70% slučajeva VL kod odraslih je povezano sa HIV infekcijom[19,59]. Pored HIV infekcije, na povećanu učestalost lajšmanijaze kao oportunističke bolesti uticao je povećani broj ljudi sa imunokompromitovanim imunitetom usled hroničnih bolesti, neoplazmi, imunosupresivnih tretmana, transplantacije[60]. Post kalaazarne kožne lezije (PKKL) mogu se javiti nakon izlečenja VL, naročito u endemskim područjima lajšmanioze uzrokovane *L. donovani*. Fizikalnim pregledom uočava se makulopapulozni nodularni osip koji je uglavnom lokalizovan oko usta i nešto manje na grudnom košu i nadlakticama. Međutim, može se javiti i generalizovani osip, čirevi i kraste, kao i heilitis i lezije na mekom i tvrdom nepcu. Bolest je hroničnog toka, može trajati godinama iako paraziti ne vrše invaziju unutrašnjih organa[19].

Kožna lajšmanijaza se karakteriše pojavom papula na koži na otkrivenim delovima tela (lice, ruke, noge) koje su praćene regionalnom limfoadenopatijom. Papule se javljaju nakon 1-2 meseca od uboda insekta, potom ulcerišu kada nastaju krateri na koži. Ivice lezija su jasno ograničene i eritematozne, a potom nastaje granulaciono tkivo. Promene su bezbolne i spontano zaceljuju kod nekomplikovanih formi KL. Međutim, patološke promene lokalizovane na vidljivim, izloženim delovima tela, sa mogućnošću destrukcije tkiva i stvaranja ožiljaka, zahtevaju medikamentoznu terapiju. Uzročnici KL su morfološki identični sa vrstama koje uzrokuju VL. U zemljama Starog sveta to vrste *L. tropica, L. major i L. aethiopica*, mada u Južnoj Evropi i zemljama mediteranskog basena uročnik KL može biti vrsta *L. infantum*. KL Novog sveta izazivaju vrste L. mexicana complex i L. braziliensis complex[19].

Kožno-sluzokožna lajšmanijaza se karakteriše lezijama na koži i sluzokoži koje delimično ili potpuno vrše destrukciju tkiva što dovodi do estetskih promena sa psihičkim poremećajima, kao i do ozbiljnih, po život opasnih, funkcionalnih promena na organima. Uzročnici KSL su *L. major, L. tropica, L. aethiopica, L. mexicana, L. brasiliensis* (Centralna Amerika, ređe Istočna Afrika). Nakon 1-4 nedelje od uboda insekta, lezija može spontano da se zaleči. Karakteristično je da se primarna lezija progresivno povećava u periodu od nekoliko nedelja i/ili godina. Bolne, destruktivne, metastatske lezije u usnoj i nosnoj duplji javljaju se u 2-50% slučajeva[19].

In this period, kala-azarwas endemic in all ex-Yugoslav republics, with the exception of Croatia and Slovenia[55]. The main infection reservoir, according to the studies, was the dog, and vectors were phlebotomi[56]. In the first decade of this century, there were 22 recorded cases of VL in Serbia and one case of HIV/leishmaniosis-coinfection in Southeastern Serbia (the city of Niš)[57,58]. One of the major threats in the control of VL is its interaction with HIV infection. In particular, VL appeared to be an important opportunistic infection (after toxoplasmosis and cryptosporidiosis) associated with HIV. In the regions endemic for VL, many people have an asymptomatic infection and concomitant infection with HIV (coinfection), which increases the risk of developing active VL one hundred to 2,320 times!

In Southern and South-Eastern Europe around 70% of cases of VL in adults are associated with HIV infection[19,59]. In addition to HIV infection, increased prevalence of leishmaniasis as an opportunistic infection is influenced by increased numbers of individuals immunocompromised due to chronic diseases, neoplasms, immunosuppressive treatments, transplantations[60]. Post-kala-azar skin lesions (PKSL) can appear after VL has been cured, especially in endemic regions for leishmaniosis caused by *L. donovani*. On physical examination, maculopapular rash is seen, primarily around the mouth and slightly less on the chest and upper arms. However, generalized rash may also occur along with boils and crusts, cheilitis and soft and hard palate lesions. The disease follows a chronic course and can last for years, although the parasites are not invading the internal organs[19].

Cutaneous leishmaniasis (CL) is characterized by the appearance of papules in the skin on the exposed parts of the body (face, arms, legs), accompanied by regional lymphadenopathy. Papules tend to occur 1–2 months after the insect bite, and after that ulcerate, producing crater-like lesions. The edges of the lesions are clearly delineated and erythematous; after that, granulation tissue is created. The changes are painless and heal spontaneously in uncomplicated forms of CL. Nevertheless, pathological changes situated in the exposed, visible parts of the body, which may destruct tissue and create scars, require medicamentous therapy. The causative agents of CL are morphologically identical to the species that cause VL. In the Old World countries these

Nekoliko godina od zalečene primarne lezije mogu se javiti metastatske lezije. Moguća su razaranja nosne pregrade, tvrdog nepca i grkljana. Takođe su opisane i deformacije usana i obraza[60-63]. Zahvatanje samo oralne duplje je veoma retko, mada su dokumentovani i takvi primeri[60,64]. Kod obolelih može se javiti: groznica, gubitak težine, anemija i sekundarna bakterijska infekcija. Anamneza i prepoznavanje kliničke slike KSL su presudne u dijagnozi bolesti. U odmakloj fazi bolesti je lečenje znatno oteženo, a takođe su mogući i relapsi. Paraziti se retko nalaze u uzorcima sa ivice primarnog ulkusa i/ili sa lezija na sluzokoži obolelog. Bolesnici su seropozitivni, a takođe je pozitivan i intradermalni test. Ozdraveli pacijenti su otporni na reinfekciju[19].

Difuzna kožna lajšmanioza se karakteriše lezijama na koži koje nalikuju lepromatoznim promenama; hroničnog je toka i teška za lečenje. Najpre se javljaju papule, potom lokalizovane lezije koje se vremenom šire na čitavu površinu tela u vidu plakova i čvorova koji su čvrsti i glatki, a kasniji i hrapavi. Promene ne ulcerišu i ne zahvataju sluzokože i unutrašnje organe[19].

Mere prevencije lajšmanijaze su različite i zavise od brojnih faktora: geografskog područja, staništa sisara domaćina i vektora. Neophodno je sistematsko otkrivanje obolelih i njihovo lečenje; periodično zaprašivanje insekticidima sa rezidualnim dejstvom, korišćenje repelenata i zaštitnih mreža oko prostora za spavanje; dispozicija đubrišta; uništavanje malih glodara i zaraženih pasa. Dijagnostikovanje oralne lajšmanijaze predstavlja izazov u medicinskoj praksi. Rana dijagnoza je neophodna da bi se obezbedio brzi tretman i da bi se izbegli recidivi[19].

Toxoplasma gondii

Rod Toxoplasma pripada kolu Apicomplex, razredu Sporozoa. Protozoa *Toxoplasma gondii* (*T. gondii*) je ubikvitarni parazit rasprostranjen po čitavom svetu. Prema podacima Centra za kontrolu i prevenciju bolesti (eng. *Centers for Disease Control and Prevencion*, CDC) prevalencija toksoplazmoze u različitim delovima sveta je više od 60% i varira u zavisnosti od geografskog područja, klimatskih prilika, načina života (ishrana, higijena)[65]. U urbanim sredinama najčešći put infekcije je konzumiranje termički nedovoljno obrađenog mesa, dok je u ruralnim sredinama češće putem prljavih ruku ili udisanjem oocista.

are *L. tropica, L. major and L. aethiopica,* although in southern Europe and the Mediterranean basin the cause of CL can be *L. infantum*. In the New World, CL is caused by *L. mexicana complex and L. braziliensis complex*[19].

Mucocutaneous leishmaniasis (MCL) is characterized by lesions in the skin and mucosa which partially or completely destruct tissue, leading to esthetic changes with resultant psychological problems, as well as to serious, life-threatening functional organ changes. The causes of MCL are *L. major, L. tropica, L. aethiopica, L. mexicana, L. braziliensis* (Central America, less commonly East Africa). One to four weeks after the insect bite, the lesion may heal spontaneously. It is characteristic that the primary lesion progressively increases in the period of several weeks and/or years. Painful, destructive, metastatic lesions in the oral and nasal cavity occur in 2–50% of cases[19]. Several years after the primary lesion has healed, metastatic lesions may appear. Destruction of the nasal septum, hard palate and larynx is possible. Deformations of the lips and cheeks have also been described[60–63]. Oral cavity involvement is rare alone, although such instances have been reported as well[60,64]. In the affected the following may occur: fever, loss of weight, anemia and secondary bacterial infections. Patient history and recognition of the MCL clinical picture are essential in the diagnosis. In more advanced disease stages the treatment is difficult, and relapses tend to occur as well. The parasites are rarely present in the samples taken from the primary ulcer edges and/or from the mucosal lesions. The patients are seropositive, and the intradermal test is also positive. The healed patients are resistant to reinfection[19].

Diffuse cutaneous leishmaniosis is characterized by lesions in the skin similar to leprous changes; it is a chronic disease, difficult to treat. Papules tend to occur first, followed by localized lesions which spread to involve the whole body surface in the form of plaques and nodules which are firm and smooth and become rough later. The changes do not ulcerate, nor they involve mucosa or internal organs[19]. The measures to prevent leishmaniosis differ and depend on a number of factors: geographical area, habitat of the mammalian host and vectors. Systematic detection of the affected and their treatment are essential; periodical dusting with residual insecticides; use of repellents and protective nets over the sleeping spaces; waste disposal; elimination of small rodents and infected dogs.

Do infekcije može doći i korišćenjem u ishrani svežih jaja domaće živine, mleka, ali i putem krvi, pljuvačke i urina zaraženih životinja (trofozoit ili pseudocista). Moguć prenos je i nesterilnim iglama, preko posteljice (transplacentarni prenos), nakon transfuzije krvi ili transplantacije organa inficiranog davaoca. Interhumani prenos je redak, a zabeležene su izolacije *T. gondii* iz pljuvačke i sa tonzila[19].

Toxoplasma gondii ima složeni životni ciklus koji se sastoji od seksualne i aseksualne faze. Brojne vrste mačaka (Felide), uključujući i domaću mačku (Felis domestica) su jedini domaćini kod kojih se odvija seksualna i aseksualna faza životnog ciklusa parazita. Mačke se, najčešće, inficiraju oocistama dospelim iz spoljne sredine (hrana), ali i putem hrane u kojoj se nalaze aseksualni oblici parazita (inficirani prelazni domaćin, obično miš). Aseksualna faza životnog ciklusa može se odvijati u različitim tkivima velikog broja domaćina uključujući i čoveka[19].

Nakon *per os* unosa pravih cisti u digestivnom traktu mačke se razgrađuje zid ciste i osobađaju se bradizoiti koji ulaze u epitelne ćelije u kojima se odvija aseksualna faza razvoja, tj. šizogonija. Formiraju se šizonti i merozoiti koji nakon oslobađanja iz dezintegrisane ćelije inficiraju nove epitelne ćelije. Nakon više aseksualnih ciklusa, pojedini merozoiti prelaze u fazu gametogonije kada nastaje zigot (nesporulisana oocista) koja fecesom mačke dospeva u spoljnu sredinu. Oociste se u fecesu mačke mogu naći nakon 1-3 nedelje od infekcije, a u spoljnoj sredini u periodu od 2 - 4 dana sazrevaju (sporulišu), odnosno postaju infektivne. Oociste su otporne u spoljnoj sredini, glavni rezervoar je zemljište, ali može biti i voda. Kada ove zrele, infektivne oociste dospeju u digestivni trakt mačke, oslobađaju se sporozoiti koji prodiru u epitelne ćelije intestinuma, transformišući se u tahizote koji se brzo razmnožavaju što dovodi do pucanja ćelije domaćina. Tahizoiti mogu inficirati susedne ćelije intestinuma, ali se mogu hematogenim i limfnim putem diseminovati po čitavom organizmu mačke. Aseksualna faza životnog ciklusa može se odvijati u ćelijama: intestinuma, CNS-a, mišićima, ćelijama retikuloendo-telijalnog sistema (RES) i dr. ćelijama stalnih, ali i prelaznih domaćina. Kod mačke se aseksualni stadijum razvoja (sem u intestinumu) odvija i u centralnom nervnom sistemu (CNS), mišićima i drugim tkivima, tzv. endodiogenija (mačke su nosioci i tkivnih stadijuma parazita), odnosno može se razviti generalizovana parazitemija.

The diagnosis of oral leishmaniosis presents a challenge in medical practice. Early diagnosis is necessary so that a timely treatment could be provided and relapses avoided[19].

Toxoplasma gondii

The genus Toxoplasma belongs to the phylum Apicomplexa, class Sporozoa. The protozoan *Toxoplasma gondii (T. gondii)* is a ubiquitous parasite present worldwide. According to the data from the Centers for Disease Control and Prevention (CDCs), the prevalence of toxoplasmosis in various parts of the world is over 60% and varies depending on the geographical area, climate, way of life (nutrition, hygiene)[65].

In urban surroundings, the infection route is most commonly by mouth through the intake of insufficiently cooked meat, while in rural areas the infection is usually contracted via dirty hands and inhalation of oocysts. The infection may also arise by using fresh eggs of domestic poultry or by milk, but also via blood, saliva and urine of infected animals (trophozoites or pseudocysts). Transmission by infected needles is also possible, as well as through the placenta (transplacental transmission) and after blood transfusions or organ transplantation from infected donors. Interhuman transmission is nevertheless rare, and T. gondiihas been isolated from the saliva and from the tonsils[19].

Toxoplasma gondii has a complex life cycle that consists of the sexual and asexual phases. Numerous cat species (Felide), including the domestic cat (Felisdomestica), are the only hosts in which sexual and asexual phases of the parasite's life cycle occur. Cats are usually infected by oocysts present in the environment (via food), but also via the food in which asexual parasite forms are present (infected intermediary hosts, usually mice). The asexual phase may take place in different tissues of a large number of hosts, including humans[19].

After a per os intake of proper cysts, the cyst wall is decomposed by the cat digestive tract, releasing the bradyzoites which enter the epithelial cells within which the asexual developmental phase takes place, i.e the schizogony. Schizonts and merozoites are formed, capable of infecting new epithelial cells after being released from the disintegrated cell.

Prelazni domaćini (čovek i drugi kičmenjaci) zaraze se unosom sporulisanih oocista iz spoljne sredine i/ili unosom pseudocisti, ali i pravih cisti koje se nalaze kod drugih prelaznih domaćina (npr. meso zaražene životinje). Oslobođeni paraziti, fagocitovani od strane makrofaga, dospevaju u ekstraintestinalne strukture prelaznog domaćina. U akutnoj fazi su zahvaćeni mezenterični limfni nodusi i jetra, dok su u hroničnoj fazi zahvaćeni CNS, srce i skeletni mišići[19].

Tahizoiti su pseudociste (ćelijski zid potiće od ćelije domaćina) ispunjene trofozoitima koji imaju intezivan metabolizam i ubrzanu deobu (endodiogenija) tokom aseksualne faze životnog ciklusa. Ekstracelularno se mogu naći u momentu prskanja ćelije domaćina kada atakuju na nove ćelije (pravi intracelularni paraziti). Mogu se javiti u akutnoj ili subakutnoj fazi toksoplazmoze. Potom, paraziti prelaze u drugi aseksualni stadijum tzv. stadijum prave ciste ispunjene bradizoitima ili cistozoitima koji takođe nastaju endodiogenijom. Bradizioti su uspavane forme parazita usporenog metabolizma koje ostaju incistirane dok su aktivni mehanizmi odbrane domaćina. Sekretuju sopstveni zid ciste formirajući pravu cistu (najbrojnije na mozgu, očima, skeletnim mišićima) koja sadrži brojne parazite (čak na hiljade) koji godinama mogu ostati vitalni. Pritom, njihov domaćin tokom života nema simptome i znake infekcije parazitom *T. gondii* bez obzira na lokalizaciju cisti (najčešće lokacije su abdominalni organi, skeletni mišići, mozak, oči, embrionalno tkivo), tzv. hronična infekcija. Međutim, zid ciste može da prsne kada se paraziti oslobađaju i pritom može doći do recidiva kliničkih manifestacija tokoplazmoze. To se obično dešava kod imunokompromitovanih domaćina kada toksoplazmoza ima akutni ili subaktni tok bolesti. Ciste nakon dužeg perioda mirovanja mogu da kalcifikuju. Ako prave ciste dospeju u spoljašnu sredinu brzo propadaju. Infektivne su ako se per os unesu zajedno sa organom u kome se nalaze[19].

Toksoplazmoza ljudi nastaje unosom oocisti *T. gondii* preko prljavih ruku, unosom hrane i vode kontaminirane fecesom mačaka tzv. horizontalna trasmisija. Moguća je i horizontalna trasmisija putem tkivnih cisti, ali i vertikalna transmisija tahizoitima. Na težinu bolesti kod infekcije parazitom *T. gondii,* pored virulencije soja, utiču i osetljivost, imunski status i starost domaćina.

After several asexual cycles, individual merozoites enter the phase of gametogony, when a zygote (non-sporulatedoocyst) is produced, which is excreted via cat feces in the environment. Oocysts can be identified in the cat feces 1–3 weeks after the infection; in the environment, they maturate (sporulate) in the period of 2–4 days, becoming infective. Oocysts are resilient in the environment; their main reservoir is soil, although it can be water as well. When these mature, infective oocysts enter the cat digestive tract, sporozoites are released, which enter intestinal epithelial cells transforming into tachyzoites which rapidly replicate, causing the host cell to burst. Tachyzoites may infect adjacent intestinal cells, or be disseminated via bloodstream or lymph throughout the cat body. The asexual phase of the life cycle can take place in the cells of the intestinum, CNS, muscles, reticuloendothelial system (RES) and other cells in the organism of definitive and intermediary hosts. In cats, the asexual phase of development (in addition to the intestines) takes place in the central nervous system (CNS), muscles and other tissues (the so called endodyogeny) – cats host the tissue stages of the parasite as well, i.e. generalized parasitemia may develop. Intermediary hosts (humans and other vertebrates) are infected by the intake of sporulatedoocysts from the environment and/or by the intake of pseudocysts or proper cysts present in other intermediary hosts (i.e. by the meat of infected animals). The released parasites, phagocytised by macrophages, reach the extraintestinal structures of the intermediary host. In the acute phase, mesenteric lymph nodes and the liver are involved, while in the chronic phase the CNS is also involved, as well as the heart and skeletal muscles[19].

Tachyzoites are in fact pseudocysts (with the cell wall originating from the host) packed with trophozoites with an intense metabolism and rapid rate of division (endodyogeny) during the asexual phase of the life cycle. Extracellularly, they can be identified in the moment of cellular burst, when they attack new cells (proper intracellular parasites). They can occur in the acute or subacute phase of toxoplasmosis. Afterwards, the parasites enter the second asexual stage, the so called proper cyst stage, with the cyst filled with bradyzoites or cystozoites, which are also produced by endodyogeny.

Mnogi ljudi inficirani parazitom *T. gondii* nemaju znake i simptome infekcije tokom stečene (akvirirana) toksoplazmoze. Ponekad, kod imunokompetentnih osoba, uključujući i zdrave trudnice, simptomi i znaci infekcije mogu biti blagi, i nalikuju gripu i/ili infektivnoj mononukleozi (temperatura, bolovi u mišićima i zglobovima, malaksalost, glavobolja, retko bol u grlu i farinksu). Često dolazi do lokalizovane limfadenopatije u predelu glave i vrata (limfni nodusi su čvrsti, bezbolni i pokretni na palpaciju)[19,66,67]. Sa razvojem imunskog odgovora dolazi do smanjenja parazitemije, a ciste toksoplazme ostaju u tkivima i sadrže žive parazite. Ciste mogu da se aktiviraju ako dođe do imunosupresije.

Kod imunokompromitovanih pacijenata *T. gondii* opisane kliničke manifestacije su većeg intenziteta, uključujući limfo-adenopatiju, a kod generalizovane infekcije može biti zahvaćen CNS. Tokso-plazmoza kod imunokompromitovanih osoba je posledica reaktivacije hronične infekcije, a znatno ređe primoinfekcije. Reaktivacija može biti lokalizovana, na mestu prskanja cisti, ili se razvija generalizovana toksoplazmoza sa teškom kliničkom slikom (toksoplazmatski encefalitis, najčešća oportunistička infekcija CNS-a kod obolelih od AIDS-a; intersticijski pneumonitis; gastrična toksoplazmoza; miokarditis) i mogućim smrtnim ishodom[19,66,67].

Iako kod tokoplazmoze u kliničkoj slici obolelih nema primarnih simptoma i znakova infekcije *T. gondii* u usnoj duplji, zbog uvećanih limfnih nodusa u predelu glave i vrata pacijenti dolaze u ordinaciju stomatologa. U ovim slučajevima, potrebno je pacijenta uputiti najpre na neinvazivne dijagnostičke procedure, u prvom redu na serodijagnostiku specifičnih antitela klase IgA, IgM i IgG prema *T. gondii*. U slučaju negativnih seroloških rezultata predložiti biopsiju suspektnih limfnih nodusa u cilju potvrde infekcije *T. gondii*[19,66,67].

Bradyzoites are dormant parasite forms, with a slow metabolism, which remain incysted while the host active defense mechanisms are active. They secrete their own cyst wall, forming a proper cyst (most numerous in the brain, eyes, skeletal muscles), that contains numerous parasites (even thousands of them) which may remain vital for years. At the same time, the host experience no symptoms and signs of infection with *T. gondii* regardless of the cysts' localization (most common sites are abdominal organs, skeletal muscles, brain, eyes, embryonal tissue) – this is a chronic infection. However, the cyst wall may burst open when parasites are released and on that occasion the clinical manifestations of toxoplasmosis may recur. This usually happens with immunocompromised hosts when toxoplasmosis have an acute or subacute disease course. After a long period of dormancy, the cysts may undergo calcification. In the environment, proper cysts tend to perish rapidly. They are infective if ingested by mouth together with the organ they are infesting[19].

Human toxoplasmosis occurs after the intake of *T. gondii* oocysts via dirty hands, with foods or water contaminated by cat feces (the so called horizontal transmission). Horizontal transmission by tissue cysts is also possible, as well as vertical transmission by tachyzoites. The severity of the disease caused by *T. gondiii* nfection is influenced by the strain virulence and sensitivity, immune status and age of the host. Many individuals infected with *T. gondii* do not have any signs and symptoms of infection during the acquired (activated) toxoplasmosis. At times, in immunocompetent individuals, including healthy pregnant women, the symptoms and signs of infection can be rather mild and resemble a flu and/or infectious mononucleosis (with symptoms such as fever, muscle and joint pain, fatigue, headache, and rarely pain in the larynx and pharynx). Localized lymphadenopathy is also common in the region of head and neck (lymph nodes are firm, painless and movable on palpation)[19,66,67]. With the development of immune response, parasitemia usually subsides, while the cysts remain in the tissues containing living parasites. If immuno-suppression develops, the cysts can undergo activation. In immunocompromised patients with *T. gondii* infection, the described clinical manifestations are more severe, including lymphadenopathy, and in cases with a generalized infection the CNS can be involved as well. Toxoplasmosis in immuno-compromised individuals represents the consequence of reactivation of a chronic infection, and rarely a primary infection.

Zaključak

Oralni mikrobiom je odraz oralnog, ali i opšteg zdravstvenog stanja organizma. Mikrobiološki stanovnici su koevoluirali zajedno sa čovekom milionima godina, tako da oralni mikrobiomi nisu nasumično kolonizovani. Razvojem tehnologije za detekciju, identifikaciju i analizu oralnih mikrobioma, danas postoje detaljnije informacije o njihovom postojanju, sastavu i specifičnim ulogama. Naredne studije trebale bi da razreše dilemu da li promene u oralnom mikrobiomu prethode kliničkim znacima bolesti ili obrnuto. U prvom slučaju, oralni mikrobiom bi omogućio utvrđivanje mogućih rizika od bolesti. Stomatolozi igraju važnu ulogu u dijagnozi oralnih oboljenja uzrokovanih protozoama usne duplje, ali i protozoa koje dovode do oboljenja koja imaju uticaja na usnu duplju. Njihovo dijagnostikovanje je svakako veliki izazov i zahteva multidisciplinarni pristup. Rana dijagnoza je neophodna da bi se obezbedilo brzo i adekvatno lečenje.

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Such a reactivation can be localized, at the cyst rupture site, or generalized toxoplasmosis may develop, with a rather serious clinical picture (toxoplasmatic encephalitis, the most common opportunistic infection of the CNS in patients with AIDS; interstitial pneumonitis; gastric toxoplasmosis; myocarditis) and possible fatal outcome[19,66,67].

Although with toxoplasmosis the typical clinical picture does not contain primary signs and symptoms of *T. gondii* infection of the oral cavity, enlarged lymph nodes in the head and neck region prompt patients to visit their dentists. In these cases it is necessary to refer the patient first for non-invasive diagnostic procedures, primarily the serodiagnosis of class IgA, IgM and IgG specific antibodies to *T. gondii*. In case that serology results are negative, the biopsy of the suspect lymph nodes should be recommended in order to confirm the infection with *T. gondii*[19,66,67].

Conclusion

Oral microbiome reflects oral and overall health status of the organism. Microbiological inhabitants of the oral cavity have evolved together with humans for millions of years, so that oral microbiomes are not colonized randomly. With the development of technology used for detection, identification and analysis of oral microbiomes, nowadays there is more detailed information about their existence, composition and specific roles they play. Further studies should resolve the dilemma whether the changes in oral microbiome precede clinical signs of disease or vice versa is the case. In the first case, oral microbiome would help in establishing possible risks for certain diseases. Dentists play an important role in the diagnosis of oral diseases caused by oral cavity protozoans, and also the protozoans which can produce systemic diseases with an impact on oral cavity. Their diagnosis represents a challenge of a kind and certainly require a multidisciplinary approach. Early diagnosis is essential in order that a rapid and adequate treatment could be initiated.

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PITANJE SAMOOBRAZOVANJA U KONTINUIRANOM PROFESIONALNOM RAZVOJU STOMATOLOGA UKRAJINE U USLOVIMA PANDEMIJE VIRUSA COVID -19

ISSUES OF SELF-EDUCATION IN THE CONTINUOUS PROFESSIONAL DEVELOPMENT OF DENTISTS OF UKRAINE IN THE CONDITIONS OF THE COVID-19 PANDEMIC

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Sažetak

Uvod: *Brzi razvoj stomatološke industrije i svakodnevna praksa stomatologa zahtevaju stalno učenje, budući da je dopunjavanje stečenih znanja i veština osnova za formiranje visokokvalifikovanog specijaliste. Samousmereno učenje, posebno čitanje i svrsishodana upotreba medicinske literature, konstantno doprinose razvoju mišljenja, koje treba da odgovara savremenom nivou nauke kod medicinskih stručnjaka, u kontekstu pandemije virusa COVID-19.*
Cilj *studije bio je da se prate i analiziraju načini dobijanja novih naučnih i praktičnih znanja od strane stomatologa, za unapređenje njihove stomatološke prakse.*
Materijali i metode. *U studiji je učestvovalo 4.026 stomatologa, koji su popunili on-line upitnike za stomatologe.*
Rezultati. *Za unapređenje svakodnevne stomatološke prakse, stomatolozi dodatno koriste informacije, koje se pružaju u sklopu predavanja na naučnim i praktičnim događajima (80,19%) i koje se mogu naći na internet resursima (71,48%). Za stomatologe, najpogodniji način čitanja naučnih i praktičnih članaka bila je elektronska verzija na sajtovima časopisa (62,20%). Informisanje putem članaka sa dobro ilustrovanim kliničkim slučajevima (72,66%) i putem predavanja, uz praktične materijale (64,75%) od najvećeg su interesa za veliku većinu stomatologa.*
Zaključak. *Analiza rezultata pokazala je to da su glavni načini dobijanja naučnih i praktičnih informacija za stomatologe, u procesu samostalnog učenja, aktivno uključivanje materijala dobijenih na predavanjima, naučnim i praktičnim događajima, podaci sa interneta, iz naučne i metodološke literature, iz naučnih članaka domaćih i stranih stručnih časopisa na engleskom jeziku.*

Ključne reči: *samousmereno učenje, naučna i praktična znanja, stručne publikacije, praćenje*

Abstract

Background: *The rapid development of the dental industry and the daily practice of dentists necessitate constant learning because replenishing the stock of acquired knowledge and skills is the basis for the formation of a highly qualified specialist. Self-directed learning, especially reading and purposeful work with medical literature, constantly contribute to the development of thinking, which should correspond to the modern level of science in medical professionals in the context of the Covid-19 pandemic.*
The aim *of the study was to monitor and analyze ways to obtain new scientific and practical knowledge by dentists to improve their dental practice.*
Materials and methods: *The study involved 4.026 dentists who filled out for dentists online.*
Results: *To improve daily dental practice, dentists additionally use information that is provided in lectures at scientific and practical events (80.19%) and Internet resources (71.48%). For dentists, the most convenient way to read scientific and practical articles was through the electronic version on the websites of the journals (62.20%). Informing doctors with articles with well-illustrated clinical cases (72.66%) and lectures along with practical materials (64.75%) are of the greatest interest to the vast majority of dentists.*
Conclusion: *According to the analytical results, it is shown that the main ways of obtaining scientific and practical information for dentists in the process of self-directed learning is the active involvement of the materials gained on the lectures, scientific and practical events, from Internet resources, from scientific and methodological literature, from scientific articles of domestic and foreign English-language professional journals.*

Key words: *self-directed learning, scientific and practical knowledge, professional publications, monitoring.*

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Uvod

Brzi razvoj stomatološke industrije, kao nauke, kao i uvođenje savremenih tehnologija u medicinsku praksu zahtevaju stalno usavršavanje stomatologa. Održavanje stručne kompetencije i kvaliteta pružanja kvalifikovane medicinske nege stanovništvu zemlje zavisi od stalnog usavršavanja, ažuriranja znanja i usavršavanja praktičnih veština stomatologa tokom njihove karijere[1].

Ovo pitanje posebno je aktuelno u kontekstu pandemije virusa COVID-19, jer je oralna sluzokoža „arena“ za efekte virusa COVID-19, u vidu kandidijaze, herpesa, aftoznih lezija i glosodinije[2,3,4]. Istovremeno, kvalitet pružene usluge i znanje stomatologa dolaze u prvi plan, kako bi se obezbedilo pružanje visokokvalifikovane nege obolelim ljudima, kroz interdisciplinarnu integraciju i kontinuirano stručno usavršavanje specijalista u ovoj oblasti medicine[5,6,7,8].

Stoga je u cilju poboljšanja kvalifikacija lekara, sistem stalnog stručnog usavršavanja ažuriran u Rezoluciji Kabineta ministara Ukrajine br. 302 „O davanju saglasnosti na Pravilnik o sistemu stalnog stručnog usavršavanja zdravstvenih radnika“28. marta 2018. godine. Prema ovoj odluci, kontinuiran proces usavršavanja i usavršavanja stručnih kompetencija stomatologa mora da se nastavi tokom čitavog perioda njihove profesionalne karijere, počevši od trenutka medicinskog obrazovanja. Sada lekari specijalisti imaju mogućnost da biraju način kontinuiranog stručnog usavršavanja, kako bi dobili 50 bodova na godišnjem nivou (CME – Continuing Medical Education – krediti) za obrazovni portfolio. Stomatolozi mogu prisustvovati predavanjima, seminarima, radionicama, simpozijumima, konferencijama, kongresima ili kursevima osvežavanja znanja u postdiplomskim medicinskim ustanovama. Međutim, kontinuirani profesionalni razvoj može biti nedovoljan ili manje efikasan, ukoliko je bez čvrste osnove, koja podrazumeva veštine stečene kroz obuku, koju su stomatolozi sami izabrali[9,10,11].

Samousmereno učenje je samostalna kognitivna aktivnost čoveka usmerena ka postizanju određenih ličnih ciljeva, odnosno zadovoljenju saznajnih interesovanja i profesionalnih potreba. Osnovni cilj samousmerenog učenja za stomatologe je kontinuirano dopunjavanje stečenih znanja i veština, koje su osnova za podršku i povećanje profesionalne kompetencije za pružanje visokokvalitetnih stomatoloških usluga.

Introduction

The rapid development of the dental industry as a science and the introduction of modern technologies in medical practice necessitate the constant development of dentists. The maintenance of professional competence and the quality of the provision of qualified medical care to the population of the country depends on the constant training, updating of knowledge and improvement of practical skills of dentists during their medical career[1].

This issue is especially relevant in the context of the Covid-19 pandemic, as the oral mucosa is an “arena” for the effects of Covid-19, in the form of candidiasis, herpes, aphthous lesions and glossodynia[2-4]. At the same time, the quality and format of knowledge of dentists come to the forefront to ensure the provision of highly qualified care to this contingent of people through interdisciplinary integration and continuous professional development of specialists in this field of medicine[5-8].

Therefore, in order to improve the qualifications of doctors, the system of continuous professional development was updated in the Resolution of the Cabinet of Ministers of Ukraine No. 302 "On Approval of the Regulations on the System of Continuous Professional Development of Healthcare Specialists" dated March 28, 2018. According to this resolution, the continuous process of training and improving the professional competencies of dentists must continue throughout the entire period of their professional activity from the moment of medical education. Now medical specialists have the opportunity to choose the format of continuous professional development in order to receive 50 points (CME – Continuing Medical Education – credits) annually for their own educational portfolio. Dentists may attend lectures, seminars, workshops, symposiums, conferences, congresses, or refresher courses in postgraduate medical institutions. However, continuing professional development may be insufficient or less effective without a solid foundation based on self-directed learning skills[9-11].

Self-directed learning is an independent cognitive activity of a person aimed at achieving certain personal goals, namely the satisfaction of cognitive interests and professional needs. The main goal of self-directed learning for dentists is the continuous replenishment of the acquired knowledge and skills that are the basis for supporting and increasing professional competence for the provision of high-quality dental services.

Godine 1997. Garison je predložio model samousmerenog učenja[12]. Ovaj model učenja zasniva se na motivaciji, koja je glavni ključ samostalnog učenja, kao i samopraćenju (odgovornost) i samoupravljanju (kontrola), koji doprinose kontinuiranom učenju i određuju njegov kvalitet i njegovu efikasnost. Danas postoji mnogo načina da se obuče medicinski stručnjaci i unaprede njihove veštine, a kako bi se obezbedili i postigli visok profesionalizam u lečenju i profesionalni razvoj samog lekara[13].

Cilj rada bila je analiza oblika i postupaka u samostalnom učenju stomatologa, u cilju formiranja profesionalnih kompetetntnih veština.

Materijali i metode

U istraživanju je učestvovalo 4026 stomatologa različitog uzrasta, koji su u martu 2021.godine popunjavali upitnik tokom on-line naučnih i praktičnih događaja i konferencija stručnih škola za stomatologe. Upitnik je pripremila NVO „Ukrajinsko stomatološko udruženje“ i uključivao je i socio-demografska pitanja i pitanja za određivanje načina i pristupa za dobijanje novih naučnih i praktičnih saznanja. Ispitanici su bili stomatolozi svih specijalnosti. Ankete stomatologa i analiza rezultata studije sprovedene su pod rukovodstvom NVO „Ukrajinsko stomatološko udruženje“, grupe kompanija „MedEkpert“ i Ukrajinske rejting agencije.

Korišćena je analitička metoda istraživanja i strukturno-logička analiza. U analizi rezultata podataka primenjene su metode statističke analize (StatSoftInc., serijski broj AGAR909E415822FA).

Rezultati

Prema rezultatima studije, od 4026 ispitanika, 70,25% činile su žene, a 29,75% činili su muškarci. Prema starosnoj dobi, 3,40% činila su lica starosti do 25 godina, 15,08% činile su osobe od 26 do 30 godina, 28,94% anketiranih stomatologa činile su osobe od 31 do 40 godina, 25,62% osobe od 41 godine do 50 godina i 26,96% osobe starije od 50 godina.

Za lekarsku praksu, uvođenje najnovijih visokotehnoloških metoda dijagnostike i lečenja teških stomatoloških oboljenja, izvori informacija su osnovni aspekt. Upitnik je obuhvatio proučavanje izvora za dobijanje stručnih informacija. Prema rezultatima studije, u cilju dobijanja novih informacija i usavršavanja praktičnih i teorijskih znanja, 80,19% stomatologa radije prisustvuje

In 1997, Garrison proposed a model of self-directed learning[12]. It is based on motivation, which is the main key to independent learning, as well as self-monitoring (responsibility) and self-management (control), which all contribute to continuous learning, and determine its quality and effectiveness. Today, there are many ways to train and improve the skills of medical professionals to ensure and achieve high professionalism in the results of treatment and professional development of the doctor himself[13].

The aim of the study was to analyze the forms and approaches in self-directed learning of dentists for the formation of professional competence skills.

Materials and methods

The study involved 4,026 dentists of different ages who filled out a questionnaire during scientific and practical events and conferences of professional schools for dentists online in March 2021. The questionnaire was prepared by the NGO "Ukrainian Dental Association" and included both socio-demographic questions and questions to determine the ways and approaches to obtain new scientific and practical knowledge. The respondents were dentists of all specialties. Surveys of dentists and analysis of the results of the study were conducted under the leadership of the NGO "Ukrainian Dental Association", the group of companies "MedExpert" and the Ukrainian rating agency.

The analytical method of research and structural-logical analysis were used. Statistical analysis methods (StatSoftInc., Serial number AGAR909E415822FA) were applied in the analysis of the data results.

Results

According to the results of the study, out of 4,026 respondents, 70.25% were females, 29.75% were males. According to age, 3.40% were persons under 25 years old, 15.08% persons from 26 to 30 years old, 28.94% of the interviewed dentists were persons from 31 to 40 years old, 25.62% persons from 41 to 50 years old, and 26.96% persons over 50 years old.

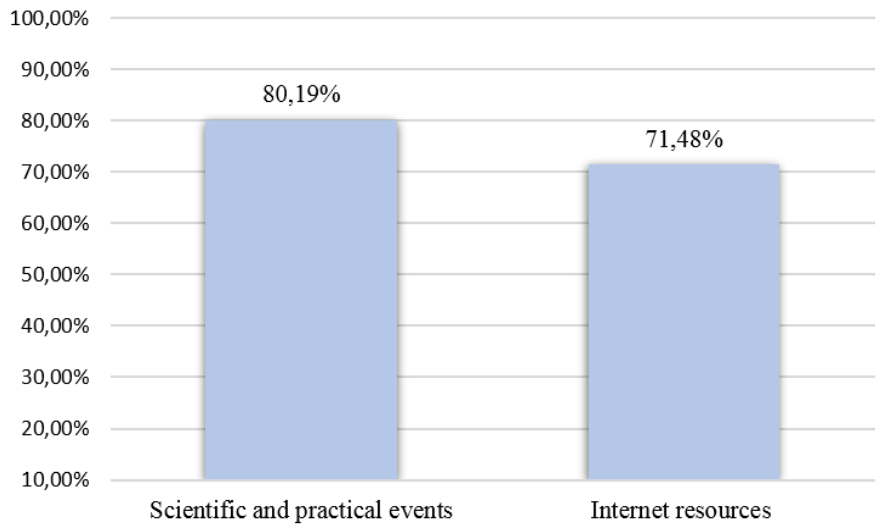
For the practice of a doctor, the introduction of the latest high-tech methods of diagnosis, treatment, and major dental diseases, the sources of information are a fundamental aspect. The questionnaire included the study of sources of professional information.

naučnim i praktičnim događajima, dok 71,48% ispitanika koristi internet, kao izvor potrebnih informacija (Slika 1.).

Svaki drugi stomatolog (54,88%) među ispitanicima bira čitanje naučne i metodičke literature (knjige i uputstva), kao glavni izvor za prikupljanje novih informacija; 40,07% bira naučne članke u domaćim stručnim časopisima. Važna tačka ankete bilo je utvrđivanje nivoa znanja stranog jezika, odnosno engleskog, na kome je nova medicinska literatura bila dostupna. Među ispitanicima, samo 18,55% stomatologa koristi naučne članke u stranim stručnim časopisima za samostalnu obradu naučnih informacija (Slika 2).

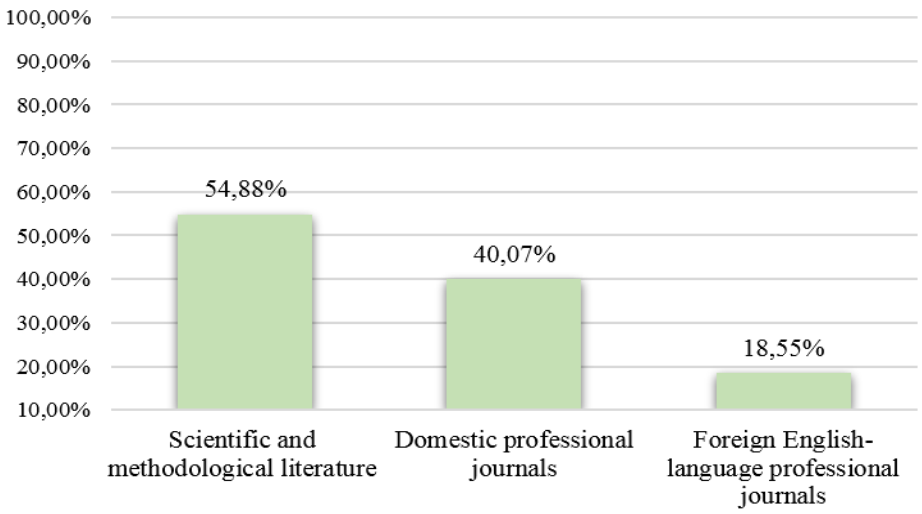
According to the results of the study, in order to obtain a new information and improve practical and theoretical knowledge, 80.19% of the dentists preferred attending scientific and practical events, while 71.48% of respondents used the Internet resources to obtain the necessary information (Figure 1).

Every second dentist (54.88%) among of the surveyed respondents chose reading of the scientific and methodological literature (books and guidelines) as the main source for replenishing new information, 40.07% chose scientific articles in domestic professional journals. An important point of the survey was to determine the level of foreign language proficiency, namely English, in order to obtain a new medical literature. Among the respondents, only 18.55% of dentists used scientific articles in foreign professional journals for independent processing of scientific information (Figure 2).



Slika 1. Korišćenje izvora informacija od strane stomatologa za sticanje novih znanja

Figure 1. Use of information sources by dentists to gain new knowledge



Slika 2. Korišćenje informacionih resursa za unapređenje stomatološke prakse

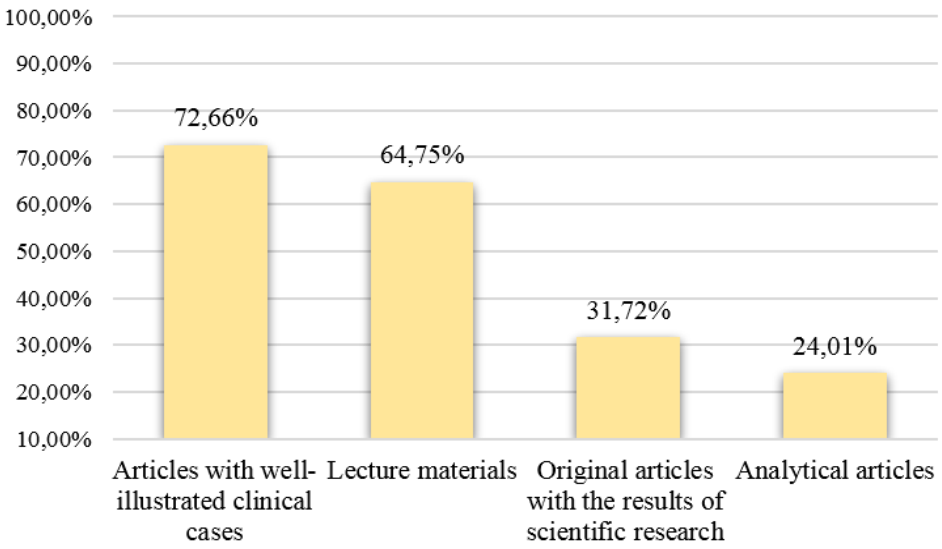
Figure 2. Use of information resources to improve dental practice

Samousmereno učenje prvenstveno podrazumeva veštine doktora za samostalan rad sa naučnom literaturom i njihovu sposobnost sistematizacije i obrade naučnih informacija. Dakle, prema rezultatima ankete, velika većina stomatologa preferirala je članke sa dobro ilustrovanim kliničkim slučajevima (72,66%) i materijale sa predavanja (64,75%) (Slika 3). Samo 31,72% stomatologa iskazalo je interesovanje za originalne članke sa rezultatima naučnih istraživanja, a 24,01% istaklo je interesovanje za analitičke članke, što ukazuje na njihovu veštinu samostalne analize literature i sposobnost obrade naučnih informacija.

Transformacija u obrazovnom sistemu, pogoršana pandemijom virusa COVID-19 i karantinskim ograničenjima, menja pristup lekara izvorima informacija. Rezultati ankete o načinima upoznavanja sa naučnim i praktičnim člancima u stručnim publikacijama pokazali su da 62,20% stomatologa radije čita članke u elektronskom formatu na sajtovima časopisa, 46,10% – zainteresovano je za čitanje članaka, koji su odabrani na relevantne teme stručne škole, 40,53% – dobija nove brojeve časopisa i članaka na e-mail adresu. Samo jedna trećina ispitanika, odnosno 34,45%, čita tekstove u papirnoj formi, objavljene u časopisima. Procenjuje se da 4,25% stomatologa posećuje medicinske biblioteke radi čitanja članaka, a 4,51% uopšte nije u mogućnosti da čita novu literature, zbog preopterećenosti poslom. Od anketiranih stomatologa, njih 1,67% navelo je da ih ne zanimaju članci u domaćim stručnim časopisima (Slika 4).

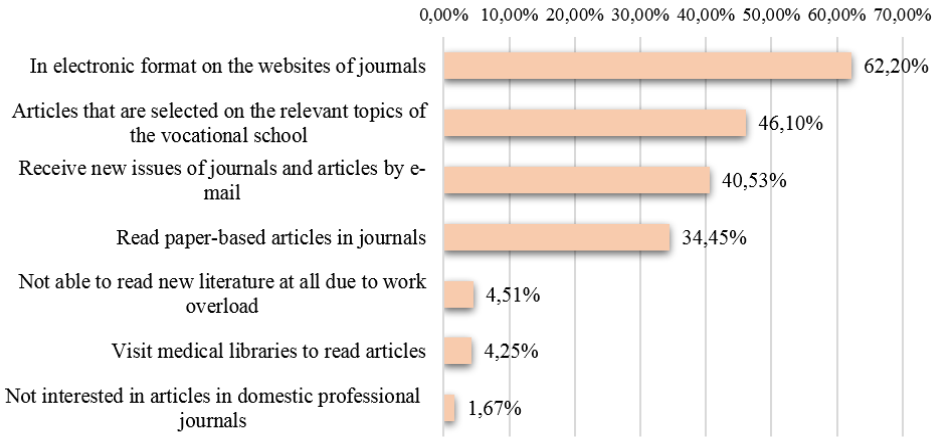
Self-directed learning primarily involves the doctor's skills for independent work with scientific literature and his or her ability to systematize and process scientific information. Therefore, according to the results of the survey, the vast majority of dentists preferred articles with well-illustrated clinical cases (72.66%) and lecture materials (64.75%) (Figure 3). Only 31.72% of dentists expressed their interest in original articles with the results of scientific research and 24.01% noted their interest in analytical articles, which indicates their skills in independent analysis of literature and the ability to process scientific information.

The transformation in the education system, exacerbated by the Covid-19 pandemic and quarantine restrictions, is changing the access of doctors to the information sources. The results of the survey on ways to get acquainted with scientific and practical articles in professional publications showed that 62.20% of dentists preferred to read articles in electronic format on the websites of journals, 46.10% were interested in reading articles that were selected on the relevant topics of the vocational school, 40.53% received new issues of journals and articles by e-mail. Only one third of the respondents, namely 34.45% read paper-based articles in journals. Four point twenty-five percent of dentists visited medical libraries to read articles, and 4.51% were not able to read new literature at all due to work overload. One point sixty-seven percent of the surveyed dentists noted that they were not interested in articles in domestic professional journals (Figure 4).



Slika 3. Vrste članaka koji su stomatolozima najzanimljiviji

Figure 3. Types of articles most interesting for dentists



Slika 4. Analiza načina upoznavanja sa naučnim i praktičnim člancima

Figure 4. Analysis of ways to get acquainted with scientific and practical articles

Prema rezultatima ankete, utvrđena je motivacija stomatologa za samostalno učenje i utvrđeno je njihovo interesovanje za čitanje stručne literature. Rezultati proučavanja učestalosti čitanja domaćih stomatoloških časopisa pokazali su to da 23,83% stomatologa redovno čita članke u domaćim časopisima, 28,32% stomatologa čita članke u domaćim časopisima nekoliko puta mesečno, 22,62% ispitanika koristi internet za pronalaženje potrebnih informacija, a 13,40% koristi informacije sa naučnih i praktičnih događaja. Članke u domaćim časopisima nekoliko puta nedeljno čita njih 8,84%, a 2,99% ispitanika ne čita domaće časopise (Slika 5).

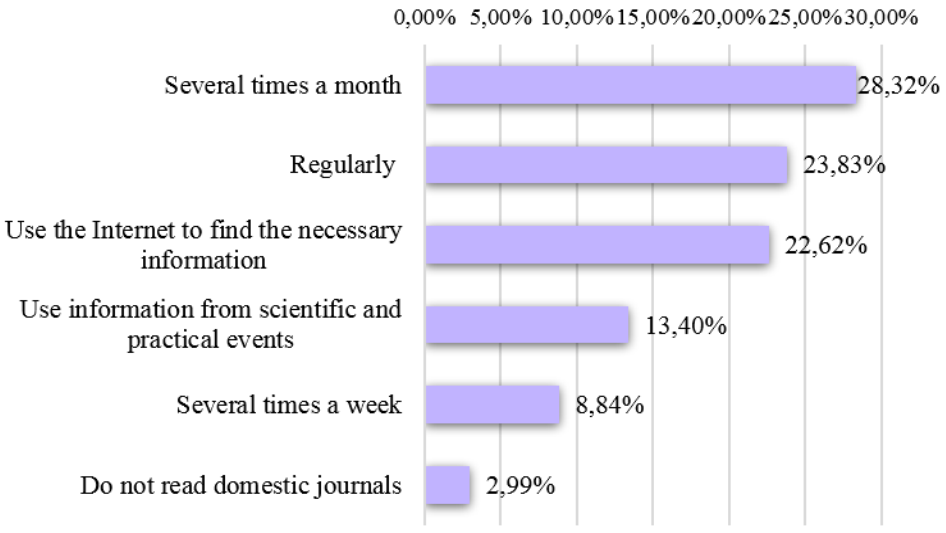
According to the results of the survey, the motivation of dentists for self-directed learning and their interest in reading professional literature were determined. The results of studying the frequency of reading domestic dental journals showed that 23.83% of dentists regularly read articles in domestic journals, 28.32% read articles in domestic journals several times a month. 22.62% of respondents used the Internet to find the necessary information, and 13.40% – used information from scientific and practical events. Eight point eighty-four percent of dentists read articles in domestic journals several times a week, and 2.99% of respondents did not read domestic journals (Figure 5).

Prema pogodnosti dobijanja novih brojeva stručnih časopisa, 53,54% stomatologa preferira elektronske verzije na sajtovima časopisa, kada istraživač može lako da pristupi i preuzme traženi članak, 24,61% ispitanika želelo je da dobija obaveštenja na e-mail adresu o novim brojevima časopisa, a 11,62% stomatologa preferira kupovinu papirnih verzija časopisa na naučnim i praktičnim događajima i izložbama. Samo 10,23% stomatologa preferira godišnju pretplatu na stručne časopise sa mogućnošću nabavke u pošti (Slika 6).

Među tri lidera domaćih stomatoloških časopisa su: časopis DentArt, koji preferira 45,68% ispitanih stomatologa, časopis Modern Dentistry, koji čita 43,49% ispitanika, i časopis Dentistry News, koji je izabralo 26,00% ispitanika (Slika 7).

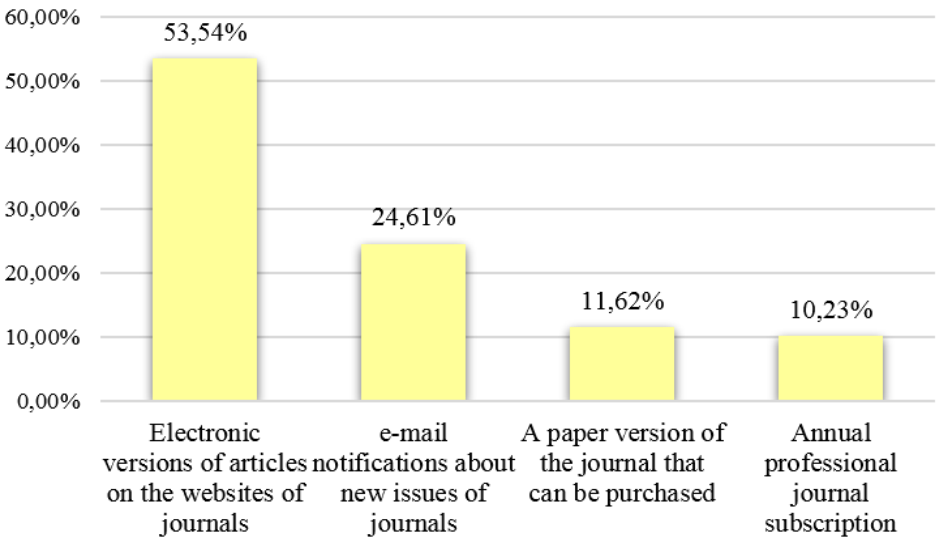
Based on the convenience of obtaining new issues of professional journals, 53.54% of dentists preferred electronic versions on the websites of journals, when the search engine could easily access and download the required article, 24.61% of respondents wished to receive e-mail notifications about new issues of journals, and 11.62% showed the readiness to purchase paper versions of journals at scientific and practical events and exhibitions. Only 10.23% of dentists preferred an annual professional journals subscription with the possibility of obtaining them at the post office (Figure 6).

Among the three leaders of domestic dental journals were DentArt Journal, which was preferred by 45.68% of the surveyed dentists, Modern Dentistry Journal, which was read by 43.49%, and Dentistry News Journal, which was chosen by 26.00% of respondents (Figure 7).



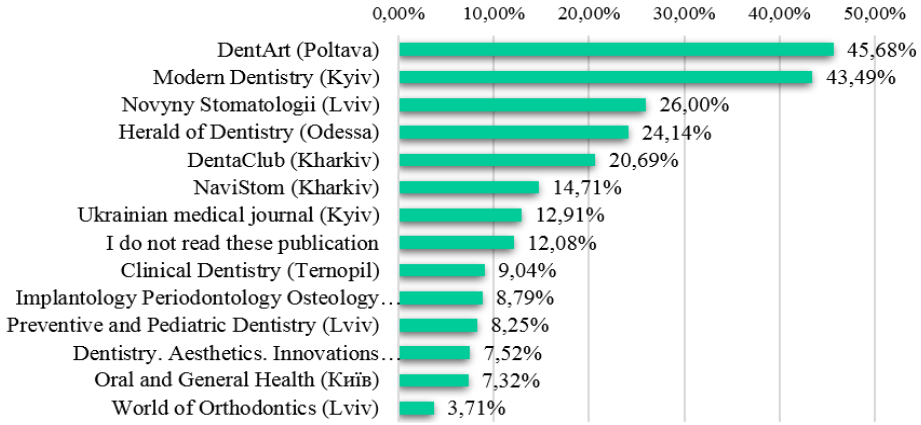
Slika 5. Utvrđivanje učestalosti čitanja naučnih i praktičnih članaka u domaćim stomatološkim časopisima

Figure 5. Determining the frequency of reading scientific and practical articles in domestic dental journals



Slika 6. Načini dobijanja novih brojeva stručnih časopisa

Figure 6. Methods of obtaining new issues of professional journals



Slika 7. Redovnost čitanja domaćih stručnih publikacija

Figure 7. Regularity of reading domestic professional publications

Diskusija

Garisonov sveobuhvatni model samo-usmerenog učenja, koji se zasniva na motivaciji, ima svoje jasno mapiranje i sistematiku u modelu učenja „po iskustvu“. Po prvi put, ovaj model samousmerenog učenja opravdao je Amerikanac D. Kolb, zasnovan na razvoju D. Djuija, K. Levina i J. Pijažea[14].

Koristeći sopstveno iskustvo, stomatolozi svoj rad usmeravaju ka produbljivanju kliničkog razmišljanja, usavršavanju praktičnih veština i pronalaženju individualnog pristupa pacijentu, kako bi u procesu samoobrazovanja identifikovali personalizovane karakteristike pacijenata i njihove reakcije u ponašanju.

Discussion

Garrison's comprehensive self-directed learning model, which is based on "motivation", has its own clear mapping and systematics in the model of learning "by experience". For the first time this self-directed learning model was justified by the American D. Kolb, based on the developments of D. Dewey, K. Levin and J. Piaget[14].

Using their own experience, dentists direct their work towards deepening clinical thinking, improving practical skills and finding an individual approach to the patient, in order to identify personalized features and their behavioral reactions in the process of self-education.

Glavni zadatak u ovoj fazi je ispravna motivacija i doktora i pacijenta. Pri tome, posebna pažnja projektuje se ne samo na praktičnu mobilnost lekara, već i na produbljivanje njegove svesti, unapređenje kliničkog i kreativnog mišljenja. U suprotnom, proces samoobrazovne obuke neće biti potpun, ako se ne unapređuju i ne uzimaju u obzir primarne profesionalne veštine i kvaliteti lekara[15].

Na osnovu analize ovog modela, proces samousmerenog učenja lekara može biti cikličan i predstavljen je kroz četiri komponente, koje se uspešno zamenjuju: konkretno iskustvo, refleksivno posmatranje, apstraktna konceptualizacija i aktivno eksperimentisanje.

U fazi konkretnog iskustva, savetuju se introspekcija i objektivna procena postojećih specifičnih znanja i veština stomatologa, koja će u budućnosti postati predmet optimizacije i diskusije u procesu „samoobrazovanja“.

Ubuduće, stečeno iskustvo dopunjuje se sveobuhvatnom analizom u toku kolektivnog i individualnog rada – produbljivanjem razmišljanja i usavršavanjem praktičnih veština (primenom različitih oblika: slušanjem predavanja, učešćem na naučnim i praktičnim događajima, redovnim čitanjem naučnih i praktičnih sadržaja, čitanjem članaka objavljenih u stručnim publikacijama i materijala dostupnog na internetu)[16].

Osnova za ovo je prelazak na fazu refleksivnog posmatranja, koja omogućava stomatolozima da analiziraju iskustvo stečeno kroz „samousmereno učenje“ i izvuku niz zaključaka u vezi sa nivoom kliničkog razmišljanja i sopstvenim veštinama u određenom delu stomatologije. Prolaz kroz ovu fazu pruža mogućnost da se stomatolozi podstaknu da traže samostalne odgovore na postavljena klinička pitanja i načine praktičnog poboljšanja. Bez takve analize, stečeno praktično iskustvo može ostati nesavršeno.

U fazi apstraktne konceptualizacije vrši se poređenje sopstvenih zaključaka sa zahtevima koje diktira nivo savremene stomatologije u Ukrajini i svetu. Njihovi prethodni zaključci dalje se razvijaju i formiraju jezikom hipoteza i mogućih sopstvenih rezultata, a zatim se testiraju u sledećoj fazi – fazi aktivnog eksperimentisanja. Ova faza pruža proveru praktičnih veština, uzimajući u obzir iskustvo stečeno kroz „samousmereno učenje“ i informacije dobijene u prethodnim fazama. Predložena faza „samoobrazovanja” lekara u procesu kontinuiranog stručnog usavršavanja stomatologa, omogućava da se fokus aktivnosti i inicijative u obrazovnom procesu pomeri ka motivaciji samog lekara.

The main task at this stage is the correct motivation of both the doctor and the patient. At the same time, special attention is projected not only on the practical mobility of the doctor, but also on the deepening of consciousness, the improvement of clinical and creative thinking. Otherwise, the process of self-education training will not be complete if it does not improve and does not take into account the primary professional skills and qualities of a doctor[15].

Based on the analysis of this model, the process of self-directed learning of doctors can be cyclical and is represented by four components that successively replace each other: concrete experience, reflective observation, abstract conceptualization and active experimentation.

At the stage of concrete experience, it is advisable to introspect and objectively assess the existing specific knowledge and skills of the dentist, which in the future will become the subject of optimization and discussion in the process of "self-education".

In the future, the acquired experience is supplemented with a comprehensive analysis in the course of collective and individual work – deepening thinking and improving practical skills (by applying various forms: listening to lectures, participating in scientific and practical events, regularly reading scientific and practical articles in professional publications, materials of Internet resources)[16].

The basis for this is the transition to the reflective observation phase, which allows dentists to analyze the experience gained through “self-directed learning” and draw up a number of conclusions regarding the level of clinical thinking and their own skills in a particular section of dentistry. The passage of this phase provides an opportunity to prompt dentists to search for independent answers to the posed clinical questions and ways of practical improvement. Without such an analysis, the acquired practical experience may remain imperfect.

At the stage of abstract conceptualization there is a comparison of own conclusions with the requirements dictated by the level of current dentistry in Ukraine and the world. Their previous conclusions are further developed and formed in the language of hypotheses and possible own results, and then tested in the next phase – the phase of active experimentation. This phase provides a test of practical skills, taking into account the experience gained through "self-directed learning" and information obtained in previous stages.

To, pak, zahteva promenu strategije postdiplomskog obrazovanja lekara, traženje novih oblika obrazovanja i tehnologija usmerenih u praktičnom smeru. Istovremeno, u prvi plan dolazi pitanje unapređenja kvaliteta samoobrazovanja stomatologa, kroz lično orijentisani model kontinuiranog profesionalnog razvoja[17].

Kombinacija ovih modela, u određenoj meri, odražava zahteve kontinuiranog stručnog usavršavanja zdravstvenih radnika, kao kontinuiranog procesa učenja i usavršavanja stručnih kompetencija specijalista, nakon sticanja visokog obrazovanja u oblasti zdravstvene zaštite i postdiplomskog pripravničkog staža, što omogućava specijalistima da ili unaprede standarde profesionalne delatnosti u skladu sa potrebama zdravstvenog sektora tokom čitavog perioda profesionalne delatnosti. Uključuje učešće u procesu formalnog, neformalnog i informalnog obrazovanja u oblasti zdravstvene zaštite[10,18].

The proposed phase of "self-education" of doctors in the process of continuous professional development of dentists, allows shifting the focus of activity and initiative in the educational process towards the motivation of the doctor himself. This, in turn, requires a change in the strategy of the postgraduate education of doctors, the search for new forms of education, and technologies in the practical direction. At the same time, the issue of improving the quality of self-education of dentists comes to the fore, through a personality-oriented model of continuous professional development[17].

The combination of these models, to a certain extent, reflects the requirements of continuous professional development of healthcare professionals – as a continuous process of learning and improving the professional competencies of specialists after they receive higher education in the field of healthcare and postgraduate education in internship. Further, this allows a specialist to improve the standards of professional activity in accordance with the needs of the healthcare sector during the entire period of professional activity. It includes participation in the process of formal, non-formal, and informal education in the field of healthcare[10,18].

Zaključak

Analiza dobijenih rezultata pokazuje to da su glavni načini dobijanja naučnih i praktičnih informacija za stomatologe, u procesu samousmerenog učenja, aktivno uključivanje materijala dobijenih na predavanjima, naučnim i praktičnim događajima, informacije dobijene putem interneta, iz naučne i metodičke literature, iz naučnih članaka domaćih i stranih stručnih časopisa, prevashodno na engleskom jeziku. Ova odredba stvara osnovu za unapređenje rezultata svakodnevne prakse. Pravovremeno i sveobuhvatno informisanje stomatologa i proširenje njihovog znanja utiče na dalji razvoj i postizanje visokoefikasnih rezultata lečenja. Važni aspekti procesa samousmerenog učenja lekara su njihova sposobnost rada sa naučnom literaturom i veštine sistematizacije i obrade medicinskih informacija.

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Zahvalnice: Nema

Conclusion

According to the analytical results, it is shown that the main ways of obtaining scientific and practical information for dentists in the process of self-directed learning is the active involvement of the materials gained on the lectures, scientific and practical events, from Internet resources, from scientific and methodological literature, from scientific articles of domestic and foreign English-language professional journals. This provision creates the basis for improving the results of daily practice. Timely and comprehensive informing of dentists and the expansion of their knowledge affects the further development and achievement of highly effective treatment results. An important aspect of the process of self-directed learning of doctors is their ability to work with scientific literature and the skills of systematizing and processing of medical information.

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PRIKAZ SLUČAJA I PREGLED LITERATURE
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ORALNI PIOGENI GRANULOM: PRIKAZ SLUČAJA I PREGLED LITERATURE

ORAL PYOGENIC GRANULOMA: A CASE REPORT AND REVIEW OF LITERATURE

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Sažetak

Uvod: *Piogeni granulom je uobičajena neoplastična izraslina u usnoj duplji, koja je po prirodi hiperplastična. Predložene su različite teorije etiopatogeneze za piogeni granulom. Obično se smatra da nastaje kao odgovor na različite lokalne iritanse, kao što su kamenac, materijal stranog tela itd. Hemoragičan je i često krvari na dodir. Obično izaziva lokalne smetnje. Eksciziona biopsija smatra se tretmanom izbora za piogeni granulom, nakon čega sledi uklanjanje lokalnih iritansa, kako bi se izbeglo ponavljanje oboljenja. U ovom članku, prikazan je slučaj oralnog piogenog granuloma na gingivi, koji se proteže do nepca, kod pacijenta starosti 54 godine, uz istovremeni prikaz pregleda literature.*
Metode: *Posle uzimanja detaljne anamneze i kliničkog pregleda, postavljena je radna dijagnoza piogenog grandoma. Urađena je eksciziona biopsija i lezija je poslata na patohistološki pregled.*
Rezultat: *Patohistološkim pregledom lezije potvrđena je klinička dijagnoza piogenog granuloma.*
Zaključak: *Piogeni granulom nije neoplastične prirode i stoga je potrebno detaljno poznavanje ove lezije, kako bi se identifikovala u ranoj fazi i na odgovarajući način lečila, pre nego što izazove bilo kakvu smetnju u normalnim rutinskim funkcijama.*

Ključne reči: *piogenost, hiperplazija, granulom, reaktivnost*

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Abstract

Uvod: *Pyogenic granuloma is a common non neoplastic growth in the oral cavity which is hyperplastic in nature. Various theories of etiopathogenesis have been suggested for pyogenic granuloma. It is commonly thought to be a response to various local irritants like calculus, foreign body material etc. It is hemorrhagic and often bleeds on touch. It usually causes local interference. Excisional biopsy is considered the treatment of choice for pyogenic granuloma followed by removal of the local irritants in order to avoid recurrence. This article presents a case of oral pyogenic granuloma in a 54-year-old patient in the gingiva extending up to the palate with a review of literature.*
Materials and methods: *A thorough case history and clinical examination was done. A provisional diagnosis of pyogenic granuloma was given. Excisional biopsy was performed and the lesion was sent for histopathological evaluation.*
Result: *Histopathological examination of the lesion confirmed the clinical diagnosis of pyogenic granuloma.*
Conclusion: *Pyogenic granuloma is non neoplastic in nature and hence a detailed knowledge of this lesion is required in order to identify it in its early stage and to manage it appropriately before it causes any hindrance in normal routine functions.*

Key words: *pyogenic, hyperplasia, granuloma, reactive*

Uvod

Piogeni granulom (PG) smatra se učestalim tumorom u usnoj duplji. Nije neoplastične prirode[1]. PG predstavlja jedan od različitih tipova inflamatornih hiperplazija u koje spadaju i fibrom, polip pulpe, *epulis fissuratum*, granulom džinovskih ćelija, papilarna hiperplazija i epulis trudnoće[2]. Hullihen[3] je 1844. godine opisao prvi slučaj PG. Termin koji se danas koristi „piogeni granulom" ili *grauloma piogenicum* predložio je Hartzell[4] 1904. godine, te je stoga nazvan i „Crockerova i Hartzellova bolest". Histološki, PG pokazuje brojne krvne sudove i upalu, pa je opisan kao „hemangiozni granulom" od strane Angelopoulosa[5] i *granuloma telangiecacticum* od strane Cawsona i sar [6]. Cawson i sar. dalje su opisali 2 oblika PG; lobularni kapilarni hemangiom i nelobularni kapilarni hemangiom[6].

Smatra se da se PG pojavljuje kao tkivo koje nastaje kao odgovor na lokalnu iritaciju i traumu[1]. Bilo koji stimulans ili bilo koja povreda prisutna u gingivalnom vratu, lokalni iritansi kao što su kamenac, strano telo i loša oralna higijena mogu postati uzročni faktor za pojavu PG i dalja iritacija tkiva rezultiraće bujnom proliferacijom granulacionog tkiva. Drugi predisponirajući faktori uključuju hormone, određene lekove, viruse i bakterije[1,7].

PG je češći kod žena i obično je zastupljeniji u drugoj deceniji života. Oralni PG ima veću sklonost ka gingivi, što mu je i najčešća lokalizacija u usnoj duplji[1].

U ovom članku predstavljamo slučaj piogenog granuloma gingive sa palatinalnim proširenjem kod pacijentkinje stare 54 godine.

Prikaz slučaja

Pacijentkinja stara 54 godine javila se našoj stomatološkoj ordinaciji žaleći se na pojavu izrasline u blizini prednjih, gornjih desnih zuba, koja je bila prisutna od 3 do 4 meseca do trenutka javljanja lekaru. Pacijentkinja je navela da je rast izrasline u početku bio mali, a zatim se postepeno povećavao do veličine koja je zabeležna na prijemu. Izraslina je bila povezana sa tupim povremenim bolom, praćen nelagodnošću i krvarenjem pri dodiru i četkanju. Pacijentkinja ne navodi u anamnezi bilo kakvo drugo vlaženje sa površine lezije. Nije bilo relevantne medicinske istorije bolesti. Pacijentkinja je bila kod stomatologa radi vađenja zuba pre oko 2 do 3 godine i period nakon vađenja protekao je bez ikakvih problema. Nije otkrivena ozbiljna asimetrija lica.

Introduction

Pyogenic granuloma (PG) is considered to be a common tumor like growth in the oral cavity. This is non-neoplastic in nature[1]. PG is one of the various types of inflammatory hyperplasias which also include fibroma, pulp polyp, epulis fissuratum, giant cell granuloma, palatal papillary hyperplasia and pregnancy epulis[2]. Hullihen[3] in 1844 described the first case of PG. The current term pyogenic granuloma or granuloma pyogenicum was coined by Hartzell[4] in 1904 and hence was also called 'Crocker and Hartzell's disease'. Histologically, PG shows numerous blood vessels and inflammation, hence was described as 'hemangiomatous granuloma' by Angelopoulos[5] and 'granuloma telangiectacticum' by Cawson et al.[6]. Cawson et al. further have described 2 forms of PG; lobular capillary haemangioma and non-lobular capillary haemangioma[6].

PG is thought to appear as an exuberant tissue of response to local irritation and trauma1. Any stimulant or injury present in the gingival crevice; local irritants like calculus, foreign body and poor oral hygiene; may become a causative factor for PG to occur and further irritation to the tissues will result in an exuberant proliferative granulation tissue. Other predisposing factors include hormones, certain drugs, viruses and bacteria[1,7].

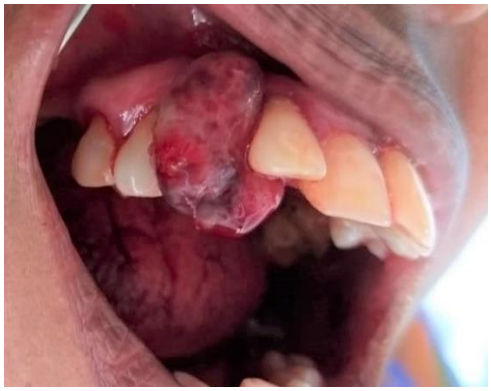
PG is more prevalent in females and usually in the second decade of life. Oral PG has a higher predilection for gingiva thus being the most common site in the oral cavity[1].

Here in this article, we present a case of pyogenic granuloma of the gingiva with palatal extension in a 54-year-old female patient.

Case Report

A 54-year-old female patient reported to our dental clinic with a chief complaint of a growth near upper right front teeth present for 3 to 4 months. The patient reported that the growth was initially small and then gradually increased to the present size. It was associated with dull intermittent type of pain with discomfort and bleeding on touching and brushing. There was no history of any other discharge from the surface of the lesion. There was no relevant medical history. The patient had visited the dentist for the extraction of the teeth around 2 to 3 years back and the post-extraction period was uneventful. No gross facial asymmetry was detected.

Pri intraoralnom pregledu uočena je izraslina ružičastocrvene boje, veličine približno 2 do 3 centimetra, koja polazi od labijalne brazde između zuba 12 i zuba 13, obuhvatajući površinu alveolarnog grebena i proteže se do palatinalnog regiona. Površina lezije je pigmentirana i glatka, osim jednog mesta u centru, koje je bilo ulcerisano. Došlo je do patološke migracije zuba 13 zbog lezije (Slika 1 i Slika 2).



Slika 1: Gingivalna izraslina koja se, posmatrano iz labijalnog pravca, nalazi između zuba 12 i 13 *(Izvor fotografije: Muralijeva kolekcija)*
Figure 1: Gingival growth from labial aspect between 12 and 13 *(Photo courtesy: Murali's Collection)*

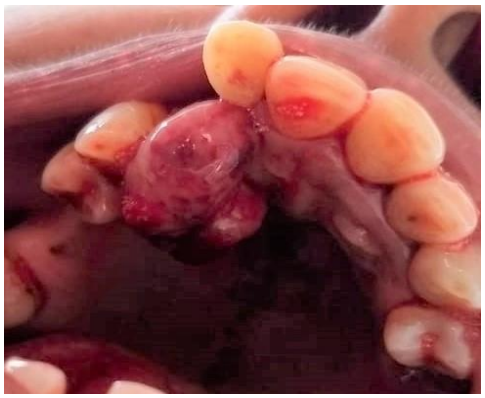
Pri palpaciji, lezija je bila meke konzistencije, osetljiva i krvarila je na dodir. Nedostajali su zubi 15, 16, 17, 25 i 36. Do 26 bili su prisutni zaostali korenovi. Bili su prisutni prebojenost i kamenac.

Na osnovu anamneze i kliničkog pregleda postavljena je privremena dijagnoza piogenog granuloma sa diferencijalnom dijagnozom perifernog gigantcelularnog granuloma, perifernog okoštajućeg fibroma i traumatskog iritacionog fibroma.

Nakon dobijanja pristanka pacijenta, urađena je eksciziona biopsija cele izrasline i poslata je na patohistološki pregled.

Patohistološka analiza pokazala je ulcerisanu površinu sa fibrinoznim eksudatom i vezivnim tkivom koje se ispod nalazilo, a koje se sastoji od obilja velikih vaskularnih prostora obloženih endotelnim ćelijama i brojnim kapilarama, koji bujaju. Gusta infiltracija mešovitih inflamatornih ćelija, ekstravaziranih eritrocita, materije i kolonija mikroba, takođe je primećena u tkivu. Ovakav nalaz bio je kompatibilan sa kliničkom dijagnozom piogenog granuloma (Slika 3).

On intraoral examination; the growth was pinkish red in colour, pedunculated, of approximately 2 x 3 centimeters in size, extending from the labial sulcus between 12 and 13 involving the surface of the alveolar ridge and extending up to the palatal region. The surface of the lesion was pigmented and smooth except for one place at the centre which was ulcerated. There was pathological migration of 13 due to the lesion (Figure 1 and Figure 2).



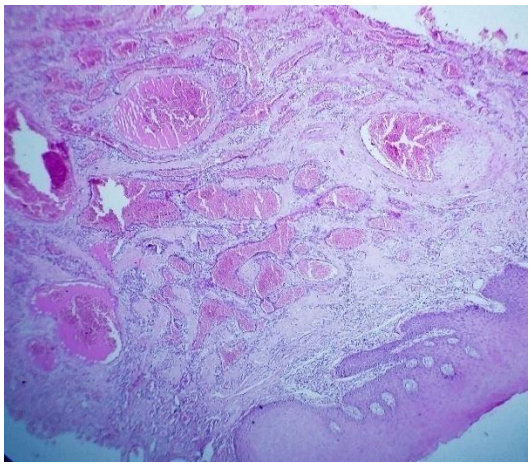
Slika 2: Gingivalna izraslina koja se proteže do palatinalnog regiona zuba 12 i 13*(Izvor fotografije: Muralijeva kolekcija)*
Figure 2: Gingival growth extending to palatal region between 12 and 13 *(Photo courtesy: Murali's Collection)*

On palpation, the lesion was soft in consistency, tender and bled on touch. There were missing teeth wrt 15, 16, 17, 25 and 36. Root stumps were present wrt 26. Stains and calculus was present.

Based on the history and clinical examination provisional diagnosis of pyogenic granuloma was made with differential diagnosis of peripheral giant cell granuloma, peripheral ossifying fibroma and traumatic (irritation) fibroma.

The patient's consent was taken and excisional biopsy of the entire growth was performed and sent for histopathological evaluation.

Histopathological evaluation showed ulcerated surface with fibrinous exudate and underlying connective tissue comprising of abundant large vascular spaces lined by endothelial cells and numerous budding capillaries. Dense infiltration of mixed inflammatory cells, extravasated RBCs, vegetable matter and microbial colonies were also seen in the tissue. This was compatible with the clinical diagnosis of pyogenic granuloma (Figure 3).



Slika 3: Histopatološke karakteristike (piogenog granuloma: Biopsija br. 277/18, ABSMIDS)
Figure 3: Histopathological features *(*of pyogenic granuloma*: Biopsy no. 277/18, ABSMIDS)*

Diskusija

Smatra se da je piogeni granulom vrsta inflamatorne hiperplazije, preuveličana reakcija na lokalne iritirajuće faktore i traumu. Različiti predisponirajući faktori mogu usloviti ovu pojavu kamenac, strani materijal, lošu oralnu higijenu, pa čak i nadoknade preteranih kontura[1,7,8].

Etiopatogeneza

PG se može javiti u svim starosnim grupama, ali češće se javlja kod mladih odraslih osoba, posebno kod žena. Ovo bi moglo biti zbog visokog nivoa cirkulišućih hormona, kao što su progesteron i estrogen[8]. Raniji izveštaji podržali su teoriju o prisustvu uvećanja gingive u trudnoći. Takođe, objavljeno je to da su morfogenetski faktori veći kod PG u poređenju sa normalnom gingivom, čime se podržava ideja o angiogenezi u trudnoći[9,10]. PG se stoga ponekad naziva tumor trudnoće ili granuloma gravidarum, kada se javlja kod trudnica[11].

U literaturi se mogu naći izveštaji u kojima je PG smatran zaraznim entitetom. U studiji sprovedenoj od strane Kerra i drugih[12] određena strana tela, stafilokoki i botriomikoza, kao i lokalizovana infekcija na zidu krvnog suda prijavljeni su kao faktori koji doprinose nastanku PG. Prisustvo gram pozitivnih i gram negativnih bacila u PG opisali su Bhaskar i sar[13]. Shafer i saradnici takođe su prijavili to da PG nastaje usled infekcije od stafilokoka i streptokoka[14]. Međutim, dominantan rast kapilara primećuje se unutar granulomatozne mase PG, a ne stvarnih piogenih organizama i gnoja, tako da je termin piogeni granulom prijavljen kao pogrešan naziv[1].

Discussion

Pyogenic granuloma is said to be a type of inflammatory hyperplasia an exaggerated reaction to local irritating factors and trauma. The various predisposing factors may include calculi, foreign material, poor oral hygiene and even over-contoured restorations[1,7,8].

Etiopathogenesis

PG can occur in all age groups but it is more frequently seen in young adults especially in females. This could be due to the high levels of circulating hormones like progesterone and estrogen[8]. Earlier reports have supported the theory of the presence of gingival enlargements in pregnancy. It's been also reported that morphogenetic factors are higher in PG when compared to normal gingiva thus supporting the idea of angiogenesis in pregnancy[9,10]. PG is therefore sometimes referred as pregnancy tumor or granuloma gravidarum when it occurs in pregnant females[11].

There have been reports in the literature which have regarded PG as an infection entity. Certain foreign bodies, staphylococci and botryomycosis, and localized infection on the wall of the blood vessel have been reported as contributing factors for PG by Kerr at al.[12]. The presence of gram positive and negative bacilli in PG has been described by Bhaskar et al.[13]. Shafer et al. have also reported PG arising due to infection from staphylococci and streptococci[14]. However, predominant growth of capillaries is seen within the granulomatous mass of PG rather than actual pyogenic organisms and pus, so the term pyogenic granuloma has been reported as a misnomer[1].

Neki autori prijavili su PG kao „reaktivni" ili „reparativni" tumorski proces.

Regezi i saradnici predložili su da se okrakteriše kao bujna proliferacija vezivnog tkiva, izazvana poznatim stimulusom ili povredom, poput kamenca ili stranog materijala unutar gingivalne pukotine[7]. Brojni drugi etiološki faktori predloženi su, kao mogući razlozi nastanka PG, kao što su hronična iritacija, lekovi, hormoni, traume, povreda mlečnog zuba, loše restauracije, impaktacija hrane, trauma četkicom za zube itd[8]. Ainamo[15] je takođe sugerisao na to da će ponavljana trauma tokom pranja zuba ili bilo koje druge funkcije koja izaziva oslobađanje različitih endogenih i angiogenih faktora doprineti povećanju vaskularnosti ove lezije.

U ovom konkretnom slučaju, pacijentkinja je bila zdrava žena od 54 godine. Verovatni etiološki faktori u ovom slučaju mogli bi da budu prisustvo velikih količina kamenca, usled loše održavane oralne higijene, ponovljene traume zuba antagonista zbog njihovog položaja i okluzalnih smetnji pri žvakanju hrane zbog njene veličine. Ovo je u skladu sa etiološkim faktorima koji su prethodno pomenuti[7,8,15].

Kliničke karakteristike

Piogeni granulom u usnoj duplji može se javiti u svim životnim dobima, a najčešće se javlja u drugoj i petoj deceniji života. Žene češće oboljevaju od muškaraca[13]. Gingiva je dominantno mesto gde se PG javlja u usnoj duplji, češće na marginalnom, nego pripojnom delu[13,16] . Primećuje se i na usnama, jeziku, bukalnoj sluzokoži, nepcu i mukobukalnom naboru; češće u maksili nego u mandibuli[13]. Veličina PG obično varira između nekoliko milimetara i nekoliko centimetara[7,11].

Intraoralno, PG se pojavljuje kao izdignuta/povišena lezija, koja može biti glatka ili egzofitna na potpornoj ili pedukuliranoj osnovi. Površina je obično prekrivena crvenim hemoragičnim i eritematoznim papulama, koje daju lobularni i bradavičasti izgled, sa ulceracijama[7,11]. Boja lezije varira od ružičaste, preko crvene do crvenkastoljubičaste u zavisnosti od starosti i vaskularnosti[1,17].U prikazanom slučaju, takođe je prestavljena ružičastocrvena izraslina sa pedukuliranom bazom približne veličine 2 cm x 3 cm, koja se proteže od labijalne brazde do palatinalne regije između zuba 12 i 13, koja je imala glatku površinu, osim ulceracije u centru izrasline. Krvarila je na dodir.

PG has been reported as ‘reactive’ or ‘reparative’ tumor process by some authors. It has been suggested as an exuberant proliferation of the connective tissue to a known stimulus or injury like calculus or foreign material within the gingival crevice by Regezi et al.[7]. Numerous other etiologic factors have been suggested like chronic irritation, drugs, hormones, trauma, injury to a primary tooth, defective restorations, food impaction, toothbrush trauma etc.[8]. Ainamo15 has also suggested that recurrent trauma while toothbrushing or any other function causing the release of various endogenous and angiogenic factors will contribute to the increase in vascularity of this lesion.

In the present case, patient was a 54-year-old healthy female. The probable etiologic factor in this case could be due to the presence of large amounts of calculus because of poorly maintained oral hygiene, repeated trauma from the opposing teeth due to its position and occlusal interference while chewing food due to its size. This is in accordance with the etiologic factors mentioned previously[7,8,15].

Clinical features

Pyogenic granuloma in the oral cavity occurs in a wide range of age, more commonly being in the second and the fifth decade of life. Females are more often affected than males[13]. Gingiva is the predominant site where PG is seen in the oral cavity, especially the marginal gingiva than the alveolar part[13,16]. It is also noticed in the lips, tongue, buccal mucosa, palate and mucobuccal fold; frequenting more often in the maxilla than in the mandible[13]. PG usually varies between few millimeters to several centimeters in size[7,11].

Intraorally, PG appears as a raised/elevated lesion which is smooth or exophytic on a sessile or pedunculated base. The surface is usually covered with red hemorrhagic and erythematous papules, which gives a lobulated and warty appearance with ulcerations[7,11]. The colour of the lesion varies from pink to red to reddish purple depending upon the age and vascularity[1,17].

The case presented here also showed a pinkish red growth with pedunculated base of approximately size 2 x 3 cm extending from the labial sulcus up to the palatal region in between 12 and 13 which had smooth surface except for an ulceration at the centre of the growth. It bled on touch.

Patohistološke karakteristike

Sloj parakeratinizovanog ili nekeratinizovanog slojevitog skvamoznog epitela prekriva piogeni granulom. Identi-fikovana su dva histološka tipa PG. Proliferacija krvnih sudova koji su organizovani kao lobularni agregati, vidi se kod prvog tipa i naziva se lobularni kapilarni hemangiom (LCH). Kod drugog tipa primećena je visoko vaskularna proliferacija koja podseća na granulaciono tkivo i to se naziva ne-LCH tipom[11,13,18,19]. Može se videti ulceracija na određenim mestima na površini PG I u takvim slučajevima edem je izražen[13].

Slične patohistološke karakteristike uočene su i u ovom slučaju.

Diferencijalna dijagnoza

U diferencijalnoj dijagnozi piogenog granuloma treba razmotriti periferni osificirajući fibrom, periferni granulom gigantskih ćelija, hemangiom, periferni odontogeni fibrom, hiperplastične upale gingive, konvencionalno granulaciono tkivo, kao i Kapošijev sarkoma i Non-Hodghogkinov sarkom[14,20].

Periferni karcinom gigantskih ćelija može se histološki isključiti zbog prisustva multinuklearnih džinovskih ćelija[7]. Takođe isključuje se prisustvo infektivnog izvora[21]. Periferni osificirajući fibrom i periferni odontogeni fibrom takođe se javljaju pretežno u gingivi, ali mogu se eliminisati zbog minimalne vaskularne komponente u poređenju sa PG[7,22]. Hemangiom se histološki razlikuje prisustvom proliferacije endotelnih ćelija, ali bez akutnog inflamatornog ćelijskog infiltrata koji se vrlo često vidi kod PG[23]. Kapošijev sarkom obično se povezuje sa sindromom stečene imunodeficijencije i pokazuje displastičnu proliferaciju, ćelije vretenaste, vaskularne pukotine, ekstravazirane eritrocite i intracelularna hijalinska tela. Ove karakteristike ne vide se kod PG[19]. Histološki hiperplastična upala gingive izgleda veoma slično PG i stoga se za postavljanje dijagnoze treba osloniti na istoriju bolesti i klinički opis[19].

Terapija

Eksciziona biopsija smatra se zlatnim standardom u lečenju piogenih granuloma. U slučaju da ekscizija izazove bilo kakav izražen deformitet, onda se može planirati inciziona biopsija[22]. Ekscizija lezije praćena uklanjanjem lokalnih predisponirajućih faktora kao što su kamenac, strani materijal i bilo koji drugi lokalni iritansi, obično se preporučuje kao opcija lečenja[11].

Histopathological features

A layer of parakeratinized or non-keratinized stratified squamous epithelium covers pyogenic granuloma. Two histological types of PG have been identified. Proliferation of blood vessels which are organized as lobular aggregates is seen in the first type and is called lobular capillary haemangioma (LCH). In the second type, highly vascular proliferation resembling granulation tissue has been observed and this is called non-LCH type[11,13,18,19]. Ulceration at certain places on the surface of PG may be seen and in such cases edema is prominent[13].

Similar histopathological features were seen in the present case as well.

Differential diagnosis

The differential diagnosis for pyogenic granuloma consists of peripheral ossifying fibroma, peripheral giant cell granuloma, haemangioma, peripheral odontogenic fibroma, hyperplastic gingival inflammation, conventional granulation tissue, Kaposi's sarcoma and Non-Hodgkin's Lymphoma[14,20].

Peripheral giant cell carcinoma can be ruled out histologically due to the presence of multinucleated giant cells[7]. There is also absence of an infectious source[21]. Peripheral ossifying fibroma and peripheral odontogenic fibroma also occur predominantly in the gingiva but can be eliminated because of the minimal vascular component when compared to PG[7,22]. A haemangioma is distinguished histologically by the presence of endothelial cell proliferation but without acute inflammatory cell infiltrate which is very often seen in PG[23]. Kaposi's sarcoma is commonly associated with Acquired Immunodeficiency Syndrome and shows proliferation of dysplastic spindle cells, vascular clefts, extravasated erythrocytes and intracellular hyaline bodies. These features are not seen in PG[19]. Hyperplastic gingival inflammation appears very similar to PG histologically and hence history and clinical description is relied on[19].

Treatment

Excisional biopsy is considered as the gold standard in the treatment of pyogenic granuloma. If in case the excision will cause any marked deformity then incisional biopsy can be planned[22]. Excision of the lesion followed by removal of local predisposing factors like calculus, foreign material and any other local irritant is usually recommended as the treatment option[11].

U ovom slučaju, eksciziona biopsija urađena je da bi se uklonila cela izraslina i ona je poslata na patohistološki pregled. Nakon ekscizije, izvršeno je skaliranje korena kako bi se uklonili svi lokalni faktori poput kamenca i stranog tela koji su mogli biti uzrok.

Različite, druge modalitete lečenja PG isprobali su različiti kliničari, a što uključuje kriohirurgiju, Nd IAG laser, pulsni laser za bojenje sa fleš lampom, laser sa ugljen-dioksidom, elektrodesikacija, skleroterapija i natrijum-tetradecil-sulfat[8].

Stopu recidiva od 16% prijavili su Taira i saradnici u svojoj studiji. Nepravilna/-nepotpuna ekscizija lezije, ponovljena trauma i neuspeh u uklanjanju lokalnih iritanasa, poput kamenca, mogu dovesti do ponovnog pojavljivanja lezije[7,22].

Zaključak

Piogeni granulom je učestala neneoplastična lezija u usnoj duplji. Obično nastaje kao odgovor na lokalne stimuluse/iritanse. Predisponirajući faktori su brojni i stoga je temeljno poznavanje lezije veoma važno, kako bi se razlikovao od drugih stanja, kao i za pravilno lečenje.

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In the present case, excisional biopsy was done to remove the entire growth and sent for histopathological evaluation. Post excision, scaling with root planning was performed in order to remove any local factors like calculus and foreign body material which could have been the cause.

Various other treatment modalities for PG have been tried by different clinicians like cryosurgery, Nd YAG laser, flash lamp pulse dye laser, carbon dioxide laser, electrodessication, sclerotherapy and sodium tetradecyl sulfate[8].

Recurrence rate of 16% has been reported by Taira et al. Improper/incomplete excision of the lesion, repeated trauma and failure to remove the local irritants like calculus may result in recurrence of the lesion[7,22].

Conclusion

Pyogenic granuloma is a common non neoplastic lesion seen in the oral cavity. It usually arises as a response to local stimuli/irritant. The predisposing factors are numerous and hence a thorough knowledge regarding the lesion is very important to differentiate it from other conditions and also for its proper management.

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PRIKAZ SLUČAJA
CASE REPORT
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MOGUĆI EFEKTI HIPERPARATIROIDIZMA NA GUBITAK OSEOINTEGRACIJE ZUBNIH IMPLANTATA: PRIKAZ SLUČAJA

POSSIBLE EFFECTS OF HYPERPARATHYROIDISM IN THE LOSS OF OSSEOINTEGRATION OF DENTAL IMPLANTS: A CASE REPORT

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Sažetak

Uvod: *Hiperparatiroidizam (HPT) je čest endokrini poremećaj sa potencijalnim komplikacijama, vezanim za skeletni, bubrežni, neurokognitivni i kardiovaskularni sistem. Njegova povezanost sa nedostatkom oseointegracije zubnih implantata nije opisana u medicinskoj literaturi.*
Prikaz slučaja: *Ovaj prikaz slučaja ima za cilj diskusiju o dva slučaja gubitka zubnih implantata, zbog viskokog nivoa parathormona (PTH,) uz odsustvo bilo kog drugog sistemskog ili lokalnog komorbiditeta, što ukazuje na moguću korelaciju između HPT i odbacivanja implantata. Oba pacijenta upućena su na Kliniku sa žalbama na protetske komplikacije, upalu gingive i pokretljivost zubne proteze. Nakon procene Cone-Beam kompjuterizovanom tomografijom, svi implantati oba pacijenta su uklonjeni, zbog odbacivanja nastalog usled periimplantitisa, a zatim su četiri implantata umetnuta pacijentu i pet implantanata pacijentu 2. Kod oba pacijenta korišćeni su kratki implantati (Bicon LLC, Boston, Massachusetts, USA), prečnika 4 mm i visine 5 mm i napravljene su protezne podstrukture od Trinia® (Bicon LLC, Boston, Masačusets, SAD).U petoj godini posle ugradnje, pacijenti su prijavili komplikacije i neuspeh implantacije. Da bi se utvrdili uzroci nesupeha, izvršena je detaljna pretraga. Pošto nisu otkriveni mogući uzroci neuspeha, pacijenti su morali da urade test krvi kako bi procenili metabolizam kostiju i posebno da bi se procenili nivoi paratiroidnog hormona (PTH), kalcijuma i vitamina D.*
Rezultati: *Rezultati analize krvi pokazali su kod oba pacijenta normalnu kalcemiju, nedostatak vitamina D i povišen nivo PTH. Posle konsultacije endokrinologa, dijagnostikovan je sekundarni hiperparatireoidizam.*
Zaključak: *Sasvim je logično pretpostaviti da gubitak oseointegracije dentalnih implantata može biti u korelaciji sa efektima HPT.*

Ključne reči: *zubni implantati; hiperparatiroidizam; implantologija; osteointegracija; parathormon.*

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Abstract

Background: *Hyperparathyroidism (HPT) is a common endocrine disorder with potential complications on the skeletal, renal, neurocognitive and cardiovascular systems. Its association with the lack of osseointegration of dental implants hasnot been describedin the medical literature.*
Case presentation: *This case report aims to discuss two cases of dental implant loss in which a high level of parathormone (PTH) was found in the absence of any other systemic or local comorbidity, suggesting the possible correlation between HPT and implant.Both patients were referred to the clinic complaining about prosthetic complications, gingival inflammation and mobility of the dental prosthesis. After a Cone-Beam computed Tomography evaluation, all implants of both patients were removed for rejection arising from periimplantitis and then four implants were inserted in the patient 1 and five implants in the patient 2. For both patientsshort implants (Bicon LLC, Boston, Massachusetts, USA), featured by 4 mm in diameter and 5 mm in height, were used and the prosthesis substructure was made of Trinia® (Bicon LLC, Boston, Massachusetts, USA). During the fifth year, the patients reported complications and the implant treatment failure. In order to establish the causes of failure, a thorough investigation was performed. Since no causes were detected, the patients were required to perform a blood test to evaluate bone metabolism and specifically to assess parathyroid-hormone levels (PTH), calcium levels and vitamin D.*
Results: *The results of the blood tests showednormal calcemia, vitamin D deficiency and elevated PTH levelsin both patients. After an endocrinologist's consultation, secondary hyperparathyroidism was diagnosed.*
Conclusion: *It is reasonable to assume that the loss of osseointegration of dental implants can be correlated with the effects of HPT.*

Key words: *dental implants, hyperparathyroidism, implantology, osseointegration, parathormone*

Uvod

Stopa uspeha ugradnje implantata je 90% do 95%. Iako je postao tretman izbora, komplikacije koje nastaju ugradnjom zubnih implantata i dalje su jedan od najvećih izazova za stomatologe[1]. Kontinuirano kliničko iskustvo ugazuje na mogućnost da nova sistemska stanja mogu biti povezana sa rizikom od odbacivanja zubnih implantata, kao što je npr. hiperparatiroidizam (HPT). Štaviše, medicinska literatura jedva da izveštava o povezanosti između HPT i odbacivanja zubnih implantata. U stvari, unošenjem ključnih reči na PubMed-u [„hiper-paratiroidizam“ i „neuspeh zubnog implantata“] dobija se samo jedan rezultat[2].

Uloga parathormona (PTH) u našem telu dobro je poznata: PTH je ključni regulator homeostaze kalcijuma i igra suštinsku ulogu u metabolizmu kostiju[3,4,5]. HPT, čak i u svom "asimptomatskom" obliku, povezan je sa potencijalnim morbiditetima, uključujući smanjenu gustinu kortikalne kosti[6].

Rai i saradnici proučavali su oro-mandibularne efekte primarnog HPT[7], što je sistemska hiperkalcemijska bolest, kod koje su gubitak lamine dure, izgled poput brušenog stakla i smanjenje širine donje vilice uobičajeni nalazi[7].

Sekundarni hiperparatiroidizam je česta komplikacija oboljenja bubrega. Kod hronične bolesti bubrega dolazi do zadržavanja fosfata, smanjene bubrežne sinteze aktivnog vitamina D (kalcitriola), sa rezultujućom hipokalcemijom i sekundarnim hiper-paratiroidizmom. Ako se ne leči, dolazi do pojave osteodistrofije (*osteitis fibrosa cistica*)[2,8].

Zbog toga je velika verovatnoća da bi neravnoteža u nivou PTH-a mogla izazvati promene u kostima, što može usloviti i odbacivanje implantata.

Ovaj prikaz slučaja ima za cilj da otkrije sistematska stanja, poput hiper-paratireoze, koja mogu direktno da doprinesu odbacivanja implantata, a koja još uvek nisu uključena među faktore rizika koji se procenjuju u preoperativnoj i postoperativnoj fazi.

Materijali i metode

2.1. Prikaz slučajeva

U 2019. godini dva pacijenta upućena su na dalje zbrinjavanje na Odeljenje za oralnu hirurgiju UOC, Stomatološke klinike, “Sapijenca” Univerziteta u Rimu, Italija, a koja su prethodno rehabilitovana fiksnom protezom, sa punim zubnim lukom fiksiranim na donjim lukovim sa četiri implantata (Pacijent 1) odnosno pet implantanata (Pacijent 2).

Introduction

The success rate of implants is reported to be 90%–95%. Although it has become the treatment of choice, the complications arising from dental implant placement are still one of the biggest challenges for dentists[1]. In continuous clinical experience, there is a possibility that new systemic conditions may be associated with a risk of failure of dental implants, such as hyperparathyroidism (HPT). Moreover, the medical literature barely reports the association between HPT and dental implants failure. In fact, the search ofthe PubMed by entering the keywords ["hyperparathyroidism" and "dental implant failure"] returned only one result[2].

The role of parathormone (PTH) within our body is well known: PTH is a crucial regulator of calcium homeostasis and plays an essential role in bone metabolism[3,4,5]. HPT, even in its "asymptomatic" form, is associated with potential morbidities, including decreased cortical bone density[6].

Rai et al. studied the oromandibular effects of primary HPT[7], which is a systemic hypercalcemic disease where loss of lamina dura, ground glass appearance, and mandibular cortical width reduction are common findings[7].

Secondary hyperparathyroidism is a frequent complication of kidney diseases. With chronic kidney disease there is phosphate retention, decreased renal synthesis of active vitamin D (calcitriol) with resultant hypocalcemia and secondary hyper-parathyroidism. If untreated, osteodystrophy (osteitis fibrosa cystica) develops[2,8].

It is therefore highly probable that an imbalance in PTH could cause bone alterations, which could lead then to implant failure.

This case report aims to bring to light systematic conditions, such as hyper-parathyroidism, which may contribute directly to implant failure and which have not yet been included among the risk factors to be assessed in the pre- and post-operative phases.

Materials and Methods

2.1. Cases Presentation

In 2019, two patients in care at the UOC Oral Surgery Department of Dental Sciences, Dental Clinic “Sapienza” University of Rome (Italy), and previously rehabilitated with a full arch cement-retained fixed prosthesis on four implants (Patient 1) and five implants (Patient 2) at the lower arch, were referred to our clinic for further management of prosthetic complications.

Pacijenti su rehabilitovani fiksnom protezom pričvršćenom cementom, sa punim lukom, po istom hirurškom i protetskom protokolu, 2014. godine.

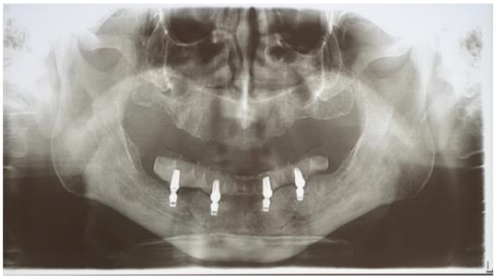
Kod oba pacijenta ugrađeni su kratki implantati (Bicon LLC, Boston, Masačusets, SAD), prečnika 4 mm i visine 5 mm. Implantat karakteriše plato dizajn, čista konusna veza, koso rame, hemisferni profil uporišta i površinska obrada kalcijum-fosfatom. Implantati i abatmenti sistema napravljeni su od legure titanijuma Ti6Al4V. Podstruktura proteze izrađena je od Trinia® (Bicon LLC, Boston, Massachusetts, SAD). Pod-konstrukciju upotpunili su zubi proteze od kompozitnog materijala.

Pacijent 1

Muškarac star 71 godinu požalio se na pokretljivost proteze i nemogućnost žvakanja hrane. Kliničkim pregledom uočena je upala gingive i klinička pokretljivost proteze. CBCT otkrivena je radiolucencija svojstvenu periimplantatu lokalizovanu na svim implantima (Slika 3). S obzirom na lokalne uslove, uklonili smo sve implantate i protezu zbog ekstremne pokretljivosti nosača.

Pacijent 2

Žena stara 70 godina javila se na kliniku zbog krvarenje gingive, pokretljivosti proteze i bola tokom žvakanja. Kliničkim pregledom uočeni su upala gingive i lokalni bol. Ortopantomografijom otkrivena je periimplantna radiolucencija, lokalizovana na implantatima postavljenim na mestima 33 i 41. Nastavili smo sa uklanjanjem proteze (implantat na mestu 41 sam je ispao tokom ove procedure; videti Sliku 4) i zabeležili kliničku pokretljivost dva implantata. Imajući u vidu lokalne uslove, uklonili smo dva implantata postavljena na mestima 33 i 42 (Slika 5) i ponovo prilagodili postojeći okvir lokalnim uslovima. Ostala tri implantata (43, 45 i 35) popustila su u narednim mesecima.



Slika 1. Pacijent 1: četvorogodišnje praćenje
Figure 1. Patient 1, four-year follow-up

The patients were rehabilitated with a full arch cement-retained fixed prosthesis, by the same surgical and prosthesis protocol, in 2014.

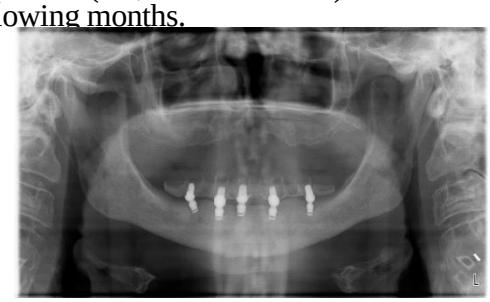
Both patients received short implants (Bicon LLC, Boston, Massachusetts, USA), featured by 4 mm in diameter and 5 mm in height. The implant is characterized by a plateau design, a pure locking taper connection, sloping shoulder, abutment hemispheric profile and calcium phosphate surface treatment. The implants and abutments of the system are made of the titanium alloy Ti6Al4V. The prosthesis substructure was made of Trinia® (Bicon LLC, Boston, Massachusetts, USA). The substructure was completed by denture teeth made of composite material.

Patient 1

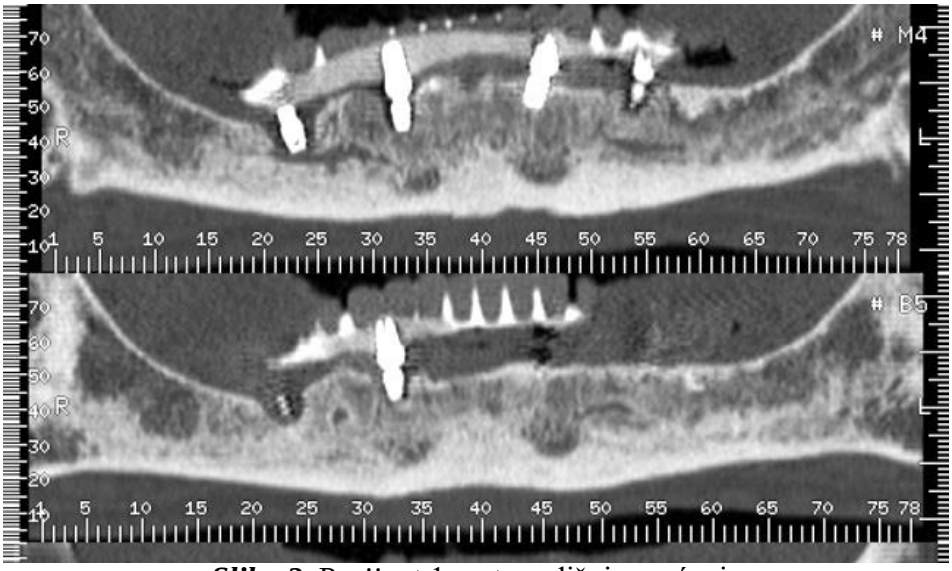
A 71-year-old man complained about prosthesis mobility and the impossibility of food chewing. By clinical examination, we detected gingival inflammation and clinical mobility of the prosthesis. The CBCT revealed a peri-implant radiolucency localized to all fixtures (Figure 3). Considering the local conditions, we removed all implants and the prosthesis due to the extreme mobility of the fixtures.

Patient 2

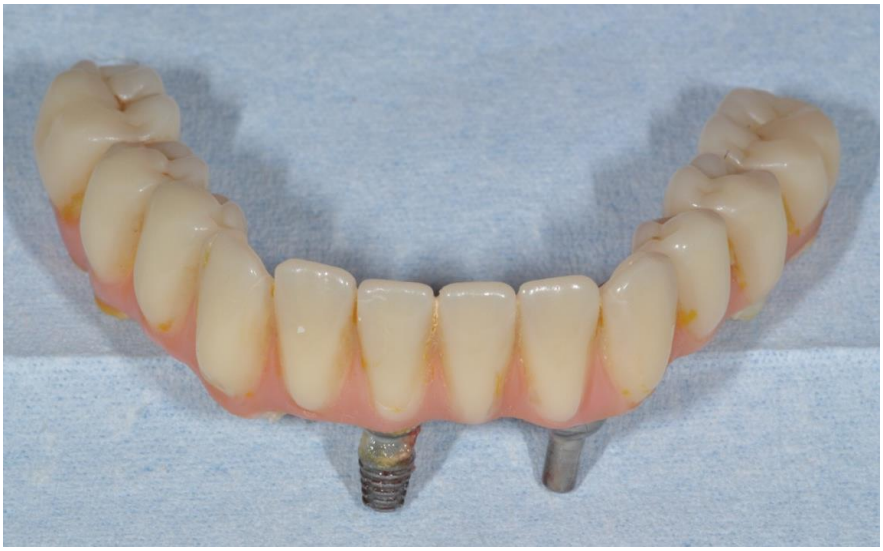
A 70-year-old womanpresented with gingival bleeding, prosthesis mobility and pain during the mastication. By clinical examination, we detected gingival inflam-mation and local pain. The orthopantomography revealed a peri-implant radiolucency localized to the implants placed in sites 3.3 and 4.1. We proceeded to remove the prosthesis (the implant in site 4.1 removed itself during this procedure, see Figure 4) and recorded the clinical mobility of the two implants. Considering the local conditions, we removed the two implants placed in sites 3.3 and 4.2 (Figure 5) and readapted the existing framework to local conditions. Other three implants (4.3, 4.5 and 3.5) failed in the following months.



Slika 2. Pacijent 2: petogodišnje praćenje
Figure 2. Patient 2, four-year follow-up



Slika 3. Pacijent 1: petogodišnje praćenje
Figure 3. Patient 1, five-year follow-up



Slika 4. Pacijent 2: Klinička fotografija kompletno uklonjene proteze sa pričvršćenim neuspelim implantom
Figure 4. Patient 2, clinical photo of the prosthesis removed in its entirety, with the failed implant attached

2.2. Hirurški protokoli

Operacija je uključivala ugradnju četiri implantata (Pacijent 1) i pet (Pacijent 2) kratkih imlantanata, respektivno.

Sledeće, navedene, procedure sprovedene su kod oba pacijenta.

Nakon lokalne anestezije mepivakainom sa adrenalinom, korišćenjem sklapelnog sečiva Bard Parker #15, urađen je režanj pune debljine; krov režnja podignut je i održavan Lagenbeck retraktorom.

Osteotomija na mestu implantata izvedena je upotrebom prvog pilot borera (prečnika 2 mm) koji radi pod vodenim hlađenjem pri konstantnoj brzini od 10000

2.2. Surgical Protocols

The surgery involved the insertion of four (patient 1) and five (patient 2) short implants.

The following procedures were performedin both patients.

After local anesthesia with mepivacaine with adrenaline, using a Bard-Parker #15 scalped blade, a full thickness flap was performed; the flap was raised and maintained with a Langenbeck retractor.

The implant site osteotomy was performed using a first pilot drill (2 mm diameter) working under irrigation at a constant speed of 10.000 rpm, followed by

o/min, a zatim četiri atraumatska borera (prečnika 2,5 mm, 3 mm, 3,5 mm i 4 mm) koji se rotiraju brzinom od 50 o/min, bez vodenog mlaza. Veličina poslednjeg zavrtnja bila je jednaka veličini implantata i implantat je postavljen pod pritiskom, linija do linije, od 1 mm do 3 mm ispod kosti. Urađen je šav sa Vicril 3.0. Postoperativno propisani su amoksicilin 1 g dva puta dnevno tokom šest dana i ibuprofen 600 mg dva puta dnevno tokom dva dana.

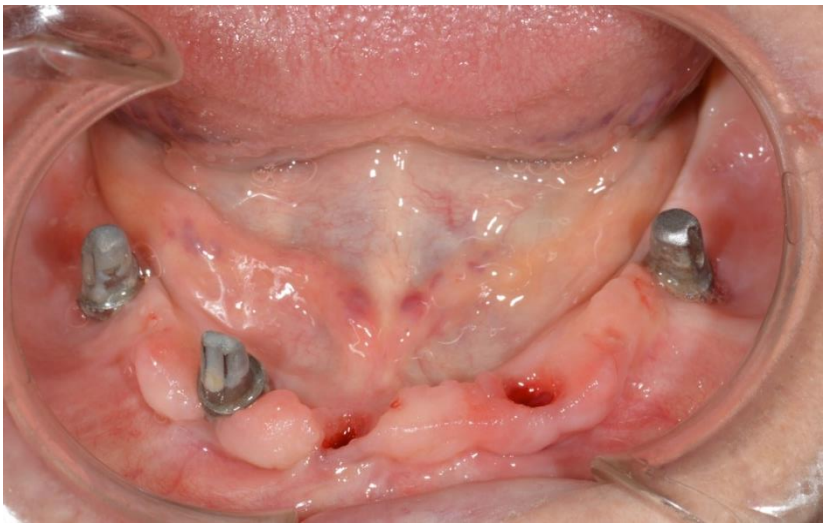
2.3. Protetski protokol

Nakon tri meseca implantati su hirurški otkriveni i postavljene su kapice za zarastanje. Dve nedelje kasnije uzet je otisak sa implantima i zuba antagonista. Proteza je cementirana upotrebom privremenog sredstva za cementiranje (Temp Bond NE, Kerr). Zatim je izvršena kontrola okluzije.

four atraumatic drills (diameter 2,5-3-3,5-4 mm) rotating at a speed of 50 rpm, without irrigation. The size of the last reamer was equal to the size of the implant and the implant was placed under pressure, line to line, from 1 to 3 mm below the bone. Suture with Vicryl 3.0 was performed. Amoxicillin 1 g twice daily for six days, and ibuprofen 600 mg twice daily for two days were prescribed as postoperative therapy.

2.3. Prosthetic protocol

After three months, implants were surgically exposed and the healing abutments were applied. Two weeks later, a full arch polyvinyl siloxane impression of the implants and the opposing teeth was taken. The prosthesis was cemented using a temporary luting agent (Temp Bond NE, Kerr). Then, the control of the occlusion was performed.



Slika 5. Pacijent 2: Klinička fotografija dobijena tokom uklanjanja implantata
Figure 5. Patient 2, Clinical photo obtained during implant removals

2.4. Praćenje

Kontrolne posete su bile zakazivane jednom godišnje nakon proteziranja pacijenata, na Odeljenju za oralnu hirurgiju UOC, Stomatološke klinike „Sapijenca“ Univerziteta u Rimu (Italija).

Tokom prve četiri godine klinička i radiografska kontrola nije pokazala komplikacije. Radili smo panoramski rendgenski snimak tokom četvorogodišnjeg praćenja (Slika 1 i Slika 2).

Tokom pete godine pacijenti su prijavili komplikacije.

2.4. Follow-up

Follow-up visits were scheduled every year after prosthetic loading, at the UOC Oral Surgery Department of Dental Sciences, Dental Clinic “Sapienza” at the University of Rome (Italy).

During the first four years, a clinical and radiographic check showed no complications. We reported the panoramic x-ray at four-year follow-up (Figure 1 and Figure 2).

During the fifth year, the patients reported complications.

Što se tiče mogućih uzroka ova dva slučaja neuspeha, razmatrali smo različite moguće faktore. Oba pacijenta su pregledana na bilo kakve sistemske i lokalne kontraindikacije za rehabilitaciju pre lečenja. Krvni testovi (krvna slika, glukoza u krvi, PT, PTT, INR) i kardiološka procena nisu pokazali nikakve kontraindikacije. Farmakološki tretman dva pacijenta nije bio povezan sa odbacivanjem implantata. Tokom posmatranog perioda nisu zabeležene sistemske promene u zdravlju, a takođe nisu prijavljene promene u farmakološkoj terapiji. Tokom godišnjeg praćenja otkrili smo da nijedna lokalna promena nije mogla da dovede do odbacivanja implantata. Okluzalno preopterećenje je već isključeno zbog toga kompletnog uklanjanja proteze sa suprotnog luka.

Zbog toga, od pacijenata smo zahtevali da urade test krvi da bi procenili metabolizam kostiju i posebno da bi procenili nivoe paratiroidnog hormona (PTH), kalcijuma i vitamina D.

Podaci testova krvi nisu bili u granicama normale. Rezultati pokazuju normalnu kalcemiju, nedostatak vitamina D i povišen nivo PTH.

Pacijente smo uputili endokrinologu koji je kod oba pacijenta dijagnostikovao sekundarni hiperparatireoidizam.

Diskusija

Sekundarni hiperparatiroidizam je sistemska bolest koja uzrokuje gubitak koštane mase. Ovo stanje se može javiti kod nedostatka vitamina D, dugotrajne terapije litijumom i hronične bubrežne bolesti.

Ding i saradnici su 2019. goine analizirali su komplikacije i preživljavanje implantata nakon hemiartroplastike kod pacijenata sa bubrežnom bolešću. Incidencija labavljenja bila je veća kod pacijenata sa hiperparatiroidizmom. Hiper-paratiroidizam nije bio povezan sa intraoperativnim prelomima, ali je bio povezan sa povećanim stopama radiografskog labavljenja u poređenju sa svim pacijentima[9].

U dva prikazana slučaja, pretpostavljamo da je gubitak oseointegracije zubnih implantata u korelaciji sa efektima HPT. Analizirali smo sve parametre koji su trenutno u korelaciji sa rizikom od kasnog odbacivanja implantata[10] i uspeli smo da ih sve isključimo. Farmakološki tretman dva pacijenta nije bio povezan sa odbacivanjem implantata i nije se menjao tokom godina. Tokom posmatranog perioda nisu zabeležene sistemske zdravstvene promene.

Concerning the possible causes of these two failure cases, we took plenty of considerations. Both patients were screened for any systemic and local contraindication for the rehabilitation before the treatment. The blood tests (blood count, blood glucose, PT, PTT, INR) and the cardiologic assessment did not show any contraindication. The pharmacologic treatment of the two patients was not related to implant failure. Neither systemic health alterations nor changes in pharmacological therapy were reportedduring the observation period. During the annual follow up, we detected that no local alteration was able to lead to implant failure. Occlusal overload was already excluded due to the presence of a complete removable denture at the opposing arch.

This being the case, we required patients to perform a blood test to evaluate bone metabolism and specifically to assess parathyroidhormone levels (PTH), calcium levels and vitamin D.

The data of the blood tests were not in the normal range. The results showed normal calcemia, vitamin D deficiency and elevated PTH levels.

We referred the patients to an endocrinologist who diagnosed secondary hyperparathyroidism.

Discussion

Secondary hyperparathyroidism is a systemic diseasecausing bone loss. This condition can occur with vitamin D deficiency, long-term lithium therapy, and chronic renal disease.

In 2019 Benjamin TK Ding et al. analyzed the complications and implant survivorship of hemiarthroplasty in patients with renal disease. The incidence of loosening was higher in patients with hyper-parathyroidism. Hyperparathyroidism was not associated with intraoperative fractures but was associated with increased rates of radio-graphic loosening when compared among all patients[9].

In the two cases presented, we assume that the loss of osseointegration of dental implants is correlated with the effects of HPT. We have analyzed all the parameters that are currently correlated with a risk of late implant failure[10] and were able to rule out all of them. The pharmacological treatment of the two patients was not related to implant failure and did not change over the years. No systemic health alterations were recorded during the observation period. During the annual follow up, we detected that no local alteration could lead to implant failure.

Tokom godišnjeg praćenja otkrili smo da nijedna lokalna promena nije mogla da dovede do odbacivanja implantata. Okluzalno preopterećenje je već isključeno zbog činjenice da je na suprotnom lulu proteza kompletno uklonjena.

Zubni implantati su u kontinuiranoj interakciji sa koštanim tkivom, prenoseći mehanička opterećenja na ekstracelularni matriks[11]. Alternacija osteogeneze i resorpcije karakteriše ovaj proces interakcije, a zakoni Volfa i Frosta[12] ga regulišu. U slučaju visokih nivoa PTH, povećanje osteoklastne aktivnosti[13] dovodi do poremećaja ravnoteže sistema u pravcu resorpciji kostiju. Osim toga, visoki nivoi PTH mogu smanjiti mineralizaciju i pogoršati kvalitet minerala i kolagena u novoformiranoj kosti[14]. Dakle, ako kortikalna kost gubi debljinu usled bolesti i trabekularna kost se formira slabije mineralizovana, onda to može ugroziti osteointegraciju potpornog implantata. Ovo možda neće biti klinički evidentno sve dok ne dođe do kasnog neuspeha u proteznoj fazi[2].

Oba efekta mogu dovesti do odbacivanja implantata, kao što se to pretpostavlja u ova dva prijavljena slučaja.

Pošto ova dva pacijenta nisu imala nikakvu analizu nivoa PTH pre rehabilitacije implantata, nema informacija o tome kada je došlo do metaboličke promene. Međutim, pošto nije bilo izveštaja o tome u periodu od 5 godina, autori smatraju da je do oboljenja došlo nakon implantacije.

S obzirom na prijavljene destruktivne efekte u ova dva slučaja, poželjno je sprovesti studije kako bi se pokazalo da li visok nivo PTH može biti povezan sa gubitkom oseointegracije.

Ako se to potvrdi, treba obratiti pažnju na mogućnost ispitivanja nivoa PTH pre podvrgavanja implantoterapiji i tokom perioda praćenja, posebno kod visoko rizičnih pacijenata[6]. Međutim, biće potrebne dalje i opsežne studije koje bi pratile ovu povezanost kak bi se potvrdila klinička hipoteza.

Autori treba da prodiskutuju rezultate i kako se oni mogu tumačiti iz perspektive prethodnih studija i radnih hipoteza. O nalazima i njihovim implikacijama treba razgovarati u najširem mogućem kontekstu. Takođe se mogu istaknuti i budući pravci istraživanja.

Occlusal overload was already excluded due to the presence of a complete removable denture at the opposing arch.

Dental implants are in continuous interaction with the bone tissue, transferring the mechanical loads to the extracellular matrix[11]. An alternation of osteogenesis and resorption characterizes this interaction process, and the laws of Wolff and Frost[12] regulate it. In the case of high PTH levels, an increase in osteoclastic activity[13] unbalances the system towards bone resorption. In addition, high PTH levels can reduce mineralization and worsen mineral and collagen quality in a newly formed bone[14]. Therefore, if the cortical bone is losing thickness because of the disease and trabecular bone is formed preferentially but not being substantially mineralized, then supportive implant osseointegration may be compromised. This may not be clinically evident until there is a late failure in the prosthetic phase[2].

Both effects could lead to implant failure, as supposed in the two reported cases.

Since the two patients did not have any analysis of PTH levels before implant-prosthetic rehabilitation, there is no information on when the metabolic alteration occurred. However, since there were no reports on this in the 5-year observation period, it is the authors' opinion that the pathogenesis occurred after the implant treatment.

Given the destructive effects reported in these two cases, it is desirable to conduct studies to demonstrate whether a high level of PTH could be related to the loss of osseointegration.

If ascertained, we should pay attention to the possibility of investigating the levels of PTH before undergoing implant therapy and during the follow-up period, especially in high-risk patients[6].

Nevertheless, further and extensive association studies will be needed to validate the clinical hypothesis.

Authors should discuss the results and how they can be interpreted from the perspective of previous studies and of the working hypotheses. The findings and their implications should be discussed in the broadest context possible. Future research directions may also be highlighted.

Zaključak

Na osnovu prikazanih slučajeva, logično je pretpostaviti da gubitak oseointegracije dentalnih implantata može biti u korelaciji sa efektima HPT. Međutim, s obzirom na ograničenje ovog prikaza slučajeva, biće potrebne dalje studije da bi se potvrdila veza HPT sa neuspehom u ugradnji implantata i gubitkom osteointegracije.

Conclusion

According to the presented cases, it is reasonable to assume that the loss of osseointegration of dental implants can be correlated with the effects of HPT. However, since the limitation of this case report, further studies will be needed to validate the relationship with HPT and implant failure and loss of osteointegration

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INDIKATORI ORALNOG ZDRAVLJA KAO PROGNOSTIČKI FAKTOR ZA KVALITET ŽIVOTA PACIJENATA SA KARCINOMOM GLAVE I VRATA U GUDŽARATU U INDIJI

ORAL HEALTH INDICATORS AS A PREDICTIVE FACTOR FOR THE QUALITY OF LIFE AMONG HEAD AND NECK CANCER PATIENTS IN GUJARAT IN INDIA

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Sažetak

Ciljevi *ove studije bili su procena veličine različitih indikatora oralnog zdravlja i određivanje indikatora oralnog zdravlja, kao prognostičkog faktora za kvalitet života pacijenata sa karcinomom glave i vrata.*
Metode. *Studija preseka sprovedena je među 400 pacijenata sa karcinomom glave i vrata, koji su zbrinuti u zdravstvenom centru na onkološkom odeljenju. Model specifičan za glavu i vrat (EORTC KLK H&N35), Evropske organizacije za istraživanje i lečenje raka, korišćen je za procenu kvaliteta života pacijenata. Indikatori oralnog zdravlja (praktikovanje oralne higijene, oralne komplikacije, posete stomatologu, oralna rehabilitacija) evidentirani su pomoću pregleda usne duplje i upitnika, odnosno razgovorom sa pacijentom. Spearmanov koeficijent korelacije korišćen je za procenu odnosa između indikatora oralnog zdravlja i različitih skala kvaliteta života. Za procenu uticaja indikatora oralnog zdravlja, kao prognostičkog faktora za kvalitet života, primenjena je multivarijantna linearna regresija.*
Rezultati. *Od 400 pacijenata, 54,25% pacijenata prijavilo je jedan ili drugi oblik oralnih komplikacija. Parodontalni problemi bili su česta oralna komplikacija među pacijentima. Postojala je slaba korelacija između indikatora oralnog zdravlja i većine skala EORTC KLK-H&N35. Utvrđeno je da su teoretski povezani indikatori oralnog zdravlja značajni prognostički faktori.*
Zaključak. *Rezultati pokazuju prisustvo visokog stepena indikatora lošeg oralnog zdravlja. Indikatori oralnog zdravlja takođe su delovali kao značajan prediktor kvaliteta života. U cilju poboljšanja oralnog zdravlja poželjan je multidisciplinarni pristup, čime bi bio poboljšan i kvalitet života pacijenata sa karcinomom glave i vrata.*

Ključne reči: *karcinom glave i vrata, oralne komplikacije, oralno zdravlje, kvalitet života*

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Abstract

Aim: *The aim of this study wasto assess themagnitude of various oral health indicators. Further, toidentify the oral health indicators as a predictive factor forthe quality of life among head and neck cancer patients.*
Methods: *A cross-sectional studywas conducted among400 head and neckcancer patients attending tertiary cancer center. The European Organization for Research and Treatment of Cancer and Head and Neck specific(EORTCQLQH&N35)modulewas used to assess the patient's quality of life. Oral health indicators (oral hygiene practices, oral complication, dental visits, oral rehabilitation) were recorded through oral examination and personal interviews. Spearman's correlation coefficient was used to assess the correlation between oral health indicators and different scales of QoL. Multivariate linear regression by a backward stepwise methodwas applied to assess the influence of oral health indicators as a predictive factor forQoL.*
Results: *Out of 400 patients, 54.25% of patients reportedhaving one or another form of oral complication. Periodontal problems were the common oral complication among the patients. There was a weak correlation between oral health indicators and most of the scales of EORTC QLQ-H&N35. Theoretically, linked oral health indicators were found to be significant predictive factors.*
Conclusion: *The results show thatthere was a high magnitude of poor oral health indicators.Oral health indicators also acted as a significant predictor of quality of life. A multi-disciplinary approach is desirable for the improvement in oral health thus improving the overall quality of life among head and neck cancer patients.*

Key words: *head and neck cancer, oral complications, oral health, quality of life*

Uvod

Preživljavanje pacijenata najveći je prioritet za osobe koje boluju od nekog oblika karcinoma. Uprkos savremenijim terapijskim tehnologijama, preživljavanje karcinoma glave i vrata (KGV) nije se poboljšalo. KGV i njegov tretman utiču na izgled, funkciju, psiho-socijalni i ekonomski status pacijenta. Kao rezultat toga, kada se odlučuje o dobrobiti preporučenog tretmana vezano za pacijenta, kvalitet života (KŽ) tog preživljavanja postaje glavna tema prilikom razmatranja[1]. Dakle, podaci o kvalitetu života postaju važan aspekt pružanja informacija o ishodima lečenja za pacijente obolele od KGV[2]. KGV zahvata skvamozni epitel ćelija usne duplje, ždrela, larinksa, paranazalnih sinusa i nosne šupljine. Ove kraniofacijalne strukture igraju glavnu ulogu u vitalnim aktivnostima, kao što su fonetika, žvakanje i gutanje. Dakle, pacijentima koji pate od KGV-a potrebna je intenzivnija nega i održavanje prihvatljivog oralnog zdravlja u poređenju sa pacijentima koji imaju karcinom druge lokalizacije[3]. Kako navode Hashim i sar.[4], različiti indikatori oralnog zdravlja kao što su oralna higijena, karijes, parodontitis, nedostatak zuba, kserostomija, upala sluzokože, protetska nadoknada i poseta stomatologu imali su značajan uticaj na kvalitet života kod pacijenata sa KGV. Postoje čvrsti dokazi koji sugerišu da su ovi pokazatelji pogođeni usled hirurške intervencije, radioterapije, hemoterapije i/ili kombinacije lečenja karcinoma[5]. Preživeli pacijenti posle tretmana prijavili su oralne komplikacije kao što su loša oralna higijena[6], smanjeno lučenje pljuvačke[7], mukozitis[8], zubni karijes[9], parodontitis[10], i smanjena mastikacija[11]. Kao rezultat toga, preživeli imaju bolove, fizičku i emocionalnu nelagodnost, deformitete, zavisnost, promene navika u ishrani i gubitak samopoštovanja, što na kraju pogoršava kvalitet života[12].

Prognostička uloga gorepomenutih indikatora oralnog zdravlja za smanjen kvalitet života među pacijentima obolelih od KGV bila je neuverljiva, zbog nedostatka informacija o indikatorima oralnog zdravlja u većini studija[13,14]. Nema dovoljno objavljenih podataka u literaturi, koji procenjuju prognostičku ulogu indikatora oralnog zdravlja o kvalitetu života pacijenata sa KGV, što je otežavalo izradu i sprovođenje plana lečenja. Zbog toga, sprovedena je ova studija procene važnosti indikatora oralnog zdravlja (praktikovanje oralne higijene, oralne komplikacije, posete stomatologu, kao i oralna rehabilitacija) među pacijentima sa KGV.

Introduction

The survival of patients is the topmost priority for patients suffering from any form of cancer. Despite recent therapeutics technologies, survival from Head and Neck Cancer (HNC) has not improved. HNC and its treatment affect the patient's appearance, function, psycho-social and economic status. As a result, when deciding on the desirability of a recommended treatment for any patient, the quality of life (QoL) of that survival becomes a major consideration[1]. Hence, QoL data is becoming an important aspect of providing information on treatment outcomes for HNC patients[2].

HNC involves the squamous cell epithelium lining of the oral cavity, pharynx, larynx, paranasal sinuses, and nasal cavity. Thesecraniofacial structures play a major role in vital activities, such as phonetics, mastication, and deglutition. Hence, the patients suffering from HNC need definite care and maintaining acceptable oral health as compared to the patients having cancers of other sites[3]. As reported by Hashim D. et al., various oral health indicators like oral hygiene, dental caries, periodontitis, missing teeth, xerostomia, mucositis, dental prosthesis, and the dental visit had a significant impact on QoL among HNC patients[4]. There is sound evidence suggesting that these indicators areunfavorably affected because of the surgical, radiotherapy, chemotherapy, and/or combination of treatment of cancer[5]. Survivorsfrom HNC treatment reported oral complications like poor oral hygiene[6], decrease salivary flow[7], mucositis[8], dental caries[9], periodontitis[10], anddecrease masticatory function[11]. As a result, the survivors suffer from pain, physical and emotional discomfort, disfigurement, dependence, change in dietary habits, and loss of self-esteem which allultimately deteriorate the QoL[12].

The predictive role of the aforementioned oral health indicators for deprived QoL among HNC patients has been inconclusive because of the lack of information on over one oral health indicator for most studies[13,14]. There is a real scarcity of published literature evaluating the predictive role oforal health indicators of HNC patient's QoL. So, the planning and intervention of treatment outline resulting in a favorable outcome might get compromised. Thus, this study was conducted to assess the magnitude of the oral health indicators (oral hygiene practices, oral complication, dental visits, oral rehabilitation) among the HNC patients.

U ovoj studiji bavili smo se procenom korelacije između indikatora oralnog zdravlja i skale kvaliteta života i indikatora oralnog zdravlja, kao prognostičkih faktora za kvalitet života kod pacijenata sa KGV. Podaci prikupljeni u ovoj studiji pomoći će da se uspostavi efikasan sistem pružanja oralne zdravstvene nege, uključivanjem stomatologa, sa ciljem sprečavanja i lečenja mogućih oralnih komplikacija tokom faze lečenja, pre i posle prisutnog karcinoma i na taj način poboljša ukupni kvalitet života pacijenata sa KGV.

Metode

Dizajn studije i etičko odobrenje

Studija preseka sprovedena je u onkološkom centru tercijarne zdravstvene zaštite u državi Gudžarat, Indija. Pre početka studije, protokol studije dostavljen je institucionalnom odboru tercijarnog centra za onkologiju. Dobijeno je odobrenje za sprovođenje studije (odobrenje etičkog komiteta: ADC/EC/13/108). Studija je sprovedena u skladu sa principima Helsinške deklaracije. Pacijentima je objašnjena svrha studije, a popunjavanje potpisanog upitnika bio je uslov za uključenje u studiju. Prema godišnjem izveštaju centra za onkologiju, stopa prevalencije KGV iznosila je 35,80%. Uzevši u obzir ovu stopu prevalencije, dozvoljenu grešku od 5% i stopu bez odgovora od 10%, sačinjen je uzorak od 400 pacijenata. Obuhvaćeno je 400 pacijenata obolelih od KGV-a u onkološkom centru tercijarne zdravstvene zaštite, koji zadovoljavaju kriterijume:

Kriterijumi za uključivanjeu studiju bili su: histo-patološki potvrđeni slučajevi KGV, pacijenti oba pola i starosti preko 18 godina, pacijenti koji su imali Karnofskijev Status Skor (KSS) preko 60; pacijenti koji su dali pismeni pristanak za učešće u studiji. Kriterijumi isključenja iz studije bili su: pacijenti stariji od 65 godina, pacijenti sa kliničkim recidivom bolesti ili pojavom sekundarnog tumora i periodom preživljavanja većim od 18 meseci nakon lečenja. *Prikupljanje podataka*: Unapred testirana, samostalno dizajnirana forma u vidu razgovora ,upotrebljena je za prikupljanje demografskih detalja (starost, pol, socio-ekonomski status (SPS), prebivalište, bračni status, vrsta porodice. SPS pacijenata procenjen je prema Kupusvamijevoj skali.[15] Glavni istraživač je sproveo oralni pregled i lične intervjue pacijenata, kako bi prikupio informacije o statusu oralnog zdravlja (praktikovanje oralne higijene, oralne komplikacije, posete stomatologu i oralna rehabilitacija). Medicinski detalji kao što su stadijum raka, lečenje su preuzeti iz medicinske dokumentacije pacijenata.

This study further evaluates thecor-relation between oral health indicators and the scales of QoLand also evaluates the oral health indicators as a predictive factor for QoL among HNC patients. The data gathered in this studywill help to establish an effective oral health care delivery system by involving dental professionals to prevent and treat oral complications duringthe preand post-cancer treatment phase and thus improving the overall QoL among HCN patients.

Methods

Study design and ethical permission

A cross-sectional study was conducted at the tertiary cancer care center in the state of Gujarat, India. Before initiating the study, the study protocol was submitted to the institutional review board of the tertiary cancer center.The protocol was reviewed and approval to conduct the study was obtained (ethical approval code: ADC/EC/13/108). The study was conductedper the Declaration of Helsinki. The purpose of the study was explained to patients and the completion of the questionnaire was a condition for entering the study and was regarded as written consent.

Study subjects and eligibility criteria

As per the annual report of the cancer centre the prevalence rate of HNC reported was 35.80%, considering this prevalence rate, allowable error of 5% and 10% non-response rate, a sample of 400 patients of HNCwas considered. Totalof 400HNC patients attending tertiary cancer center and satisfying the following eligibility criteria were enrolled:

Inclusion criteria: histopathologically confirmed cases of HNC, patients of both gender and above 18 years of age, patients who had Karnofsky's Performance Status score (KPS) over 60, and those patients who gave written consent to take part in the study.

Exclusion criteria: patients above 65 years of age, had clinical evidence of disease recurrence or a secondary tumor and had survived for over 18 months after treatment in any form. *Data collection*:A pretested self-designed proformawas used to collect the demographic details (age, gender, socioeconomic status (SES), residence, marital status, type of family) through a personal interview. The SES of the patients was assessed as per Kuppuswamy's scale[15]. The principal investigator conducted an oral examination and personal interviews among the patients to gather information regarding oral health status (oral hygiene practices, oral complications, dental visits, and oral rehabilitation).

Kvalitet života pacijenata je procenjivan korišćenjem prilagođenog upitnika za procenu kvaliteta života pacijenata po specifičanom modelu Evropske organizacije za istraživanje i lečenje karcinoma glave i vrata (EORTC KLK-H&N35)[16]. Korišćena je prethodno upotrebljavana gudžarati verzija ovog upitnika[17]. EORTC KLK-H&N35[16] je tumor-specifičan model koji se koristi za procenu kvaliteta života kod pacijenata sa KGV. Ovaj model upitnika sadrži sedam skala simptoma sa više stavki i jedanaest skala simptoma sa jednom stavkom. Pacijenti su morali da odgovore na pitanja na Likertovoj skali sa odgovorom u rasponu od '1=ni malo' do '4=veoma'. Dok je poslednjih pet stavki EORTC KLK-H&N35 imalo dihotomnu skalu sa formatom ne/da.

Analiza podataka:

Demografske i kliničke karakteristike sumirane su kao učestalost i % starosti. Spearmanov koeficijent korelacije korišćen je za procenu korelacije između indikatora oralnog zdravstvenog statusa i različitih skala kvaliteta života. Uticaj indikatora oralnog zdravlja kao prediktivnog faktora kvaliteta života ispitan je primenom multivarijantne linearne regresije. Korišćena je metoda korak po korak sa eliminacijom unazadza P = 0,05 i P = 0,10 za izbor nezavisnih promenljivih. Za analizu podataka korišćen je statistički paket softver društvenih nauka (SPSS® verzija 22; IBM Corp., Armonk NI, SAD). Nivo značajnosti ograničenja je na P<0,05.

Rezultati

Demografske i kliničke karakteristike pacijenata prikazane su u tabeli 1. Prosečna starost bolesnika bila je 45,47 godina ± 10,31 godina. Pacijenti muškog pola (n = 354, 87,50%) oboleli su u većem broju, u poređenju sa pacijentima ženskog pola, od KGV. Polovina pacijenata (n = 214, 53,50%) pripadala je seoskim zajednicama sa nižim socio-ekonomskim statusom (57,50%). Broj pacijenata koji su se prijavili sa uznapredovalim stadijumom bolesti (III/IV) bio je visok. Kod većine pacijenata primenjena je kombinovana terapija, a kod manjeg broja monoterapija. Četkica za zube bila je najpopularnije sredstvo za oralnu higijenu (n = 1, 20 pacijenata, 30%). Skoro polovina pacijenata (n = 190, 47,50%) nikada u životu nije posetila stomatologa. Više od polovine pacijenata (n = 217, 54,25%) prijavilo je oralne komplikacije (Tabela 2), bilo samo zbog karcinoma ili zbog lečenja. Samo 11% (n = 44) pacijenata imalo je dobro oralno zdravlje. Parodontalni problemi (n = 109, 27,25%) i ograničeno otvaranje usta (n = 9, 8 pacijenata, 24,50%) bile su uobičajene oralne komplikacije pacijenata.

Medical details like the stage of cancer, treatment of cancer, and KPSwere retrieved from patient medical records. The QoL of patients was assessed by using aself-administeredquestionnaire-European Organization for Research and Treatment of CancerHead and Neck specific module (EORTCQLQ-H&N35)[16] was used to assess the QoL of patients. Thepre-validated Gujarati version of this questionnaire was used[17].

The EORTC QLQ-H&N3516 is a tumor-specific module used for the assessment of QoL in HNC patients. It contains seven multi-item symptom scales and eleven single-item symptoms scales. The patients have to answer the questions on a Likert scale with a response ranging from '1=not at all' to '4=very much.' Whereas the last five items of EORTC QLQ-H&N35 have a dichotomous scale having a no/yes format.

Data Analysis

The demographic and clinical characteristics were summarized as frequencies and %ages. Spearman's correlation coefficient was used to assess the correlation between oral health status indicators and different scales of QoL. The influence of oral health indicators as a predictive factor on QoLwas examined using multivariate linearregression.The backward stepwise method was used as having entry with P=0.05 and removal with P=0.10 to select independent variables. Statistical Package for Social Science software (SPSS® version 22; IBM Corp., Armonk NY, USA) was used for data analysis. The level of significance was kept at P<0.05.

Results

The demographic and clinical characteristics of the patients are shown in Table 1. The mean age of the patients was 45.47±10.31 years. Male patients (n=354, 87.50%)outnumbered their female counterparts, showing the predominance of HNC among male subjects. Half of the patients (n=214, 53.50%) belonged to rural communities and had lower socioeconomic status (57.50%). The number of patients reporting at the advanced stage (III/IV) was high. Most of the patients received combined treatment modalities as compared to the single-modality treatment. A toothbrush was the most popular means of oral hygiene aid used (n=120, 30%). Nearly half of the patients (n=190, 47.50%), had never visited the dentist in their lifetime. More than half (n=217, 54.25%) of patients reported oral complications (Table 2) either due to cancer alone or because of its treatment.

Tabela 1. Demografske i kliničke karakteristike pacijenata sa karcinomam glave i vrata
Table 1. Demographic and clinical characteristics of head and neck patients

Variables/Varijable	Number (n=400)/	Variables/Varijable
Mean age (in years)/Prosečna starost(u godinama)	45.47 ± 10.31	
Gender(Pol)		
Men/Muški	350	87.50
Women/Ženski	50	12.50
Location/Lokalizacija		
Urban/Gradsko područije	186	46.50
Rural/Seosko područije	214	53.50
Marital status/Materijalni status		
Unmarried/Neoženjeni	35	8.75
Married/Oženjeni	357	89.25
Divorced/Widow/Razvedeni/Udovci	8	2.00
Socio-economic status/Socio ekonomski status		
Upper/Višisloj	7	1.75
Upper middle/Srenji ka višem	45	11.25
Lower middle/Srednji	80	20.00
Upper lower/Srednji ka nižem	230	57.50
Lower/NIži	38	9.50
Family type/Tip porodice		
Nuclear family/Uža porodica	82	20.50
Joint family/Šira porodica	318	79.50
Site of Tumour/Lokalizacija tumora		
Oral cavity/Usna duplja	340	85.00
Pharynx/hypopharynx /Ždrelo ili hipofarings	26	6.50
Larynx/Grkljan	34	8.50
Stage of cancer/Stadijum karcinoma		
I/ II	122	30.50
III/ IV	278	69.50
Treatment Modalities/Načini lečenja		
No treatment (newly diagnosed)Bez tretmana/ upravo dijagnostikovan	80	20.00
Only surgical/Samo hirurški	39	9.75
Only radiotherapy/Samo radioterapija	25	6.25
Only chemotherapy/Samo hemoterapija	28	7.0
Surgical + Radiotherapy/Hirurški i radioterapija	92	23.00
Radiotherapy + Chemotherapy/Hirurški i hemoterapija	65	16.25
Combination of all/Kombinacija svih terapija	71	17.75

Devijacija otvaranja usta i kserostomija takođe su prijavljeni kao neželjeni efekti operacije i radioterapije. Nakon hirurškog lečenja, skoro polovina pacijenata imala je deformitete. Veoma mali broj pacijenata (n = 38, 9,50%) bio je rehabilitovan uz pomoć maksilofacijalnih proteza, u vidu obturatora i pločastih proteza. Uočena je slaba korelacija između indikatora oralnog zdravlja i većine teorijski povezanih skala EORTC KLK-H&N35 (Tabela 3). Kako bi se procenili prognostički znaci za kvalitet života, primenjena je multivarijantna linearna regresija (Tabela 4). Teoretski povezani indikatori oralnog zdravlja imali su značajan uticaj i zadržani su u modelu posle "backward stepwise" eliminacije.

Only 11% (n=44) of the patients had good oral health. Periodontal problems (n=109, 27.25%) and restricted mouth opening (n=98, 24.50%) were the common oral complications of the patients. Deviated mouth opening and xerostomiawere also reported as the side effects of surgery and radiotherapy, respectively. Following surgical treatment, nearly half of the patients had adisfigurement. Very few patients (n=38, 9.50%) had received rehabilitative service asmaxillo-facial prostheses like obturators and guiding plates.

A weak correlation was observed between oral health indicators and most of the theoretically linked scales of EORTC QLQ-H&N35 (Table 3). To evaluate the predictors for QoL, multivariate linear regression was applied (Table 4).Theoretically linked oral health indicators had significant influence and were retainedin the model after doing backward stepwise elimination.

Tabela 2. Indikator iralnog zdravlja kod pacijenata
Table 2. Oral health indicatorsof patients

Variables/Varijable	Number (n)/Broj(n)	Percent (%)/Procenat(%)
Oral hygiene aids/Sredstva za oralnu higijenu		
None/Ne koristi	10	2.50
Toothbrush/Četkica za zube	120	30.00
Datun/Neem stick/Štapići	26	6.50
Finger/Prst	41	10.25
Mouthwash/Oralni rastvor	76	19.00
Tooth brush + mouthwash/Četkica za zube + oralni rastvor	127	31.75
Dental Visit/Posete stomatologu		
Before diagnosis/Pre dijagnoze	33	8.25
During treatment/U toku tretmana	121	30.25
After diagnosis/Posle dijagnoze	56	14.00
Never/Nikada	190	47.50
Oral complications/Oralne komplikacije		
Yes/Da	217	54.25
No/Ne	183	45.75
Oral health status/Status oralnog zdravlja		
Good oral health/Dobro oralno zdravlje	44	11.00
Periodontal problems/Periodontalni problemi	109	27.25
Mucositis/Mukozitis	41	10.25
Restricted mouth opening/Otežano otvaranje usta	98	24.50
Deviated mouth opening/Devijacija pri otvaranju usta	25	6.25
Edentulous/Bezubi	13	3.25
Pain in mouth/Bol u ustima	20	5.00
Xerostomia/Kserostomija	25	6.25
Dental caries/Karijes	25	6.25
Type of disfigurement /Tip narušavanja izgleda		
Single/Jedna	183	45.75
Multiple/Multile	8	2.00
None/Nema	209	52.25
Rehabilitation /Rehabilitacija		
Yes/Da	38	9.50
No/Ne	362	90.50

Tabela 3. Korelacija između indikatora a oralnog zdravlja i EORTC QLQ H&N35 skala
Table 3. Correlation between the oral health indicators and scales of EORTC QLQ H&N35

Scales/Skale	Dental visit/ Posete stomatologu	Oral complication/Oralne komplikacije	Disfigurement/ Narušavanje izgleda	Rehabilitation/ Rehabilitacija
Pain/Bol (HNPA)	0.04	-0.18**	0.04	0.06
Swallowing/Gutanje (HNSW)	0.11*	-0.06	0.02	0.07
Senses/Čula (HNSE)	0.07	-0.07	-0.02	0.04
Speech/Govor (HNSP)	0.07	-0.02	0.04	0.007
Social eating/Društvena ishrana (HNSO)	0.08	-0.14**	-0.12*	-0.06
Social contact/Društveni kontakti (HNSC)	0.03	-0.11*	-0.24**	-0.05
Sexuality/Seksualnost (HNSX)	-0.13*	0.01	-0.006	-0.11*
Problem in Teeth /Problemi sa zubima(HNTE)	-0.21**	0.01*	-0.11*	-0.07
Opening mouth /Otvaranje usta(HNOM)	0.09	-0.42**	-0.27**	-0.05
Dry mouth/Suvoća usta (HNDR)	0.17**	-0.13*	-0.10*	-0.02
Sticky saliva/Lepljiva pljuvačka (HNSS)	0.12*	-0.17**	-0.13*	0.05
Coughing/Kašalj (HNCO)	0.01	0.03	0.10*	0.13**
Felt ill/Osećaj bolesti (HNFI)	0.08	-0.08	0.04	0.07
Pain Killers /Analgetici(HNPK)	0.25**	-0.09	-0.008	0.18**
Nutritional supplement /Dodaci ishrani(HNNU)	-0.09	0.001	-0.04	-0.04
Feeding tube/Ishrana preko cevi (HNFE)	0.02	-0.15**	-0.21**	-0.13*
Weight loss/Gubitak težine (HNWL)	0.10*	-0.07	-0.09	0.05
Weight gain /Dodavanje težine(HNWG)	-0.14**	0.05	0.05	-0.10*

Spearmanov rank koeficijenta koleracije
Spearman's Rank correlation co-efficient, *Significant P<0.05, **Significant P<0.01

Tabela 4 Multivarijantna linearna regresija između indikatora oralnog zdravlja i EORTC KŽ H&N35
Table 4 Multivariate linear regression between oral health indicators and EORTC QLQ H&N35

Dependent Variables	Predictors	β coefficient	SE	95% CI	P value
Pain (HNPA)	Constant	24.41	5.15	14.27 to 34.54	<0.001**
	Dental visit	3.73	1.99	-0.55 to 7.29	0.09
	Oral complication	-7.83	2.05	-11.86 to -3.79	<0.001**
	Disfigurement	3.90	2.04	-0.10 to 7.90	0.05*
Swallowing (HNSW)	Constant	-71.09	193.72	-451.93 to 309.76	0.71
	Dental visit	-142.99	86.43	-312.91 to 26.94	0.09
	Disfigurement	150.64	86.41	-19.24 to 320.52	0.08
Senses (HNSE)	Constant	8.99	3.31	2.48 to 15.51	0.01*
	Dental visit	3.70	2.13	-0.48 to 7.89	0.08
Speech (HNSP)	Constant	13.02	4.04	5.08 to 20.96	0.001*
	Dental visit	5.39	2.59	0.29 to 10.48	0.04*
Social eating (HNSO)	Constant	46.67	5.05	36.74 to 56.59	<0.001**
	Oral complication	-5.85	2.63	-11.03 to -0.67	0.03*
	Disfigurement	-5.15	2.63	-10.32 to 0.02	0.05*
Social contact (HNSC)	Constant	23.07	3.14	16.89 to 29.24	<0.001**
	Disfigurement	-6.35	1.96	-10.20 to -2.50	0.001*
Sexuality (HNSX)	Constant	-338.66	516.17	-1353.43 to 676.11	0.51
	Disfigurement	-546.07	322.14	-1179.37 to 87.23	0.09
Problem in Teeth (HNTE)	Constant	149.23	274.51	-390.44 to 688.89	0.59
	Oral complication	-308.19	178.22	-658.56 to 42.17	0.08
Opening mouth (HNOM)	Constant	86.66	6.08	74.69 to 98.62	<0.001**
	Oral complication	-27.01	3.17	-33.26 to -20.77	<0.001**
	Disfigurement	-10.31	3.17	-16.54 to -4.09	0.001*
Dry mouth (HNDR)	Constant	47.06	8.96	29.43 to 64.68	<0.001**
	Dental visit	6.09	3.47	-0.73 to 12.92	0.08
	Oral complication	-6.52	3.56	-13.53 to 0.49	0.07
	Disfigurement	-6.32	3.54	-13.29 to 0.63	0.07
Sticky saliva (HNSS)	Constant	48.11	4.58	39.10 to 57.12	<0.001**
	Oral complication	-10.94	2.97	-16.79 to -5.09	<0.001**
Coughing (HNCO)	Constant	-8.85	8.57	-25.69 to 7.98	0.30
	Disfigurement	4.35	2.55	-0.67 to 9.37	0.09
	Rehabilitation	9.61	4.35	1.06 to 18.16	0.03*
Felt ill (HNFI)	Constant	9.10	4.04	1.17 to 17.04	0.02*
	Dental visit	5.97	2.59	0.88 to 11.07	0.02*
Pain Killers (HNPK)	Constant	21.06	12.19	-2.90 to 45.02	0.08
	Dental visit	25.39	3.77	17.99 to 32.80	<0.001**
	Rehabilitation	12.06	6.41	-0.55 to 24.67	0.06
Nutritional supplement (HNNU)	Constant	9.42	2.75	4.01 to 14.84	<0.001**
	Dental visit	-4.18	1.77	-7.67 to -0.71	0.02*
Feeding tube (HNFE)	Constant	70.48	13.02	44.89 to 96.08	<0.001**
	Oral complication	-8.19	3.71	-15.51 to -0.89	0.03*
	Disfigurement	-12.35	3.77	-19.76 to -4.94	0.001*
	Rehabilitation	-12.19	6.26	-24.51 to 0.12	0.05*
Weight loss (HNWL)	Constant	42.15	7.57	27.27 to 57.04	<0.001**
	Dental visit	12.61	4.86	3.05 to 22.16	0.001*
Weight gain (HNWG)	Constant	30.07	4.78	20.67 to 39.48	<0.001**
	Dental visit	-12.93	3.07	-18.97 to -6.89	<0.001**

*P<0.05 significant; **P<0.001 highly significant, CI= confidence interval

Diskusija

Pacijenti sa KGV žive pod stalnom pretnjom razvoja fizičkih, emocionalnih i funkcionalnih komplikacija tokom lečenja, što na kraju utiče na njihov kvalitet života. Kvalitet života je važan za onkološka i psiho-socijalna istraživanja o bitnim parametrima, kao što su ishodi lečenja, preživljavanje, mortalitet i stopa komplikacija[18]. Utvrđeno je to da oralne komplikacije vezane za govor, unos hrane, fizički izgled, kserostomiju i bol najviše utiču na kvalitet života[19]. Fokus je stavljen na procenu indikatora oralnog zdravlja i perspektivu pacijenta, vezanu za kvalitet života u ovoj studiji. Nalazi ove studije pokazali su to da je većina pacijenata koristila četkice za zube za održavanje oralne higijene. Mali broj pacijenata koristio je prst za čišćenje zuba, a razlog koji su pacijenti naveli tokom intervjua je nemogućnost upotrebe četkica za zube zbog ograničenog otvaranja usta, izazvanog karcinomom ili hirurškim lečenjem. Određeni broj pacijenata (31,75%) u ovoj studiji koristi vodice za ispiranje usta, kao pomoćno sredstvo, uz četkicu za zube. Razlog ovome je propisivanje ove metode za održavanje oralne higijene, kao redovne terapije kod pacijenata podvrgnutim radioterapiji. U ovoj studiji, većina pacijenata pripada ruralnim zajednicama i ima niži socio-ekonomski status, pa stoga mogu zanemariti svoje oralno zdravlje i na taj način izbegavati posete stomatologu. Osim toga, u zemljama u razvoju, kao što je Indija, oralno zdravlje smatra se veoma zanemarenim za razliku od oralnog zdravlja u zapadnim zemaljama, gde je oralno zdravlje od najveće važnosti, kao i zdravlje svakog drugog dela tela. Zbog neredovnih poseta stomatologu i nedovoljnoj svesti o oralnom zdravlju, većini pacijenata dijagnostikovana je terminalna faza KGV[20]. Parodontalni problemi bili su uobičajene oralne komplikacije u ovoj studiji, te je rezultat predstavljen u ovoj studiji bio sličan rezultatima predstavljenim u prethodnim studijama[4,9,21]. Loša oralna higijena povezana sa KGV-om dovodi do trauma i inflamacije. Uzroci traume i zapaljenja posledica su koegzistirajuće bolesti i/ili zanemarivanja oralne higijene. Dakle, ovi indikatori mogu pokazati promenu u oralnoj flori[22], abraziju zuba[23], mehaničku traumu[24] i zanemarivanje opšteg zdravstvenog stanja. Hemoterapeutski lekovi menjaju protok i viskozitet pljuvačke i količinu antikariogenih enzima, kao što su lizozim, laktoperoksidaza, imunoglobulini, histamin i laktoferin[25]. Ove promene mogu izazvati poteškoće prilikom gutanja, formiranje plaka i posledične promene u ishrani bogatoj ugljenim hidratima, kao i povećanje učestalosti karijesa zuba.

Discussion

Both the HNC patients and the survival patients are living under constant threat of developing physical, emotional, and functional complications during the treatment,which ultimately affects their QoL.QoL is important for oncological as well as psycho-social research about important parameters like treatment outcomes, survival, mortality, and complication rates[18]. The oral complicationsrelated to speech, food intake, physical appearance, xerostomia, and pain have been found to bear on QoL[19]. Thus, a focus was made on the assessment of oral health indicators and the patient's perspective on QoL in this study.

Thefindings of this study showed mostof the patientsused toothbrushesfor maintaining their oral hygiene. Few patients usedthe finger to clean their teeth. The reason given by the patients during the interview was their inability to use toothbrushesbecause of restricted mouth opening due to cancer or after surgical treatment. A good number of patients (31.75%) in the present study used mouthwashes as an adjuvant with a toothbrush. This is because themouth wash was prescribed regularly to the patients undergoing radiotherapy for an effective means for oral hygiene maintenance. In the present study, most of the patients belonged to rural communities and had lower socioeconomic status hence, they may have neglectedtheir oral health and thus avoided dental visits. Besides, in developingcountries like India,the oral cavity is considered a highly neglected part of the body in contrast with western countries where the oral cavityis paramount important like any other part of the body. Because of the lack of dental visits and unawareness regarding oral health,the majority of the patients were diagnosed at the terminal stage ofHNC[20].

Periodontal problems were common oral complicationsin the present study, this result was similar to the previous studies[4,9,21]. Poor oral hygiene associated with HNC falls into categories of trauma and inflammation.

Causes of trauma and inflammation are due to coexisting disease and/or negligence of oral hygiene. Thus, these indicators may show the shift in the oral flora[22], tooth wear[23], mechanical trauma[24], and general health maintenance, all of which are linked to cancer. Chemotherapeutic drugs alter salivary flow and viscosity and the amount of anti-cariogenic enzymes like lysozyme, lactoperoxidase, immunoglobulins, histamine, and lactoferrin[25].

Redovne posete stomatologu igraju značajnu ulogu u gubitku zuba tokom lečenja karcinoma, pa je bezubost pacijenata manja nakon lečenja. Zbog toga je dentalna rehabilitacija parcijalnom protezom bila moguća[9]. Rogers i sar.[26] prijavili su značajno gori kvalitet života pacijenata sa potpunom bezubošću u poređenju sa pacijentima kod kojih postoji parcijalna bezubost. Izrada maksilofacijalne proteze najbolja je alternativa za hiruršku rekonstrukciju posle operacije za poboljšanje oralne funkcije[27] i kvaliteta života[28,29]. Nažalost, rezultati pokazuju loš odziv posetama stomatologu i lošu rehabilitaciju.

U ovoj studiji, indikatori oralnog zdravlja i većina skala EORTC KLK-H&N35 pokazuju značajnu korelaciju. Ovaj rezultat bio je očigledan, pošto je EORTC KLK-H&N35 upitnik specifičan za bolest i mesto (glava i vrat) karcinoma. Prema istraživanjima MacEntee i sar. [30], oralno zdravlje proističe od tri faktora: udobnost (uključujući bol i ishranu), oralna higijena i opšte zdravlje. Ovo je potkrijepljeno nalazima ove studije. Postojala je značajna korelacija između bola, problema u socijalnoj interakciji i oralnih komplikacija. Kao što je očigledno, u studiji je prijavljena značajna korelacija između oralnih komplikacija i simptoma povezanih sa suvoćom usta, lepljivom pljuvačkom i poteškoćama pri otvaranju usta. Uočena je značajna korelacija između prisustva deformiteta, kao posledice hirurškog zahvata i problema sa otvaranjem usta i socijalnom interakcijom. Hirurška resekcija često dovodi do značajne estetske deformacije i pacijenti se suočavaju sa ograničenim otvaranjem usta i postaju socijalno hendikepirani. Usluge rehabilitacije, kao što su obturatori i druge maksilofacijalne proteze poboljšavaju funkcionalnost, estetiku i emocionalni status pacijenta, koji se leče od karcinom. Međutim, rezultat pokazuje to da je vrlo mali broj pacijenata (9,50%) imao stomatološku rehabilitaciju u bilo kom obliku. Zbog toga, preporučeno je da se pacijentima promoviše zdravlje i upoznavanje sa mogućnošću korišćenja maksilofacijalne proteze pre hirurškog lečenja. Takođe, potrebno je obezbediti rehabilitacione usluge u postoperativnom periodu. Rezultati ove studije pokazali su to da postoji značajna zabrinutost za kvalitet života među pacijentima koji pate od KGV. Neophodno je formirati multidisciplinarni tim sa širokim spektrom specijalista za dijagnostiku, planiranje lečenja i praćenje svih pacijentata tokom bolesti i rehabilitacije.

Thesechanges can cause difficulty in swallowing, plaque formation, and consequent changes to a pasty carbohydrate-rich diet, increasing the incidence of dental caries. Regular dental visits play a significant role in teeth loss during cancer treatment, and thus the edentulousness of the patient is less post-treatment. Therefore, dental rehabilitation with a partial prosthesis was possible[9]. Rogers SN[26] reported significantly poor QoL among fully edentulous patients as compared to partially edentulous patients. The fabrication of maxillofacial prosthesis is the best alternative for surgical reconstruction post-operatively for the improvement in oral function[27] and QoL[28,29]. Unfortunately, the results show poor compliance with dental visitsand poor rehabilitation.

In the present study, the oral health indicators and most of the scales of EORTCQLQ- H&N35 show a significant correlation. This result was obvious, as the EORTC QLQ-H&N35 is a disease and site-specific (head and neck) questionnaire. According to MacEntee et al. [30], oral health is a mixture of three themes: comfort (including pain and eating), oral hygiene, and general health. This was supported by the present findings. There was a significant correlation between the pain, problems in social interaction, and oral complications. As obvious,a significant correlation between the oral complication and symptoms related to dryness of the mouth, sticky saliva, and difficulty in mouth openingwas reported in the study. A significant correlation was observed between the disfigurement and the problems with mouth opening and social interaction. The disfigurement was associated with the surgical procedure. This might be because surgical resection often leads to a considerable estheticdeformation andpatients experience restricted mouth opening hence, they become socially handicapped. The rehabilitative services like gliding flange, obturators, and other maxillo-facialprostheses will enhance the functionality, esthetics, and sense of well-being among the patients receiving cancer treatment. However, the result shows that very few patients (9.50%) were having dental rehabilitation in any form. Hence, it hasbeen recommended that the patients should be given health promotion and made aware of themaxillo-facial prosthesisbefore the surgical treatment. Also, provision should be made as a part of rehabilitative services postoperatively.

Preporučuju se savetovanje, edukacija i podrška preživelima. Poseban naglasak treba staviti na odgovarajuću stomatološku procenu za: a) ranu dijagnozu bilo kakvih stomatoloških promena, koje treba identifikovati i odmah tretirati, pre nego što počne lečenje karcinoma; b) selektivno vađenje zuba treba uraditi pre radioterapije i omogućiti dovoljno vremena za izlečenje; c) oralni higijeničar treba da radi sa ovim pacijentima, kako bi postigao visoke standarde oralne higijene, u cilju smanjenja komplikacija posle tretmana; d) stomatolog treba da proceni bezubo područje (ako ga ima), kao i postoperativne defekte. U ovu studiju uključen je veliki broj uzoraka pacijenata sa KGV-om, koji su bili podvrgnuti hirurškoj intervenciji, hemioterapiji, zračnoj terapiji i/ili kombinaciji modaliteta lečenja. Međutim, treba uzeti u obzir nekoliko ograničenja i rezultate treba tumačiti sa oprezom. Prvo, studija je dizajnirana kao studija preseka, tako da se ne može utvrditi uzročna-posledična veza. Zato je potrebna longitudinalna studija sa ciljem daljeg istraživanja problema kvaliteta života. Drugo, procena indikatora oralnog zdravlja bila je subjektivna. Bilo bi bolje kada bi se neki indeksi (OHI-S, DMFT, indeks pljuvačke i indeks mukozitisa) uzeli u obzir za objektivnu procenu različitih problema oralnog zdravlja. Ovo bi pomoglo za tačno tumačenje stanja oralnog zdravlja i kvaliteta života pacijenata. Konačno, ova studija bila je ograničena na samo jedan institut. Međutim, to je regionalni bolničko-tercijarni centar za karcinome i smatra se jednim centrom za registraciju karcinoma, što utiče na poboljšanje eksterne validnosti studije.

The results of thepresent study showed that there was a significant concern for QoL among the patients suffering from HNC. A multidisciplinary team with a wide range of specialists has to be established for diagnosis, treatment planning, and management of all patients throughout their disease and rehabilitation.Their advice, education, and support to the survivor are recommended. Special emphasis should be made by proper dental assessment by the dentist fora) Early diagnosis of any dental problems needs to be identified and should be treated promptly before cancer treatment begins, b) Selective dental extraction should be done beforeradiotherapyallowing sufficient time to heal, c) A dental hygienist should work with these patients to achievehigh standards of oral hygiene, toreduce complication after treatment,d) The prosthodontist should assessthe edentulous area (if any) and the postoperative defects.

This study enrolled a good number of samples of HNC patients who underwent surgical, chemo-radiation, and/or a combination of treatment modalities. However, few limitationsshould be considered and results should be interpreted with caution. First, the study design was cross-sectional, and thus a causal relationship cannot be established. Hence, a longitudinal study is required to further investigate the QoL issues. Second, the assessment of oral health indicators was subjective.It would have been better if some indices (OHI-S, DMFT, index for salivary flow, index for mucositis) have beentaken into account for assessing various oral health problemsobjectively. This would have helped theaccurate interpretation ofthe oral health status and QoL of the patients. Finally, the present study was limited to only one institute. However, it is the regional hospital-tertiary cancer center and considered as one centerfor registration of cancer, which thus improves the external validity of the study.

Zaključak

U okviru ograničenja ove studije, može se zaključiti da je intenzitet loših pokazatelja oralnog zdravlja bio veoma visok. Uočena je slaba korelacija između indikatora oralnog zdravlja i skala kvaliteta života pacijenata sa KGV. Indikatori oralnog zdravlja bili su značajani u prognozi kvaliteta života pacijenata sa KGV. Dakle, treba osmisliti i primeniti različite strategije, kako bi se sprečile oralne komplikacije i održalo dobro stanje oralnog zdravlja. Multidisciplinarni pristup, koji uključuje onkološko, medicinsko, stomatološko, fizioterapeutsko i medicinsko osoblje bio bi efikasan. Ovakav tim imaće vitalnu ulogu, ne samo u dijagnostici karcinoma i tokom njegovog lečenja, već i tokom perioda rehabilitacije i na taj način poboljšati kvaliteta života ovakvih pacijenata.

Conclusion

Within the limitation of this study, it can be concluded that the intensity of poor oral health indicators was very high. Weak correlation between oral health indicatorsand scales of QoLin the HNC patientswas observed. Oral health indicators werea significant predictor ofQoL among HNC patients. So, different strategies should be framed and implemented to prevent oral complications and to maintain good oral healthstatus. A multi-disciplinary approach involving the oncology, medical, dental, physiotherapist, and nursing staff would be effective. This team will play a vital role not only during the diagnosis of cancer, during its treatment but also during the rehabilitative treatment andthus improving the quality of life.

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ANTROPOMETRIJSKI PARAMETRI I ESTETIKA U IZRADI FIKSNIH STOMATOLOŠKIH NADOKNADA – 2 deo

ANTHROPOMETRIC PARAMETERS AND AESTHETICS IN THE MAKING OF FIXED PROSTHODONTIC RESTAURATIONS – Part 2

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Sažetak

Uvod: *Uloga estetske stomatologije u domenu fiksne stomatološke protetike jeste redizajniranje osmeha, što ne podrazumeva samo tretman zuba, već i obradu okolnih mekih tkiva. Uspešna terapija može se ostvariti uspostavljanjem sklada između statičkih (zubi i gingiva) i dinamičkih faktora (usne, obrazi i mimični mišići) u stanju mirovanja i pri vršenju različitih funkcija orofacijalnog sistema.*
Cilj rada: *bila je analiza parametara mekih oralnih tkiva (zdravlje gingive, visina gingive, gingivalni zeniti, linija usana i simetrija i ravnoteža zubnog niza),koji utiču na estetiku fiksnih protetičkih nadoknada. Korišćeni su podaci iz literature i kliničko iskustvo.*
Zaključak: *Poštovanje opisanih paramtara od velikog je značaja u izradi estetskei funkcionalne fiksno protetičke nadoknade.*

Ključne reči: *estetika, gingiva, linija usana*

Abstract

Introduction: *The role of aesthetic dentistry in the field of fixed dental prosthetics is to redesign the smile, which means not only the treatment on the teeth, but also the treatment of the surrounding soft tissues. Successful therapy can be achieved by establishing the harmony between the static (teeth, gingiva) and dynamic factors (lips, cheeks, mimic muscles) at rest and when performing various functions of the orofacial system.*
The aim: *of the study was to analyze the parameters of the oral soft tissues (gingival health, gingival height, gingival zeniths, lip line and symmetry and balance of the dentition) that affect the aesthetics of fixed prosthodontic restorations. Literature data and clinical experience were used.*
Conclusion: *Adherence to the described parameters is of great importance in the development of aesthetic and functional fixed prosthetic restoration.*

Key words: *aesthetics, gingiva, lip line*

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Uvod

Nesumnjivo je da je estetika lica oduvek zauzimala važno mesto u samopercepiji čoveka i determinisala njegov stav prema životnim vrednostima. Naime, samo-ulepšavanje i težnja ka očuvanju mladalačkog izgleda načini su ponašanja duboko ukorenjeni u čovekovo postojanje. Skladnost lica, posebno njegove donje trećine, može se poboljšati stomatološkim tretmanom, individualnim pristupom ili, daleko češće, timskim radom parodontologa, ortodonta, protetičara i, ponekad, maksilofacijalnog hirurga. Okluzalnom rehabilitacijom i adekvatnim tretmanom oralnih mekih tkiva, rad stomatologa obezbeđuje funkcionalnost oro-facijalnog sistema, kreativnost u dizajniranju osmeha i socijalno-psihološku rehabilitaciju pacijenta. Imajući u vidu dominantnu ulogu, koju estetika ima u savremenoj stomatologiji, sve moderene koncepte u orofacijalnoj rehabilitaciji pacijenta možemo podvesti pod pojam estetske stomatologije.

Uloga estetske stomatologije u domenu fiksne stomatološke protetike jeste redizaj-niranje osmeha, pod kojim se ne podrazumeva samo tretman zuba, već i obrada okolnih mekih tkiva. Protetska nadoknada svojim dizajnom i odnosom prema strukturama sa kojima dolazi u kontakt (usne i obrazi) utiče i na estetiku lica, te je od nepobitne važnosti za celokupnu skladnost izgleda pacijenta[1].

Imajući u vidu velikobrojnosti raznolikost izgleda pacijenata, od posebne je važnosti ustanoviti i poštovati kriterijume oblikovanja osmeha, koji obezbeđuju univer-zalnu dopadljivost. Kada su u pitanju tvrda zubna tkiva, to je odnos središnje linije zuba i lica, dužine zuba, interdentalne kontaktne tačke i površine, oblika, veličine i proporcije zuba i njihova boja[2]. Analiza mekih oralnih tkiva obuhvata poziciju zenitnih tački, gingivni pripoj, liniju osmeha, odnosno liniju usana. Smatra se da se uspešna terapija može ostvariti uspostavljanjem sklada između statičkih (zubi i gingiva) i dinamičkih faktora (usne, obrazi i mimični mišići) u stanju mirovanja i pri vršenju različitih funkcija orofacijnog sistema[3].

Cilj rada bila je analiza parametara mekih oralnih tkiva,koji utiču na estetiku fiksnih protetičkih nadoknada, na osnovu podataka iz literaturei kliničkog iskustva.

Introduction

There is no doubt that facial aesthetics has always occupied an important place in a person's self-perception and determined his attitude towards life values. Namely, self-beautification and striving to preserve a youthful appearance are a way of behaving deeply rooted in human existence. The harmony of the face, especially its lower third, can be improved by dental treatment, individual approach or, far more often, teamwork of periodontists, orthodontists, prosthodontists and, sometimes, maxillofacial surgeons. With occlusal rehabilitation and adequate treatment of oral soft tissues, the work of a dentist ensures the functionality of the orofacial system, creativity in designing a smile and social and psychological rehabilitation of the patient. Having in mind the dominant role that aesthetics has in modern dentistry, all modern concepts in orofacial rehabilitation of the patient can be summed up as aesthetic dentistry.

The role of aesthetic dentistry in the field of fixed dental prosthodontics is the redesign of the smile, which means not only the treatment on the teeth but also the treatment of the surrounding soft tissues. Prosthodontic compensation with its design and relation towards the structures with which it comes into contact (lips, cheeks) also affects the aesthetics of the face, and is of undeniable importance for the overall harmony of the patient's appearance[1].

Given the infinity of different patient appearances, it is of particular importance to establish and adhere to smile-shaping criteria that seek to ensure universal appeal. When it comes to dentalhardtissues, it is the relationship between the midline of the teeth and the face, the length of the teeth, the interdental contact points and surfaces, the shape, size and proportions of the teeth and their color[2]. The analysis of the oral softtissues includes the position of the zenith points, gingival attachment, smile line, or lip line. It is believed that successful therapy can be achieved by establishing the harmony between the static (teeth, gingiva) and dynamic factors (lips, cheeks, mimic muscles) at rest and when performing various functions of the orofacial system[3].

The aim of this study was to analyze the parameters of the oral soft tissues that affect the aesthetics of fixed prosthodontic restorations based on the literature data and clinical experience.

Zdravlje gingive

Pretprotetska parodontološka priprema i usvajanje postulata optimalne oralne higijene preduslov su za uspešnost i trajnost protetske terpije. Zdrava gingiva je bledo roze boje, matirane površine i karakterističnog izgleda „kore narandže“. Proteže se oko gleđno-cementne granice, u vidu okvira. Različito je vidljiva u zavisnosti od dužine i konture usana, a nepoštovanje njenog anatomorfološkog oblika smanjuje estetski efekat nadoknade i može biti uzrok funkcionalnih oštećenja. Pojedini autori smatraju da je širina pripojne gingive od 2mm optimalna da ujedno zadovolji estetske kriterijume i obezbedi trajno zdravlje parodontalnog tkiva nakon cementiranja fiksnih protetskih konstrukcija[3]. Loša oralna higijena i konsekutivne zapaljenske promene menjuju arhitektoniku gingive, dovode do njenog povlačenja i remete estetiku i funkcionalnost stomatološkog rada. Sa druge strane, recesija gingive i sledstvene parodontalne promene mogu biti i jatrogene prirode, a obično su izazvane postojanjem marginalne pukotine između protetskog rada i brušenog zuba (kratke ili široke krune) ili subgingivalnom pozicijom demarkacije preparacije[4]. Kako su zdrava marginalna gingiva i interdentalni prostori ispunjeni papilom neophodni za lep izgled mostova i osmeh pacijenta, neophodno je maksimalno precizno izgraditi sinergiju mekih oralnih tkiva i veštačkih materijala od kojih su oni napravljeni, kao i obučiti pacijenta kako da štiti oralno zdravlje.

Visina gingive

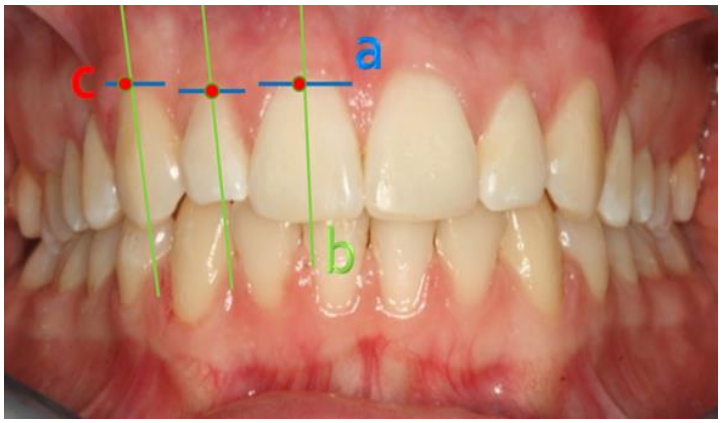
Kontura gingive gornjih centralnih sekutića i očnjaka ima elipsiodni, a lateralnih sekutića polukružni oblik. Za pravilno oblikovanje osmeha neohodno je pravilno pozicioniranje nivoa gingive. Posmatrano u horizontalnoj ravni, najviša pozicija gingivalne konture gornjih centralnih sekutića nešto je više pozicionirana u odnosu na poziciju lateralnih sekutića. Visina gingive gornjih lateralnih sekutića nalazi se 0,5 mm do 0,2 mm ispod nivoa gingive centralnih sekutića[5]. Najviša tačka gingivalne konture gornjih očnjaka postavljena je nešto apeksnije u poređenju sa najvišom tačkom gingivalne konture centralnih sekutića. Razlike u visini nivoa gingive gornjih prednjih zuba čine osmeh zanimljivijim i atraktivnijim (Slika 1).

Gingival health

Pre-prosthodontic periodontal pre-paration and adoption of the postulates of optimal oral hygiene are a precondition for the success and durability of prosthodontic therapy. The healthy gingiva has a pale pink color, matte surface and the characteristic appearance of "orange peel". It extends around the enamel-cement border in the form of a frame. It is different depending on the length and contour of the lips, and disrespecting its anatomical and morphological shape,the gingiva reduces the aesthetic effect of compensation and can be the cause of functional damage. Some authors believe that the width of the adhered gingiva of 2 mm is optimal to meet the aesthetic criteria and ensure lasting health of periodontal tissue after cementation of fixed prosthodonticstructures[3]. Poor oral hygiene and consequent inflammatory changes modifythe architecture of the gingiva, lead to its withdrawal and disrupt the aesthetics and functionality of dental work. On the other hand, gingival recession and consequent periodontal changes can be iatrogenic in nature, and are usually caused by the existence of a marginal crack between prosthodontic work and a prepared tooth (short or wide crown) or a subgingival position of preparation demarcation[4]. Sincethe healthy marginal gingiva and interdental spaces filled with papillae are necessary for the beautiful appearance of bridges and the patient's smile, it is necessary to makethe synergy betweenoral soft tissues and artificial materials they areproduced of, as well as teach the patient how to protect oral health.

Gingival height

The contour of the gingiva of the upper central incisors and canines has an ellipse shape, and the lateral incisors have a semicircular shape. Proper gingival leveling is necessary for proper smile formation. Observed in the horizontal plane, the highest position of the gingival contour of the upper central incisors is somewhat more positioned in relation to the lateral incisors. The height of the gingiva of the upper lateral incisors is 0.5 to 0.2 mm below the level of the central incisors gingiva[5]. The highest point of the gingival contour of the upper canines is set somewhat more apically compared to the central incisors. Differences in the level of the gingiva of the upper front teeth make the smile more interesting and attractive (Figure 1).



Slika 1. Estetika gingive a) cervikalna visina gingive maksilarnog lateralnog sekutića nalazi se oko 0,5–0,2 mm ispod nivoa gingive centralnih sekutića i očnjaka; b) uzdužna osovina zuba c) gingivalni zeniti
//www.sfzg.unizg.hr › estetika_u_ortodonciji

Figure 1. Aesthetics of the gingiva a) the cervical height of the gingiva of the maxillary lateral incisor is about 0.5–0.2 mm below the level of the gingiva of the central incisors and canines; b) longitudinal axis of the tooth c) gingival zeniths
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Gingivalne konture gornjih prednjih zuba nejednake su visine, sa prividnom nesavršenošću i tada govorimo o klasi I gingivalnih visina. Klasa II gingivalnih visina podrazumeva apeksnije postavljene gingivalne konture lateralnih sekutića u odnosu na gingivalne konture centralnih sekutića i očnjaka.

Pri fiksnoprotetskoj rekonstrukciji, bitno je prepoznati kojoj klasi gingivalnih kontura pripada posmatrani slučaj, jer od pravilne rekonstrukcije mekih tkiva, koja okružuju zube, zavisi kako estetski tako i funkcionalni uspeh terapije[3]. Ukoliko je pozicija gingive značajno izmenjena nakon destrukcije ili gubitka zuba, pre izrade protetskog rada neohodna je gingivoplastika.

Gingivalni zeniti

Gingivalni zeniti ili zenitne tačke najviše su apikalne tačke zuba na spoljašnjoj konturi gingive. Obično su lokalizovani distalnije od uzdužne osovine maksilarnih sekutića i očnjaka. Kod lateralnih sekutića gornje vilice, ona je u pravcu uzdužne osovine zuba (Slika 1). O položaju gingivalnih zenita treba voditi računa tokom brušenja zuba i otiskivanja, kao i prilikom modelovanja članova fiksnog protetskog rada.

The gingival contours of the upper front teeth are unequal in height, with apparent imperfection, and then we talk about class I gingival heights. Class II gingival heights include more apically placed gingival contours of the lateral incisors in relation to the central incisors and canines.

During fixed prosthodontic reconstruction, it is important to recognize which class of gingival contours the observed case belongs to, because both aesthetic and functional success of therapy depends on the correct reconstruction of soft tissues surrounding teeth[3]. If the position of the gingiva is significantly changed after the destruction or loss of the tooth, gingivoplasty is necessary before making prosthodontic work.

Gingival zenith

The gingival zeniths or zenith points are the most apical points of the tooth on the outer contour of the gingiva. They are usually located distal to the longitudinal axis of the maxillary incisors and canines. In the lateral incisors of the upper jaw, it is in the direction of the longitudinal axis of the tooth (Figure 1). The position of the gingival zeniths should be taken into account during tooth preparation and impression, as well as during the modeling of members of fixed prosthodontic work.

Linija usana

Ekponiranost gornjih zuba i gingive zavisi od pozicije linije gornje usne. Sa druge strane, linija osmeha donje usne blago dodiruje sečivne ivice gornjih prednjih zuba[6].

U odnosu na vidljivost postoje tri tipa linija gornje usne: visoka, srednja i niska linija, što utiče na vidljivost zuba i, samim tim na estetski izgled lica[7] (Slika 2). Niska linija usana najmanje je estetski prihvatljiva, jer prekriva gingivu i veći deo zuba, pa su oni jedva vidljivi. Ukoliko je moguće, vidljivost zuba može se povećati produžavanjem kliničkih kruna zuba[8]. Starenjem, gornja usna postaje opuštenija gornja usna je opuštenija i u većoj meri prekriva gornje centralne sekutiće, te su donji zubi vidljiviji u odnosu na gornje[9].

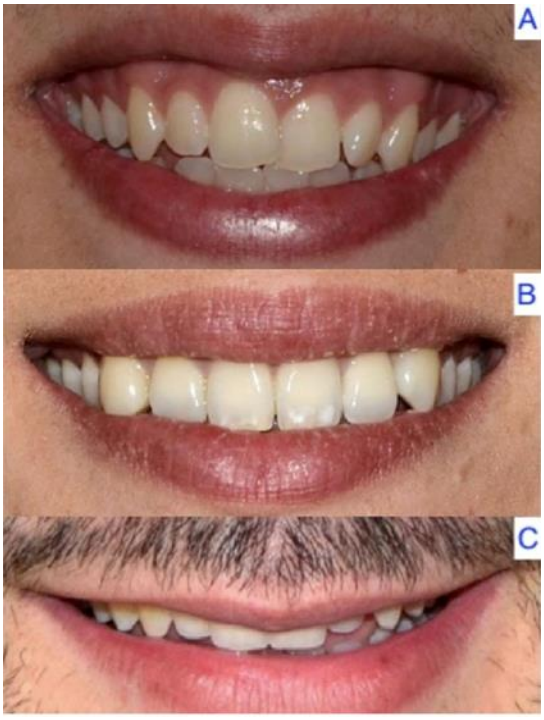
Srednja linija usana dozvoljava vidljivost zuba od 1 mm do 3 mm i smatra se estetski najprihvatljivijom. Kod visoke linije usana, desni i zubni su vidljivi, što ne izgleda lepo, a klinički se teško koriguje[10].

Lip line

The exposure of the upper teeth and gingiva depends on the position of the upper lip line. On the other hand, the smile line of the lower lip lightly touches the cutting edges of the upper front teeth[6].

In relation to visibility, there are three types of upper lip line: high, middle and low, which affects the visibility of the teeth and thus the aesthetic appearance of the face[7] (Figure 2). The lower lip line is the least aesthetically pleasing because it covers the gingiva and most of the teeth, so they are barely visible. If possible, tooth visibility can be increased by lengthening the clinical crowns of the teeth[8]. With age, the upper lip is more relaxed and covers the upper central incisors to a greater extent, so the lower teeth are more visible than the upper ones[9].

The middle line of the lips allows the visibility of the teeth from 1 to 3 mm and is considered the most aesthetically pleasing. Withthe high lip line, the gums and teeth are very visible, which does not look nice, and it is clinically difficult to correct[10].



Slika 2. Visoka (a), srednja (b) i niska (c) linija usana[8]
Figure 2. High (a), middle (b) and low (c) lip line[8]

Simetrija i ravnoteža zubnog niza

Simetričnost zubnog niza posmatra se u odnosu na središnju liniju lica. Sredina zubnog luka i sredina zubnih nizova treba da se poklapaju, što se posebno odnosi na zube gornje vilice (Slika 3). Nepodudarnost srednje linije lica i sredine donjeg zubnog niza češća je, ali sa estetskog stanovišta nije od bitnog značaja[8].

Za skladnu kompoziciju osmeha poželjana je paralelnost linije koja prolazi kroz komisure usana i linije koja spaja vrhove očnjaka[11].

Symmetry and balance of the dentition

The symmetry of the dentition is observed in relation to the midline of the face. The middle of the dental arch and the middle of the dental rows should coincide, which is especially true for the teeth of the upper jaw (Figure 3). The mismatch between the middle line of the face and the middle of the lower dentition is more common, but from an aesthetic point of view it is not important[8].

For a harmonious composition of the smile, the parallelism of the line passing through the commissures of the lips and the line connecting the tips of the canines[11] is desirable.

Slika 3. Blaga nepodudarnost središnje linije lica i sredine gornjeg zubnog niza [12]

Figure 3. Mild mismatch of the center line of the face and the middle of the upper dentition[12]

Zaključak

Poštovanje opisanih funkcionalnih i estetskih paramtara važno je u izradi fiksnih protetičkih nadoknada, kojim treba težiti kako bi se postigli elementarni postulati lepog. Ipak, ljudska lepota ne može biti apsolutno definisana opisanim kriterijumima. Ona je stvar raznolikosti, lične percepcije, stanja duha, pa je stoga individualna vrednost svakog pojedinca, uz opasku da i nesavršenost može biti i te kako zanimljiva.

Conclusion

Observance of the described functional and aesthetic parameters is important in the creation of fixed prosthodontic restorations, which should be strived for in order to achieve the elementary postulate of the beautiful. However, human beauty cannot be absolutely defined by the described criteria. It is a matter of diversity, personal perception, state of mind, so it is the personal value of each individual, for imperfection can be very interesting.

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ORALNA LEUKOPLAKIJA: PREGLED KLINIČKIH KARAKTERISTIKA I TRENDOVA U LEČENJU

ORAL LEUKOPLAKIA: A REVIEW OF CLINICAL FEATURES AND TRENDS IN MANAGEMENT

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Sažetak

Uvod: *Oralni, potencijalno maligni poremećaji (OPMD) čine grupu bolesti od velike važnosti za stomatologa. Oralna leukoplakija (OL) dugo je bila predmet debate brojnih istraživača. Uobičajeni etiološki faktor je duvan, koji je povezan sa karcinomom usne šupljine.*
Cilj studije *je ukazati na ozbiljnost lezije, najčešću kliničku sliku i lokalizaciju. Prevalencija leukoplakije u svetu je 2,6% sa stopom maligne konverzije u rasponu od 0,1% do 17,5%. Nalazi u literaturi o prevalenci i godišnjoj stopi maligne transformacije od približno 2%, ukazuju da ove promene traba ozbiljno shvatiti i redovno pratiti*
Zaključak: *Umeće postavljanja tačne dijagnoze pruža ključ za sprečavanje progresije premaligne ka malignoj transformaciji. Opisani su različiti medicinski i hirurški modaliteti lečenja ove lezije. Ovaj članak naglašava različite trendove u dijagnostici i lečenju oralne leukoplakije.*

Ključne reči: *potencijalno maligni poremećaj, leukoplakija, maligna transformacija*

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Abstract

Introduction: *Oral potentially malignant disorders (OPMD)conisit of the group of diseases of great importance for dentists. Oral leukoplakia (OL) has long been the subject of debate by numerous researchers. A common etiologic factor is tobacco, which is associated with oral cancer.*
The aim *of the study is to indicate the severity of the lesion, the most common clinical characreistics and localization. The prevalence of leukoplakia in the world is 2.6% with a rate of malignant conversion ranging from 0.1% to 17.5%. Literature data about the prevalence and annual rate of malignant transformation, approximately 2%, indicate that these changes should be taken seriously and regularymonitored*
Conclusion: *Occurate diagnosis provides the key to preventing to malignant transformation. Various medical and surgical treatment modalities for this lesion have been described. This article highlights various trends in the diagnosis and treatment of oral leukoplakia.*

Key words: *potentially malignant disorder, leukoplakia, malignant transformation*

Uvod

Termin leukoplakija prvi je upotrebio Švimer 1877. godine[1]. Termin leukoplakija izveden je od grčke reči leucos što znači belo i plakija što znači fleka[2]. Butlin je 1885. godine povezao ove lezije sa pušenjem i smatrao je da je ova promena kod pušača rana faza naprednije lezije belog tumefakta, koji je nazvao leukom[3]. Akell je 1996. godine definisao leukoplakiju kao belu mrlju od 5 mm ili više, koja se ne može otkinuti i ne može se pripisati nijednoj drugoj dijagnostikovanoj bolesti[4]. Leukoplakija predstavlja oblik hiperkeratoze oralnog epitela. Faktor rizika za ovu bolest je duvan, kako u vidu cigareta, sa dimom, tako i u formama bez dima. Drugi faktori koji doprinose razvoju leukoplakije su alkohol, hronična iritacija sluzokože, oralna kandidijaza, nedostaci u ishrani, polno prenosive lezije, kao što je sifilis i izlaganje ultraljubičastom zračenju[5]. Predloženi su različiti načini prevencije, sa ciljem sprečavanja napredovanja leukoplakije u oralni karcinom skvamoznih ćelija. U ovom radu opisani su različiti klinički tipovi, dijagnostičke metode i strategije lečenja leukoplakije.

Definicija oralne leukoplakije

Tokom godina, predložene su različite definicije oralne leukoplakije. Na prvoj međunarodnoj konferenciji o oralnoj leukoplakiji (Malme, Švedska, 1984. godina), definisana je leukoplakija kao „bela mrlja ili plak koji se ne može klinički ili patološki okarakterisati kao bilo koja druga bolest i nije povezana ni sa jednim fizičkim ili hemijskim uzročnikom osim sa upotrebom duvana"[6]. Ovo je pojednostavljeno 1994. godine kao „pretežno bela lezija oralne sluzokože, koja se ne može okarakterisati kao bilo koja druga lezija, koja se može definisati"[7]. Akell i sar.[4] definisali su 1996. godine leukoplakiju kao „belu mrlju veličine 5 mm ili više, koja se ne može ostrugati i ne može se pripisati nijednoj drugoj bolesti". Svetska zdravstvena organizacija (SZO) je 1997. godine modifikovala definiciju kao „pretežno belu leziju oralne sluzokože, koja se ne može okarakterisati kao bilo koja druga definisana lezija"[7,8]. SZO je 2005. godine definisala leukoplakiju kao „beli plak sumnjivog rizika, koji je isključio (druge) poznate bolesti ili poremećaje, koji ne nose povećan rizik od raka"[9]. Varnakulasuriia i sar. 2007. godine[10] predložili su sledeću definiciju: „beli plak sumnjivog rizika, koji je isključio druge poznate bolesti ili poremećaje, koji ne nose povećan rizik od raka".

Introduction

The term leukoplakia was first coined by Schwimmer in 1877[1]. Leukoplakia is derived from the Greek word Leucos which means white and plakia which means a patch[2]. In 1885, Butlin related these lesions to smoking and considered smokers patch to be an early stage of a more advanced white raised lesion that he termed leukoma[3]. In 1996, Axell defined leukoplakia as a white patch measuring 5 mm or more which cannot be scrapped off and cannot be attributed to any other diagnostic disease[4]. It represents a form of hyperkeratosis of the oral epithelium. The risk factors for this disease include tobacco, both in smoked and smokeless form. Other contributing factors include alcohol, chronic mucosal irritation, oral candidiasis, nutritional deficiencies, sexually transmitted lesions like syphilis and exposure to ultraviolet light[5]. Various management strategies have been proposed to halt the progress of leukoplakia into oral squamous cell carcinoma. The present review describes the various clinical types, diagnostic methods and management strategies of leukoplakia.

Definitions of oral leukoplakia

Various definitions for oral leukoplakia have been proposed over the years. The first International Conference on Oral Leukoplakia, Malmo, Sweden, 1984, defined leukoplakia as "A white patch or plaque that cannot be characterized clinically or pathologically as any other disease and is not associated with any physical or chemical causative agent except the use of tobacco"[6]. This was simplified in 1994 as "A pre-dominantly white lesion of the oral mucosa that cannot be characterized as any other definable lesion"[7]. In 1996, Axell et al.[4] defined leukoplakia as "A white patch measuring 5 mm or more, which cannot be scraped off and cannot be attributed to any other diagnostic disease". In 1997, the WHO modified the definition as "A predominantly white lesion of the oral mucosa that cannot be characterized as any other definable lesion"[7,8]. In 2005, WHO defined leukoplakia as "a white plaque of questionable risk having excluded (other) known diseases or disorders that carry no increased risk for cancer"[9]. Warnakulasuriya et al. in 2007[10] proposed the following definition "A white plaque of questionable risk having excluded other known diseases or disorders that carry no increased risk of cancer".

Epidemiologija

Prevalencija leukoplakije u svetu je 2,6%, sa stopom maligne konverzije u rasponu od 0,1% do 17,5%[11]. U Indiji, prevalencija leukoplakije je između 0,2% i 5,2%, sa stopom maligne transformacije od 0,13% do 17,5%[5,12]. U studiji koju su sproveli Martorell-Calataiud i sar.[13], utvrđeno je da je prevalencija leukoplakije u rasponu od 0,4% do 0,7%[13]. Gopinath D i sar.[12] pronašli su žarište oralnih karcinoma kod 11,9% biopsiranih oralnih leukoplakija. Feller i sar.[14] pokazali su to da se stopa prevalencije leukoplakije kreće od 0,5% do 3,46%. Takođe, pokazali su to da se stopa maligne transformacije leukoplakije kretala od 0,7% do 2,9%. Brouns i sar.[15] izvestili su o prevalenciji i godišnjoj stopi maligne transformacije od približno 2% i 1%.

Starost i pol

Leukoplakija se obično javlja kod osoba srednjih godina i starijih osoba, pretežno kod muškaraca[16]. Manje od 1% slučajeva leukoplakije javlja se kod muškaraca mlađih od 30 godina[11]. Espinoza i sar.[17] pokazali su to da leukoplakiju u svim starosnim grupama sa višom stopom prevalencije kod starije populacije, u rasponu od 0,35% do 18,6%. Bokor-Bratiket i sar.[18] pokazali su to da se oralna leukoplakija javlja u vidu crvenila kod muškaraca preko 40 godina i kod žena preko 50 godina. Leukoplakija je češća kod muškog pola, verovatno zbog povećane prevalencije navika konzumiranja duvana i alkohola u poređenju sa ženama[19].

Lokalitet leukoplakije

Leukoplakija se može videti na bukalnoj sluzokoži, labijalnoj sluzokoži, podu usta, gingivi i jeziku. Ramia i sar.[20] izvestili su o tome da je bukalna sluzokoža najčešće mesto za leukoplakiju. Na mesto leukoplakije utiče povezana navika. Pušači beedi cigareta imaju veću incidenciju leukoplakije u prednjoj bukalnoj sluzokoži, pri čemu je, kao i kod žvakanja duvana, veća verovatnoća da će se leukoplakija pojaviti u zadnjoj bukalnoj sluzokoži[21].

Klasifikacija

Mnogi autori predložili su različite klasifikacije leukoplakije. Leukoplakija se uglavnom klasifikuje kao homogena i nehomogena, gde je homogena leukoplakija uniformno bela mrlja, koja se ne može strugati, dok se nehomogena leukoplakija sastoji od mešanih crvenih i belih područja i uključuje pegastu, nodularnu i verukoznu leukoplakiju[22,23].

Epidemiology

The prevalence of leukoplakia worldwide is 2.6% with a malignant conversion rate ranging from 0.1% to 17.5%[11]. In India, the prevalence rate of leukoplakia is between 0.2% and 5.2% with a malignant transformation rate from 0.13% to 17.5%[5,12]. In a study done by Martorell-Calatayud et al.[13] the prevalence of leukoplakia was found to be in the range from 0.4% to 0.7%[13]. Gopinath D et al.[12] found oral foci of carcinoma in 11.9% of biopsied oral leukoplakias. Feller et al.[14] showed that the prevalence rate of leukoplakia was found to be ranging from 0.5% to 3.46% in his study. He also showed that the malignant transformation rate of leukoplakia ranged from 0.7% to 2.9%. Brounset al.[15] reported a prevalence and annual malignant transformation rate of approximately 2% and 1%, respectively.

Age and gender

Leukoplakia commonly occurs in middle aged and older individuals predominantly in males[16]. Fewer than 1% cases of leukoplakia occur in males less than 30 years of age[11]. Espinoza et al.[17] showed leukoplakia in all age groups with a higher prevalence rate in the elderly population, ranging from 0.35% to 18.6%. Bokor-Bratić et al.[18] showed that oral leukoplakia occur red in men over 40 years and in women over 50 years of age. Leukoplakia is more prevalent in male gender probably due to the increased prevalence of habits in males when compared to females[19].

Site of Leukoplakia

Leukoplakia can be seen in the buccal mucosa, labial mucosa, floor of the mouth , gingiva, and the tongue. Ramya et al.[20] reported that the buccal mucosa was the most common site for leukoplakia. The site of leukoplakia is affected by the associated habit. Beedi smokers have greater incidence of leukoplakia in the anterior buccal mucosa, where as in tobacco chewing, leukoplakia is more likely to occur in the posterior buccal mucosa[21].

Classification

Various classifications have been suggested by many authors. Leukoplakia is mainly classified as homogenous and non-homogenous where homogenous leukoplakia is uniformly white non scrapable patch while non-homogenous leukoplakia consists of mixed red and white areas and includes speckled, nodular and verrucous leukoplakia[22,23].

Leukoplakija se takođe može klasifikovati kao tanka, glatka leukoplakija, debela, fisurna leukoplakija, granularna, veruciformna leukoplakija i eritro-leukoplakija[24]. U daljoj modifikaciji 2002. godine, SZO podelila je leukoplakiju u četiri faze: faza I koja se sastoji od tanke, glatke leukoplakije; faza II kao gusta, pukotinasta leukoplakija; faza III kao proliferativna verukozna leukoplakija (PVL) i faza IV kao eritroleukoplakija[21]. Proliferativna verukozna leukoplakija (PVL) je podtip verukozne leukoplakije sa ekstenzivnim širenjem, otpornošću na terapiju i visokim stepenom maligne transformacije. PVL je klasifikovana kao oblik nehomogene leukoplakije[25]. Nasuprot tome, van der Vaal pominje to da sve ekstenzivne leukoplakije imaju povećan potencijal za malignu transformaciju, te PVL ne treba klasifikovati kao poseban entitet. Dalje, PVL se može smatrati vrstom homogene leukoplakije, jer je pretežno bele boje[23].

Histopatološka klasifikacija

Histopatološka klasifikacija zasniva se na stepenu epitelne displazije u leukoplakiji. Tri glavne klasifikacije uključuju klasifikaciju SZO, binarni sistem klasifikacije i Brothvellovu klasifikaciju[26]. Klasifikacija SZO koristi citološke i ćelijske arhitektonske promene, kako bi podelila leukoplakiju na blagu, umerenu ili tešku epitelnu displaziju. „Blagu displaziju“ karakterišu ćelije koje pokazuju nuklearni hiperhromatizam i pleomorfizam bazalnih i parabazalnih epitelnih regiona. „Umerena displazija“ karakteriše se ćelijama sa nuklearnim hiperhromatizmom i pleomorfizmom u bazalnom, parabazalnom i spinoznom sloju. Lezije „teške displazije“ karakterišu lukovičasti zaravnjeni procesi sa hiperhromatskim jedrima i pleomorfizmom po celoj debljini epitela[26]. Brothvellov sistem sličan je klasifikaciji SZO, sa dodatnim nivoom „karcinoma in situ“, koji karakterišu displastične promene u celom epitelu, koje sugerišu na invaziju u osnovno tkivo, ali bez dokaza o istom[27]. Binarni sistem kategoriše lezije kao visokorizične i niskorizične[28].

Etiologija

Duvan: Oralna leukoplakija ima multifaktorsku etiologiju, ali najčešće impliciran uzročnik je upotreba duvana u vidu cigareta za pušenje ili bez dima. Duvan oslobađa karcinogene, koji se vezuju za DNK, izazivajući mutaciju. Oni, takođe, mogu dovesti do stvaranja visokoreaktivnih slobodnih radikala, koji uzrokuju oštećenje ćelijske membrane i DNK[25].

Leukoplakia can also be classified as thin, smooth leukoplakia, thick, fissured leukoplakia, granular, verruciform leukoplakia and erythro leukoplakia[24].

In a further modification in 2002, the WHO categorised leukoplakia into Phase I consisting of thin, smooth leukoplakia; Phase II as thick, fissured leukoplakia; Phase III as proliferative verrucous leukoplakia (PVL) and Phase IV as erythro leukoplakia[21].

Proliferative verrucous leukoplakia (PVL) is a subtype of verrucous leukoplakia with extensive involvement, resistance to therapy and high degree of malignant transformation. PVL has been classified as a form of non-homogenous leukoplakia[25]. In contrast, van der Waal mentions that since all extensive leukoplakias have increased potential for malignant transformation, PVL need not be classified as a separate entity. Further, PVL could be considered as a type of homogenous leukoplakia since it is predominantly white[23].

Histopathologic classification

Histopathologic classification is based on the degree of epithelial dysplasia in the leukoplakia. The three main classification include WHO classification, Binary classification system and Brothwell's classification[26].

WHO classification uses cytological and cellular architectural changes to classify leukoplakia as having mild, moderate or severe epithelial dysplasia.

"Mild dysplasia" is characterized by cells showing nuclear hyperchromatism and pleomorphism in the basal and parabasal epithelial regions; "Moderate dysplasia": is characterised by cells with nuclear hyperchromatism and pleomorphism in the basal, parabasal, and spinous layers; while "Severe dysplasia"lesions are characterized by bulbous straight processes with nuclear hyperchromatism and pleomorphism throughout the epithelial thickness[26].

Brothwell's system is similar to WHO classification with an additional 'carcinoma in situ' level characterised by dysplastic changes throughout the epithelium suggestive of invasion into underlying tissue but without evidence of the same[27]. The binary system categorises lesions as high risk and low risk[28].

Etiology

Tobacco: Oral leukoplakia has a multifactorial etiologybut the most commonly implicated agent is the use of tobacco in either smoking or smokeless form.

Toplota od pušenja i iritacija trenjem od duvanskih proizvoda za žvakanje mogu izazvati stimulaciju keratinocita i hiperkeratinizaciju. Bezdimni duvan može se udisati, žvakati ili pušiti. U južnoj Aziji često se meša sa arekanom, listom betela, gašenim krečom i začinima[25].

Postupci transplantiranja

Alkohol: Alkohol deluje kao ko kancerogen i ima sinergistički efekat sa duvanom u razvoju leukoplakije[29]. Alkohol ima dehidrirajući efekat na oralnu sluzokožu, čineći je podložnijom dejstvu duvana[30]. Pored gore navedenih etioloških agensa, ulogu u nastanku ove lezije imaju mehaničke traume usled loših protetskih nadoknada i oštrih zuba, kao i virusi poput humanog papiloma virusa i Epstein Barr virusa[29].

Leukoplakija povezana sa kandidom: Kandida oslobađa nitrozamine koji mogu da konvertuju etanol u acetaldehid kod konzumenata alkohola i izazivaju leukoplakiju povezanu sa duvanom. Nutritivni faktori kao što su nedostatak gvožđa, folne kiseline, vitamina A, B_1 i B_2 mogu imati ulogu u njegovoj etiologiji. Displazija je 4 – 5 puta veća kod leukoplakije povezane sa kandidom[31,32].

Viadent leukoplakija: Sangvinarna leukoplakija povezana je sa leukoplakijom u predelu vestibuluma maksile i alveolarnoj sluzokoži i uzrokovana je biljnim ekstraktom prisutnim u viadent pastama za zube i rastovrima za ispiranje usta[19,30,33].

Nutritivni faktori

Smanjeni nivoi vitamina A, B_{12}, C, beta karotena i folne kiseline u serumu primećeni su kod subjekata sa oralnom leukoplakijom[34]. Pretpostavlja se da atrofija epitela povezana sa ovim nedostacima u ishrani, kao kod nedostatka gvožđa, može povećati osetljivost na razvoj leukoplakije[35].

Dijagnoza

Dijagnoza leukoplakije može se postaviti na osnovu kliničkih nalaza i dopunskih ispitivanja. Leukoplakija se može definitivno dijagnostikovati na osnovu istorije bolesti, kliničkih karakteristika i histopatološke procene. Suština dijagnostike je isključiti leukoplakiju . Leukoplakija je klinički termin tako da je neophodna patohistološka dijagnoza, kako bi isključili druge bele lezije[25].

Uobičajena karakteristika leukoplakije je prisustvo bele mrlje koja se ne može skinuti, što je generalno povezano sa konzumiranjem duvana[36].

Tobacco releases carcinogens that bind to DNA causing mutation. They may also lead to the formation of highly reactive free radicals causing cell membrane and DNA damage[25]. The heat from smoking and the frictional irritation from chewing tobacco products may cause keratinocyte stimulation and hyper-keratinisation. Smokeless tobacco can be inhaled, chewed, or smoked. In South Asia, it is often mixed with arecanut, betel leaf, slaked lime, and spices[25].

Transplatation protocol

Alcohol: Alcohol acts as a co-carcinogen and has synergistic effect with tobacco in the development of leukoplakia[29]. Alcohol has a dehydrating effect on the oral mucosa rendering it more susceptible to the effects of tobacco[30].

In addition to the above etiological agents, mechanical trauma from ill-fitting dentures and sharp teeth as well as viruses like human papilloma virus and Epstein Barr virus has been implicated[29].

Candida-associated leukoplakia: *Candida* releases nitrosamines which can convert ethanol into acetaldehyde in alcohol consumers and cause leukoplakia in association with tobacco. Nutritional factors such as deficiency of iron, folic acid, vitamins A, B_1, and B_2 may have a role in its etiology. Dysplasia is 4-5-fold higher in candida-associated leukoplakia[31,32].

Viadent leukoplakia: Sanguinaria-associated leukoplakia Sanguinaria has been associated with leukoplakia in maxillary vestibule and alveolar mucosa and is caused by aherbal extract present in toothpastes and mouth rinses[19,30,33].

Nutritional factors

Decreased serum levels of vitamin A, B_{12}, C, beta carotene, and folic acid have been noted in subjects with oral leukoplakia[34]. It is hypothesized that the epithelial atrophy associated with these nutritional deficiencies, as in iron deficiency and OSMF, can increase susceptibility to the development of leukoplakia[35].

Diagnosis

The diagnosis of leukoplakia can be done on the basis of clinical findings and chair side investigations. Leukoplakia can be definitively diagnosed based on subject history, clinical features and histopathologic evaluation. It is essentially a diagnosis of exclusion. Leukoplakia is a clinical term; a biopsy is essential to confirm the diagnosis and to rule out other white lesions[25].

Homogena leukoplakija je bela mrlja koja može biti naborana (poput peščane plaže) sa finim linijama poznatim kao kriste ili naborana forma, koja se obično opisuje kao izgled suvog, ispucanog blata[36]. Nehomogena leukoplakija može biti nodularna ili pegasta. To su keratotični čvorići ili mrlje prisutne na eritematoznoj bazi sluzokože[36]. Verukozni oblik leukoplakije ima gusto keratinizovane projekcije površine sluzokože[36]. Proliferativnu verukoleukoplakiju karakteriše prisustvo egzofitnih i proliferativnih keratotskih plakova koji nisu mnogo povezani sa upotrebom duvana[37]. Ima najveći potencijal za malignu transformaciju među leukoplakijama[16,25,37]. Uobičajena mesta za oralnu leukoplakiju su dno usta, jezik, bukalna sluzokoža, usne gingive, nepce i crna ivica usne. Kada lezija zahvata dno usta i jezika, veća je verovatnoća da će doživeti malignu transformaciju[38].

Ispitivanje

Vitalno bojenje

Vitalno bojenje je postupak prikom koga žive ćelije preuzimaju određene boje, koje ih selektivno boje. Upotreba vitalnog bojenja toluidin plavim ili jodom može ocrtati prisustvo displazije i identifikovati mesto biopsije u velikim lezijama[16]. Toluidin plavo boji nukleohistone u DNK[39]. Njegova upotreba *in vivo* zasniva se na činjenici da displastične i anaplastične ćelije sadrže kvantitativno više nukleinskih kiselina nego normalna tkiva, pokazuju gubitak ćelijske kohezije i povećanu mitozu. Lugolov jod boji glikogen citoplazme. Pošto displastične i maligne ćelije imaju manje glikogena, a normalna tkiva više, on selektivno boji normalna tkiva braon u crno[39,40,41].

Optičke tehnike: Optičke tehnike zasnivaju se na sposobnosti tkiva da fluoresciraju. Vizilit je hemiluminiscentna metoda koja se koristi za otkrivanje displastičnih područja oralne sluzokože. Kada se koristi u kombinaciji sa toluidin plavim, efikasan je u identifikaciji područja displazije za biopsiju[42]. Velscope koristi sposobnost autofluorescencije, dajući fluorescentnu boju normalnim tkivima i boju od tamno zelene do crne boje abnormalnim tkivima[43,44].

Glavni nedostatak navedenih metoda je učestalost lažno pozitivnih i lažno negativnih rezultata[16,33].

Ostalo: fluorescentno endoskopsko snimanje posredovano 5-aminolevulinskom

A common feature in leukoplakia is the presence of a non-scrapable white patch, generally associated with tobacco consumption[36]. Homogeneous leukoplakia is a white patch which can be either corrugated (like a beach with ebbing tide) with fine lines known as cristae or a wrinkled form, which is commonly described as dry, cracked mud appearance[36]. Non-homogeneous leukoplakia may be nodular or speckled. These are keratotic nodules or specks present on an erythematous base of mucosa[36]. Verrucous form of leukoplakia has densely keratinized projections of the mucosal surface[36].

Proliferative verrucous leukoplakia is characterized by the presence of exophytic and proliferative keratotic plaques which are not much associated with the use of tobacco[37]. It has the highest potential for malignant transformation among the leukoplakias[16,25,37].

Common sites for oral leukoplakia are the floor of the mouth, tongue, buccal mucosa, gingiva lips, palate, and vermilion border of the lip. When the lesion involves floor of mouth and tongue, it is more likely that it will undergo malignant transformation[38].

Investigations

Vital Staining

Vital staining is a procedure where living cells take up certain dyes, which selectively stains them. Use of vital staining with toluidine blue or lugol's iodine can delineate the presence of dysplasia and identify the site of biopsy in large lesions[16]. Toluidene blue stains the nucleohistones in DNA[39]. Its use *in vivo* is based on the fact that dysplastic and anaplastic cells contain quantitatively more nucleic acids than normal tissues, show loss of cell cohesion and increased mitosis. Lugol's iodine stains the glycogen of the cytoplasm. Since dysplastic and malignant cells have less glycogen and normal tissues have more, it selectively stains the normal tissues brown to black[39,40,41].

Optical techniques: These are based on the ability of the tissues to fluoresce. Vizilite is a chemiluminescent method used to detect dysplastic areas of the oral mucosa.

When used in combination with toluidine blue, it is effective in identifying areas of dysplasia for biopsy[42]. Velscope utilises the ability of autofluorescence giving fluorescent colour to normal tissues and dark green to black colour to abnormal tissues[43,44].

kiselinom (ALA), digitalizovano fluorescentno endoskopsko snimanje posredovano ALA i autofluorescentna spektroskopija koriste se za usmeravanje biopsija i otkrivanje margina za hirurško resekciju[16].

Histopatološke metode

Histopatološke metode uključuju eksfolijativnu citologiju, biopsiju četkicom i biopsiju. Eksfoliativna citologija je histopatološka studija eksfolijiranih ćelija za određivanje karakteristika displazije. Suština metode je da displastične ćelije u dubljim epitelnim slojevima, postaju labavije u malignim stanjima i sidaju se zajedno sa ćelijama površnog sloja[45]. Nedostaci su lažno pozitivni i lažno negativni rezultati[45].

Biopsija četkicom, takođe poznata kao oralna CDk biopsija ili transepitelna biopsija, prikuplja ćelije iz svih slojeva oralnog epitela i smatra se reprezentativnijom od eksfoliativne citologije. Rezultati se procenjuju korišćenjem kompjuterske analize[16,46]. Biopsija može biti inciziona ili eksciziona. Inciziona biopsija savetuje se za lezije manje od 1 cm, dok se kod većih lezija biopsira reprezentativno područje. Odabir ovog područja može se izvršiti nakon bojenja toluidin plavim, kako bi se identifikovala područja displazije[42].

Histološke karakteristike

Kod leukoplakije, epitelna displazija može biti prisutna u rasponu od blage do teške. Displastične promene kod leukoplakije uključuju ćelijski pleomorfizam, nuklearni hiperhromatizam, povećan nuklearno-citoplazmatski odnos, uvećane nukleole, smanjenje ćelijske kohezije, keratinizaciju jedne ćelije, gubitak polariteta bazalnih ćelija, rete pege u obliku kapi, povećan broj mitotičkih figura, prisustvo mitotičke figure, i prisustvo više od jednog sloja ćelija koje izgledaju kao ćelije bazalnog sloja (VHO, 1978)[47]. Molekularni markeri Mib-l, Ciclin Dl i CENP-F i eksprimirani su u bazalnim suprabazalnim i površinskim slojevima oralne sluzokože sa leukoplakijom[48]. Markeri proliferacije i kontrole ćelijskog ciklusa koriste se za određivanje malignog potencijala lezije.

Određivanje malignog potencijala lezije uključuje Ki-67, ciklin D1 i proteine kao što su p53, p16 i pRb[26]. Prekomerna ekspresija p53 i smanjeni p16 smatraju se najranijim markerima maligne

The main disadvantage of the above methods is the incidence of false positive and false negative results[16,33].

Others: 5-Aminolevulinic acid (ALA) mediated fluorescence endoscopic imaging, ALA mediated digitized fluorescence endoscopic imaging and autofluorescence spectroscopy are used to direct biopsies and detect the margins for surgical resection[16].

Histopathological Methods

These include exfoliative cytology, brush biopsy and biopsy.

Exfoliative cytology is the histopathologic study of exfoliated cells for features of dysplasia. The rationale is that dysplastic cells in the deeper epithelial layers become loose in malignant conditions and are shed along with superficial cells[45]. Disadvantages are false positive and false negative results[45].

Brush biopsy, also known as oral CDx biopsy or transepithelial biopsy, collects cells from all layers of the oral epithelium and is considered more representative than an exfoliative cytology. Results are evaluated using computer analysis[16,46].

Biopsy can be incisional or excisional. Incisional biopsy is advised for lesions less than 1 cm in size while in larger lesions a representative area is biopsied. Selection of this area can be done following a toluidine blue staining to identify areas of dysplasia[42].

Histological features

In leukoplakia, epithelial dysplasia may be present ranging from mild to severe. Dysplastic changes in leukoplakia include cellular pleomorphism, nuclear hyper-chromatism, increased nuclear- cytoplasmic ratio, enlarged nucleoli, reduction of cellular cohesion, single cell keratinization, loss of basal cell polarity, drop shaped rete pegs, increased number of mitotic figures, presence of mitotic figures, drop shaped rete pegs and presence of more than one layer of cell having basaloid appearance (WHO, 1978)[47].

Molecular markers

Mib-l, Cyclin Dl, and CENP-F i are expressed in basal suprabasal and superficial layers of oral mucosa with leukoplakia[48].

Markers of proliferation and cell cycle control are used to determine malignant potential of a lesion.

transformacije. Ovo je posebno relevantno kod nedisplastične leukoplakije, prilikom koje promene p53, Ki-67 i p16 ukazuju na progresiju u malignitet[22,26].

Morfometrijska analiza uz pomoć kompjutera ispituje ćelijski i nuklearni perimetar korišćenjem kompjuterskih slika histoloških preseka. Primećeno je to se veličina ćelije i jedra progresivno povećavaju od normalne sluzokože prema leukoplakiji do oralnog skvamoznog karcinoma[22].

AgNOR tehnika: Ova tehnika detektuje proteine povezane sa transkripcionom aktivnošću nukleolarnih organizacionih regiona (NOR) kroz impregnaciju koloidnog srebra, nazvane AgNOR proteini. NOR se mogu vizualizovati pod mikroskopom kao male, dobro definisane tamne mrlje unutar ćelijskog jezgra[26]. AgNOR se smatraju markerima proliferacije epitela i pretpostavlja se da se njihov broj povećava sa malignitetom. Međutim, autori nisu uspeli da pokažu definitivnu vezu između AgNOR-a i maligne transformacije[26,49,50].

Diferencijalna dijagnoza

Diferencijalna dijagnoza leukoplakije uključuje lichen planus, leukoedem, amelanotični nevus, sifilitičnu sluzokožu, eritematozni lupus discoideus, bradavice, hemijsku opekotinu i hroničnu mehaničku povredu usled ujeda obraza[29]. Asimetrična bela mrlja koja se ne može skinuti, odsustvo Vikamovih strija bez okolne upale pomaže u postavljanju kliničke dijagnoze leukoplakije[51]. PVL, posebno nehomogeni tip, može se pomešati sa lichen planusom zbog njegovog multifokalnog i bilateralnog širenja[25].

Stopa maligne transformacije i prognostički indikatori

Globalna stopa maligne transformacije leukoplakije kreće se od 0,7% do 2,9% 12. Poznato je da se leukoplakija javlja 5 godina pre početka oralnog karcinoma skvamoznih ćelija[32]. Postoje različiti faktori koji povećavaju sklonost leukoplakije ka malignoj transformaciji. To su: ženski pol, dugo perzistentna lezija koja ne reaguje na terapiju, I lokalizacija visoko rizičnim mestima kao što su dno usta, ventrolateralna strana jezika i meko nepce, prisustvo lezije kod nepušača ili idiopatska leukoplakija.

Veću tendenciju maligne transformacije imaju nehomogena leukoplakija egzofitnog i verukoznog izgleda i leukoplakija sa epitelnom displazijom[52].

These include Ki-67, cyclin D1 and proteins such as p53, p16 and pRb[26]. Overexpression of p53 and decreased p16 are considered as the earliest markers of malignant transformation. This is especially relevant in non-dysplastic leukoplakia where p53, Ki-67, and p16 alteration are suggestive of progression to malignancy[22,26].

Computer-assisted morphometric analysis: analyses cell and nuclear perimeter using computer images of histologic sections. The cell and nuclear size was observed to increase progressively from normal mucosa to leukoplakia to oral squamous cell carcinoma[22].

AgNOR technique: This technique detects proteins associated with the transcriptional activity of nucleolar organizing regions (NORs) through colloidal silver impregnation, named AgNOR proteins. NORs can be visualized under the microscope as small, well-defined dark spots within the cell nucleus[26].

AgNORs are considered as markers of epithelial proliferation and their numbers are hypothesized to increase with malignancy. However, authors have failed to show a definite relation between AgNORs and malignant transformation[26,49,50].

Differential diagnosis

Differential diagnosis of leukoplakia includes lichen planus, leukoedema, white sponge nevus, syphilitic mucous patch, discoid lupus erythematosus, verruca vulgaris, chemical burn, and chronic cheek bite[29]. Asymmetric, non-scrapable white patch, absence of Wickham's striae without surrounding inflammation helps establish a clinical diagnosis of leukoplakia[51]. PVL, especially the non-homogenous type, may be confused with lichen planus due to its multifocal and bilateral involvement[25].

Malignant transformation rate and prognostic indicators

Global rates of malignant transformation of Leukoplakia range from 0.7% to 2.9%[12]. Leukoplakia has been known to occur 5 years prior to the onset of oral squamous cell carcinoma[32].

There are various factors that increase the tendency of aleukoplakia to turn malignant.

This includes female gender, leukoplakias persisting over prolonged periods and resistant to treatment, OL in high risk sites such as the floor of the mouth, ventrolateral tongue and soft palate, OL among non-smokers or idiopathic leukoplakia.

Homogena leukoplakija ima najmanji potencijal za malignu transformaciju, dok PVL ima najveći maligni potencijal od oko 70-80%[29]. Prema Varnakulasuria i sar[10], ženski pol, dugotrajna leukoplakija, leukoplakija kod nepušača (idiopatska leukoplakija), lokalizacija na jeziku ili dnu usta, veličina veća od 200 mm2, nehomogena leukoplakija, prisustvo kandide i prisustvo epitelne displazije imaju povećanu tendenciju maligne transformacije. Displastični epitel ima stopu maligne transformacije od oko 41% dok nedisplastični epitel ima potencijal maligniteta od samo oko 9,5%[53,54]. Molekularni markeri kao što su Ki-67, bromodeoksiuridin i kombinacija hromozomske polisomije, gubitak heterozigotnosti i p5 veruje se da tačno predviđaju potencijal maligne transformacije[53]. Subjekti sa višestrukim područjima leukoplakije skloniji su malignoj transformaciji od onih sa pojedinačnim lezijama[53]. Leukoplakija sa gubitkom heterozigotnosti (LOH) na 3p14 i/ili 9p[21] bila je povezana sa većim rizikom od razvoja invazivnog karcinoma[33]. Gopinath i sar.[12] su izvestili da korisnici duvana imaju četiri puta veći rizik od maligne transformacije u poređenju sa onima koji ne koriste duvan.

Režim praćenja: Potreba za praćenjem određena je stepenom displazije i mestom leukoplakije. Šestomesečno praćenje preporučuje se za lezije bez displazije, tromesečno za blagu/umerenu displaziju, a mesečno za tešku displaziju / karcinom *in situ*[33,55].

Lečenje

Prvi cilj u lečenju leukoplakije je prevencija maligne transformacije56. Lečenje leukoplakije može se podeliti na konzervativno, medicinsko i hirurško lečenje. Pre nego što se odluči o lečenju, mora se proceniti stepen epitelne displazije. Hirurško lečenje poželjnije je kod umerene do teške displazije, dok u slučajevima sa blagom displazijom, odluke o upravljanju treba da se procene u kontekstu drugih karakteristika kao što su mesto, veličina, prestanak upotrebe duvana, itd[22].

Konzervativno lečenje

Prvi korak u lečenju oralne leukoplakije je uklanjanje etioloških faktora kao što su duvan, alkohol i žvakanje betel kuida.

Ovo se može uraditi kroz savetovanje o navikama. Oko 60% leukoplakije može regresirati ako se prestane sa pušenjem. Pokazalo se da redovno savetovanje povećava

Non homogenous leukoplakia with exophytic and verrucous appearance and leukoplakia with epithelial dysplasia have a higher tendency for malignant transformation[52]. Homogenous leukoplakia has the least potential for malignant transformation while PVL has the highest malignant potential of around 70-80%[29].

According to Warnakulasuriya et al[10], female gender, long term leukoplakia, leukoplakia in non-smokers (idiopathic leukoplakia), location in the tongue or the floor of the mouth, size greater than 200 mm^2, non homogenousleukoplakia, presence of *Candida Albicans and* presence of epithelial dysplasia have increased tendency for malignant transformation. Dysplastic epithelium has a malignant transformation rate of around 41% while non-dysplastic epithelium has a malignancy potential of only around 9.5%[53, 54]. Molecular markers such as Ki-67, bromodeoxyuridine and a combination of chromosomal polysomy, loss of heterozygosity and p53 are believed to accurately predict the potential for malignant transformation[53]. Subjects with multiple areas of leukoplakia are more prone to malignant transformation than those with single lesions[53]. Leukoplakia with loss of heterezygosity (LOH) at 3p14 and/ or 9p[21] was associated with more risk of developing invasive cancer[33]. Gopinath et al[12] reported that tobacco users had four fold increased risk of malignant transformation when compared to non-users.

Follow up Regimen: The need for follow-up is determined by the degree of dysplasia and the site of leukoplakia. Six-monthly follow up is recommended for lesions without dysplasia, three-monthly for mild/moderate dysplasia, and monthly for severe dysplasia/carcinoma *in situ*[33,55].

Management

The first aim in the management of leukoplakia is the prevention of malignant transformation[56]. Management of leukoplakia can be divided into conservative, medical and surgical management. Prior to deciding the treatment, the degree of epithelial dysplasia must be assessed. Surgical management is preferred in moderate to severe dysplasia while in cases with mild dysplasia, management decisions need to be evaluated in the context of other features like site, size, discontinuation of tobacco use, etc[22].

Conservative Management

The first step in the management of oral leukoplakia is the removal of etiological-factors such as tobacco, alcohol and betel quid chewing.

stopu odvikavanja od duvana[22,53]. Martin i sar. prijavili su regresiju leukoplakije nakon prestanka navike žvakanja duvana[57]. Enameloplastika oštrih zuba i zamena neispravnih nadoknada predstavljaju početni tretman u slučajevima sa hroničnom iritacijom izazvanom leukoplakijom. Upotreba lekova protiv gljivica korisna je u slučajevima leukoplakije povezane sa kandidom. Preporučuje se prekid konzumacije alkohola i uvođenje zdrave ishrane i dobre oralne higijene. Drugi pristup je metoda „čekaj i vidi" po kojoj se pacijenti redovno prate kako bi se otkrili početni znaci maligne transformacije, kada se može uvesti odgovarajući tretman[22].

Medicinski tretman

Medicinski tretman poželjniji je kod pacijenata sa osnovnim zdravstvenim stanjima koja predstavljaju rizik za hirurške procedure. Prednosti ove metode su minimalni neželjeni efekti, niska cena i jednostavnost. Ovo je preporučeni metod u slučajvima u kojima je lezija široko rasprostranjena ili u slučajevima u kojima je lezijom zahvaćeno više mesta [52]. Hemoprevencija je metoda upotrebe hemijskih agenasa za preokretanje, suzbijanje ili sprečavanje razvoja maligniteta. Neke od metoda medicinskih tretmana su:

Beta karoten: je prekursor vitamina A. Njegov način delovanja je uklanjanje slobodnih radikala. Kombinuje se sa reaktivnim vrstama kiseonika i deluje kao antioksidans smanjujući šanse da lezija postane maligna. Prijavljeno je da je beta karoten efikasniji kod pušača koji imaju nizak nivo vitamina C i beta karotena. Doziranje varira u različitim studijama u rasponu od 20-90 mg/dan tokom 3 do 12 meseci. Studije su prijavile minimalne neželjene efekte kao što su bol u mišićima i glavobolja. Regresija leukoplakičnih lezija je zabeležena kod 4-54% ispitanika nakon tretmana. Međutim, određene studije pominju recidiv i malignu transformaciju nakon prestanka uzimanja leka[52,53].

Likopen: Likopen je karotenoid koji se nalazi u zrelom paradajzu. To je efikasan antioksidans koji neutrališe slobodne radikale i veruje se da štiti ćelije od progresije u displaziju inhibiranjem proliferacije tumorskih ćelija[52].

Singh M i sar.[58] procenili su efikasnost likopena kod leukoplakije i otkrili da je 8 mg/dan bolje od 4 mg/dan u lečenju leukoplakije. Patel JS i sar.[59] su otkrili da je likopen zajedno sa vitaminom E i selenom pokazao kliničko i histološko poboljšanje u poređenju sa placebom.

This can be done through habit counselling. Around 60% of leukoplakia can regress if tobacco habits are stopped. Use of habit counselling also increases tobacco quit rates[22,53]. Martin et al. reported regression of leukoplakia after stopping ~~the~~tobacco chewing habit[57]. Enameloplasty for sharp teeth and replacement of faulty restorations form the initial management in cases with chronic irritation induced leukoplakia. Use of anti-fungal medication is useful in cases of Candida associated leukoplakia. Stoppage of alcohol and institution of a healthy diet and good oral hygiene is recommended.

Another approach is the 'wait and see' method where patients are kept onregular follow up to detect initial signs of malignant transformation, at which time, appropriate treatment can be instituted[22].

Medical Management

Medical management is preferred in patients with underlying medical conditions which pose a risk for surgical procedures. The advantages of this method are minimal adverse effects, low costand ease of use. It is the recommended method in widespread cases or cases with multiple sites of involvement[52].

Chemoprevention is the method of using chemical agents to reverse, suppress, or prevent development of malignancy. Some of the methods of medical management include:

Beta Carotene: is a precursor of Vitamin A. It's mode of action is through scavenging of free radicals. It combines with reactive oxygen species and acts as an antioxidant decreasing the chances of the lesion turning malignant. Beta carotene has been reported to be more effective in smokers who have inherently low levels of vitamin C and beta carotene. The dosage varies in different studies ranging from 20-90 mg/day for 3 to 12 months. Studies have reported minimal side effects such as muscle pain and headaches. Regression of OL lesions has been noted in 4-54% subjects after treatment. However, certain studies mention recurrence and malignant transformation after stoppage of the medication[52,53].

Lycopene: Lycopene is a carotenoid found in ripe tomatoes. It is an effective antioxidant which neutralises free radicals and is believed to protect cells from progression into dysplasia by inhibiting tumour cell proliferation[52].

Terapija vitaminom A (retinoična kiselina):

Vitamin A je potreban za normalnu diferencijaciju epitelnih ćelija i formiranje keratina. Retinoidi deluju svojim delovanjem na proizvodnju keratina, rast ćelija, diferencijaciju ćelija i gubitak ćelija. Nedostatak je povezan sa malignitetima epitela[53]. Kod oralne leukoplakije preporučuje se retinoid 13-cis-retinoična kiselina (13-cRA, izotretinoin). Lokalni 0,1% izotretinoin gel je pokušavan za oralnu leukoplakiju tokom 4 meseca, pri čemu je jedna trećina ispitanika pokazala potpunu regresiju leukoplakije. Studije sa sistemskom primenom pokazale su različite rezultate. Sistemska 13-cis retinoična kiselina (1-2 mg/kg dnevno) tokom perioda od 3 meseca bila je povezana sa smanjenjem veličine lezije u 67% slučajeva[60]. Glavni nedostatak terapije izotretinoinom je ponavljanje lezije nakon prestanka uzimanja leka. Neželjeni efekti kao što su glavobolja, bol u mišićima, primećeni su uz delimično ili potpuno povlačenje lezija. Ostali prijavljeni neželjeni efekti su hipervitaminoza, teratogenost i promene u različitim organskim sistemima. Fenretinid je analog vitamina A sa manje toksičnosti i testiran je sa različitim rezultatima kod OL-a i oralnog lihen planusa (OLP). Lokalna primena dva puta dnevno tokom jednog meseca ili sistemska primena od 200 mg/dan tokom 3 meseca dala je prihvatljive rezultate u OL i OLP[53,61].

Vitamin C i vitamin E su testirani zbog njihovog antioksidativnog dejstva sa nekoliko studija koje su pokazale delimičnu ili potpunu regresiju leukoplakije[61].

Topikalni bleomicin: Studija je koristila 1% topikalni bleomicin tokom 14 uzastopnih dana nakon čega je usledila biopsija odmah nakon tretmana. Rezolucija displazije je zabeležena kod 75% pacijenata uz poboljšanje od najmanje dva stepena displazije. Zaključili su da bleomicin može usporiti napredovanje displazije u malignitet[62]. Bleomicin se takođe može koristiti kod ekstenzivnih leukoplakija da bi se smanjila veličina lezije nakon čega sledi hirurška ekscizija[63].

Antifungalna terapija: savetuje se 2-4 nedelje antifungalne terapije kod mogućih leukoplakijskih lezija, uz uklanjanje mogućih uzročnika kao što je pušenje kako bi se procenila regresija lezije.

Vizhi i sar.[64] su prijavili konverziju 14% slučajeva nehomogene leukoplakije u homogenu leukoplakiju nakon tretmana sa 1% topikalnog klotrimazola tri puta dnevno tokom 3 nedelje. Takođe je primećeno smanjenje veličine lezije i poboljšanje kliničkog stadija, čime se smanjuju šanse za malignu transformaciju[64].

Singh M[58] et al evaluated the efficacy of lycopene in leukoplakia and found that 8 mg/day was better than 4 mg/day in management of leukoplakia. Patel JS et al[59] found that lycopene along with Vitamin E and selenium showed clinical and histologic improvement when compared with placebo.

Vitamin A (Retinoic acid) therapy: Vitamin A is needed for normal epithelial cell differentiation and keratin formation. Retinoids act through their action on keratin production, cell growth, cell differentiation and cell loss. Deficiency has been associated with epithelial malignancies[53]. In oral leukoplakia, the retinoid 13-cis-retinoic acid (13-cRA, isotretinoin) is recommended. Topical 0.1% isotretinoin gel was tried for oral leukoplakia for 4 months with one-third of subjects showing complete regression of leukoplakia. Studies with systemic administration have shown varied results. Systemic 13-cis retinoic acid (1–2 mg/kg per day) for a period of 3 months was associated with decreased lesion size in 67% cases[60]. The main drawback of isotretinoin therapy is the recurrence of the lesion after the medication is stopped. Side effects such as headaches, muscle pain, were noted with partial or complete resolution of lesions. Other reported side effects are hypervitaminosis, teratogenicity and alterations in various organic systems. Fenretinide is a Vitamin A analogue with less toxicity and has been tried with varied results in OL and oral lichen planus(OLP). Topical application twice daily for one month or systemic use of 200 mg/day for 3 months gave acceptable results in OL and OLP[53,61].

Vitamin C and Vitamin E have been tried for their antioxidant effect with few studies showing partial or complete regression of leukoplakia[61].

Topical bleomycin: A study used 1% topical bleomycin for 14 consecutive days followed by immediate post treatment biopsy. Resolution of dysplasia was noted in 75% patients with improvement of at least two grades of dysplasia. They concluded that bleomycin may retard the progression of dysplasia into malignancy[62]. Bleomycin can also be used in extensive leukoplakias to decrease the size of the lesion followed by surgical excision[63].

Antifungal therapy: A 2-4 week course of antifungal therapy is advised in possible leukoplakia lesions along with removal of possible of causative agents like smoking in order to evaluate for lesion regression.

Fotodinamička terapija (PDT): je neinvazivna metoda lečenja OL. Daje dobre kozmetičke rezultate, dobro se podnosi; može se koristiti kod osoba kod kojih nije preporučljivo hirurško lečenje, kao što su osobe sa pejsmejkerima ili sklonostima krvarenju. PDT deluje tako što proizvodi reaktivne vrste kiseonika koje mogu da ubiju displastične ćelije direktnim dejstvom, oštećenjem vaskulature ili imunološkom aktivacijom. Selvam i sar.[65] su koristili 10% ALA emulziju kao afotosenzibilizator u slučajevima OL nakon čega je usledila primena svetlosti pomoću ksenonske lampe tokom 1000 sekundi. Ova terapija je nastavljena tokom 6-8 sesija sa intervalom od 1 nedelje između sesija. Od 5 ispitanika u studiji, potpuna i delimična rezolucija OL-a zabeležena je kod po 2 subjekta. Neželjeni efekti su uključivali prolazni osećaj pečenja[65].

Hirurške opcije

Hirurško lečenje se savetuje u prisustvu umerene do teške epitelne displazije. U slučajevima niskog do umerenog rizika, potrebno je proceniti druge faktore pacijenta, kao što je prestanak navika. Kriohirurgija: Ovo je metoda izlaganja tkiva ekstremnoj hladnoj temperaturi. Ćelijska smrt se javlja na -20 stepeni Celzijusa. Koristi se krio sonda hlađena tečnim azotom. Zamrzavanje se vrši 1 minut, a zatim odmrzavanje od 5 minuta. Ova procedura se ponavlja 2-3 puta da bi se postiglo maksimalno uništenje tkiva[66].

Elektrohirurgija: Ova tehnika koristi struju visokog napona koja se kontroliše pomoću pokretne elektrode. Izaziva destru-kciju tkiva uz laku kontrolu krvarenja[67]. Laseri su povezani sa smanjenim intraoperativnim krvarenjem, smanjenim edemom lica i smanjenim ožiljcima tkiva. Međutim, otkriveno je da su post-hirurški bol i otok slični kod ekscizije skalpelom[68].

Karbonski laser: Sadrži ugljen-dioksid, azot i helijum. Ima dubinu prodiranja u tkiva od 0,2 do 0,3 mm i talasnu dužinu od 10.600 nm u infracrvenom spektru. Kod laserske ablacije postiže se površinska dubina vaporizacije od 0,5 mm, što obično rezultira dobrom sekundarnom reepitelizacijom[69,70].

Kalijum-titanil fosfatni (KTP) laseri: Imaju talasnu dužinu od 532 nm i proizvode se propuštanjem Nd: IAG laserskog zraka (1064 nm) kroz KTP kristal, čime se njegova talasna dužina prepolovi do 532 nm. Ima sposobnost ablacije krvnih sudova hraneći leziju uz očuvanje biološke obloge sluznice koja se nalazi iznad[69].

Vizhi et al[64] reported conversion of 14% cases of non-homogenous leukoplakia into homogenous leukoplakia after treatment with 1% topical clotrimazole thrice daily for 3 weeks. Decreased lesion size and improvement in clinical staging thereby reducing the chances of malignant transformation[64].

Photodynamic therapy (PDT): is a non-invasive method of OL management. It produces good cosmetic results it is tolerated well; can be used in subjects where surgical management is not advisable such as subjects with pacemakers or bleeding tendencies. PDT acts by production of reactive oxygen species which can kill dysplastic cells through direct effect, damage to vasculature or through immune activation. Selvam et al[65] used 10% ALA emulsion as aphotosensitizer in OL cases followed by light application using a xenon lamp for 1000 sec. This therapy was continued for 6-8 sessions with interval of 1 week between sessions. Out of 5 subjects in the study, complete and partial resolution of OL was noted in 2 subjects each. Side effects included transient burning sensation[65].

Surgical options

Surgical management is advised in the presence of moderate to severe epithelial dysplasia. In cases of low to moderate risk, other patient factors need to be assessed such as habit cessation.

Cryosurgery: Here tissue is exposed to extreme cold temperature. Cell death occurs at -20 degree Celsius. Cryo probe refrigerated by liquid nitrogen is used. Freezing is done for 1 minute, followed by a thaw of 5 minutes. This procedure is repeated 2-3 times to achieve maximum tissue destruction[66].

Electrosurgery: This technique employs high voltage current that is controlled by a movable electrode. It causes tissue destruction with easy control of haemorrhage[67].

Lasers are associated with decreased intraoperative bleeding, decreased facial edema and decreased scarring of tissue. Post-surgical pain and swelling, however were found to be similar in scalpel and laser excision[68].

Carbon dioxide LASER: It contains carbon dioxide, nitrogen and helium. It has a tissue depth of 0.2 to 0.3 mm and 10.600 nm wavelength in the infrared spectrum. In laser ablation a surface vaporization depth of 0.5 mm is achieved which normally results in good secondary re-epithelization[69,70].

Menadžment PVL

Najveće poteškoće/prepreke u zbrinjavanju nastaju zbog pojave recidiva nakon lečenja i toksičnosti na propisane lekove. Kod PVL, laserska ablacija i topikalna fotodinamička terapija daju bolje rezultate od ostalih tradicionalnih metoda. Međutim, potpuna ekscizija sa marginama bez bolesti u kombinaciji sa dugotrajnim praćenjem čini oslonac lečenja u PVL[37]. Ponavljanje OL nakon hirurškog lečenja prijavljeno je u 10–35% slučajeva[52,71]. Različite studije su pokazale da se čak i nakon hirurškog lečenja leukoplakija može ponoviti u 13-42% slučajeva, a maligna transformacija može doći u 3-11% slučajeva na mestu ekscizije[70]. Još jedan važan nalaz je da recidiv leukoplakije nije bio povezan sa korišćenim protokolom lečenja[71]. Sundberg i sar.[71] sproveli su prospektivnu studiju kako bi procenili karakteristike pacijenata i metode lečenja leukoplakije sa stopama recidiva. Otkrili su ukupan recidiv od 42% nakon hirurškog uklanjanja. Glavni faktori koji su doveli do recidiva bili su nehomogena leukoplakija i upotreba burmuta. Utvrđeno je da savetovanje o prestanku pušenja pomaže ljudima da ostave pušenje i povezano je sa smanjenim recidivom. Takođe su otkrili da se 9% slučajeva rekurentne leukoplakije transformiše u karcinom skvamoznih ćelija[71]. Ovo implicira da je rekurentna OL povezana sa većim rizikom od maligne transformacije. Moguće objašnjenje za recidiv leukoplakije može se naći u konceptu kancerizacije polja gde je genomska nestabilnost prisutna u celoj sluzokoži što dovodi do generalizovanog povećanog rizika od maligne transformacije. Kuribajashi i sar.[72] su pronašli stopu recidiva od 15.1% i stopu maligne transformacije od 1.9% nakon hirurške ekscizije. Stepen displazije nije bio u korelaciji sa malignom transformacijom[72].

Drugi agensi za hemoprevenciju

Agensi uključuju inhibitore ciklo-oksigenaze-2 (COKS2) poput celekoksiba i ketorolaka[73,74]; polifenoli zelenog čaja poput epigalokatehin-3-galata (EGCG)75; p53-ciljani agensi koji koriste modifikovani adenovirus[76]; tiazolidindioni kao što je pioglitazon[77] i inhibitori EGFR koji su pokazali promenljive rezultate[33].

Potassium-Titanyl phosphate (KTP) lasers: It has a wavelength of 532 nm and is produced by passing a Nd: YAG laser beam (1064 nm) through a KTP crystal, thus halving its wavelength to 532 nm.

It has the ability to ablate the underlying vasculature feeding the lesion while preserving a biological dressing of overlying mucosa[69].

Management of PVL

The major difficulties/ hurdles in the management are due to recurrence after treatment and toxicity to the prescribed medications. In PVL, laser ablation and topical photodynamic therapy have given better results than the other traditional methods. However, total excision with disease free margins combined with long term follow up forms the mainstay of treatment in PVL[37]. Recurrence of OL after surgical treatment has been reported in 10%–35% of cases[52,71]. Various studies have shown that even after surgical management leukoplakia can recur in 13-42% of cases and malignant transformation can occur in 3–11% of cases at the excision site[70]. Another important finding is that leukoplakia recurrence was not related to the treatment protocol used[71].

Sundberg et al.[71] carried out a prospective study in order to evaluate patient characteristics and leukoplakia management methods with recurrence rates. They found an overall recurrence of 42% after surgical removal. The major factors promoting recurrence were nonhomogenous leukoplakia and the use of snuff. Tobacco cessation counselling was found to help people quit smoking and associated with decreased recurrence. They also foundthat 9% of cases of recurrent leukoplakia transformed into squamous cell carcinoma[71]. This implies that recurrent OL is associated with higher risk of malignant transformation.

A possible explanation for leukoplakia recurrence could be found in the concept of field cancerisation where genomic instability is present throughout the mucosa leading to a generalised increased risk of malignant transformation. Kuribayashi et al[72] found a recurrence rate of 15.1% and a malignant transformation rate of 1.9% after surgical excision. The degree of dysplasia was not correlated to malignant transformation[72].

Izazovi u lečenju leukoplakije

Jedan od glavnih faktora koji utiču na lečenje leukoplakije je nedostatak znanja o prirodnoj istoriji bolesti uprkos ogromnoj količini objavljenih podataka. Neke leukoplakije će ostati statične godinama, neke će se povući nakon prestanka navika, dok će se neke od nedisplastičnih leukoplakija transformisati u maligne lezije[33]. Drugi izazov je koncept „kancerizacije polja" koji podrazumeva da zdrava sluzokoža kod pacijenata sa potencijalno malignim i malignim lezijama takođe može imati displastične promene. Upotreba vitalnog bojenja može pomoći u identifikaciji takvih područja[33].

Zaključak

Leukoplakija je oralna potencijalno maligna lezija koju treba pravilno pregledati jer ima velike šanse za malignu transformaciju. Lekar bi trebalo da ima temeljno znanje o kliničkoj dijagnozi, različitim metodama ispitivanja i terapijskim protokolima koji će obezbediti lečenje lezije, koja bi trebalo da se završi obnavljanjem normalne zdrave sluzokože. Prestanak štetnih navika putem savetovanje važan je deo lečenja leukoplakije. Dugotrajno praćenje neophodno je u svim slučajevima oralne leukoplakije, čak i nakon hirurške ekscizije.

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Other chemoprevention agents

These include cyclooxygenase-2 (COX2) inhibitors like celecoxib and ketorolac[73,74]; green tea polyphenols like epigallocatevhin-3-gallate (EGCG)[75]; p53-targeted agents using modified adenovirus[76]; thiazolidinediones such as pioglitazone[77], and EGFR inhibitors with variable results[33].

Challenges in the management of leukoplakia

One of the major factors affecting the management of leukoplakia is the absence of knowledge regarding the natural history of the disease despite the huge amount of published data. Some leukoplakias will remain static for years, few will regress after stoppage of habit while few non-dysplastic leukoplakias will transform into malignant lesions[33]. Another challenge is the concept of 'field cancerisation' which implies that healthy-appearing mucosa in patients with potentially malignant and malignant lesions, may also present with dysplastic changes. The use of vital staining, can help identify such areas[33].

Conclusion

Leukoplakia is an oral potentially malignant lesionwhich should be screened properly as it has a high chance of malignant transformation. The clinician should have a thorough knowledge about the clinical diagnosis, the various investigativeand managementprotocols which will ensure the resolution of lesion followed by the restoration of normal healthy mucosa. Cessation of adverse habits through habit counselling is an important part of the management in leukoplakia. Long-term follow up is essential in all cases of oral leukoplakia even after surgical excision.

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DIGITALNA DENTALNA FOTOGRAFIJA – NEIZOSTAVNI DEO PARODONTOLOŠKE PRAKSE

DIGITAL DENTAL PHOTOGRAPHY – INDISPENSABLE PART OF PERIODONTAL PRACTICE

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Sažetak

Uvod: *Fotografija igra veoma važnu ulogu u interakciji sa pacijentom. Defekti koji nisu lako uočljivi pacijentu postaće očigledni na fotografijama. Stoga, dentalna fotografija omogućava pacijentu da vidi stanje svoje usne duplje i da se osmehne sa istom percepcijom, kakvu ima stomatolog. Upotreba dentalne fotografije značajna je u dokumentaciji, ali i u mnogim drugim segmentima, kao što su društveni, mediji ili marketing.*
Zaključak: *Upotreba odgovarajućih uređaja i dodatne opreme poboljšava rezultat dentalne fotografije. Ovaj informativni članak daje pregled važnosti dokumentacije, upotrebe digitalnih kamera i raznih intraoralnih dodataka, koji mogu pomoći kliničaru da postigne najbolje rezultate.*

Ključne reči: *dentalna fotografija, DSLR fotoaparat, dokumentacija*

Abstract

Introduction: *Photographs are fundamental in interacting with patients. Defects that are not readily noticeable to the patient will be obvious in still pictures. Thus, dental photography permits the patient to visualize their oral condition and smile with the same perception as the dentist. The use of dental photography is for documentation and many more other purposes like social media or marketing.*
Conclusion: *The use of proper devices and additional accessories enhances the outcome of dental photography. This informative article gives the overview of importance of documentation, use of digital cameras and various intraoral accessories which can help the clinician to obtain the best results.*

Key words: *dental photography, DSLR camera, documentation*

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Uvod

Fotografija je nauka i umetnost dokumentovanja slika. Dentalna fotografija je deo fotografije kao celine i ima svoju primenu u naprednoj stomatologiji. Trenutno, tehnološki napredak omogućio je stomatolozima da dentalnu fotografiju jednostavno koriste u svojoj rutinskoj, stomatološkoj praksi[1]. Od početka dijagnoze do poslednje faze postoperativne pretrage i čuvanja zapisa, slikovna dokumentacija igra vitalnu ulogu za svakog kliničkog stomatologa. Sa pojavom digitalne tehnologije, slikanje je postalo jednostavnije i dostupnije.

Mnogi praktičari tek treba da prihvate ovu promenu i počnu da dokumentuju svoj rutinski klinički rad. Znanju se može pristupiti iz principa fotografije, pribora, osvetljenja, podešavanja, naknadne obrade i svrhe njegove upotrebe[2].

Ovaj sažeti članak naglašava značaj upotrebe digitalne dentalne fotografije, zajedno sa dodatnim intraoralnim priborom u opštoj stomatološkoj i/ili parodontalnoj praksi.

Upotreba fotografije u stomatologiji

Dentalna fotografija igra centralnu ulogu u poboljšanju "licem u lice" i virtuelne brige o pacijenatu u savremenoj opštoj stomatološkoj praksi. Od prve posete stomatologu do svake naknadne kontrole nakon operacije, ovi vizuelni otisci obezbediće odgovarajuće akreditive i za pacijente i za kliničara. U nastavku će biti prikazana upotreba dentalne fotografije u svakom koraku kliničke prakse.

1. Preoperativno:
    a. dijagnoza;
    b. planiranje tretmana;
    c. edukacija pacijenata.
2. Operativno:
    a. praćenje napretka snimanjem;
    b. samokritika;
    c. podudaranje nijansi;
    d. komunikacija sa tehnikom;
    e. dizajniranje osmeha;
    f. interdisciplinarna komunikacija.
3. Postoperativno:
    a. medicinsko-pravni dokaz;
    b. evidencija;
    c. istraživanje/teza;
    d. diskusije/prezentacije;
    e. publikacije;
    f. deljenje na društvenoj mreži;
    g. stomatološko osiguranje.

Introduction

Photography is a science and art of documenting pictures. Dental photography is a part of it and upholds an essential share in advanced dentistry. Currently, technological progress has made it simpler for the dentists to employ it in their routine dental practice[1]. Since the beginning of diagnosis to the last phase of postoperative investigation and upholding records, pictorial documentation plays a vital role for every clinical practitioner. With the advent of digital technology, imaging has become simpler and readily accessible.

Many practitioners are yet to embrace this change and start documenting their routine clinical work. The knowledge can be accessed from the principles of photography, accessories, lighting, setups, post-processing and purpose of its use[2].

This concise article highlights the significance of using digital dental photography along with additional intra oral accessories in a general dental and/or periodontal practice.

Uses of photography in dentistry

Dental photography plays a central role in enhancing face-to-face and virtual patient care in contemporary general dental practice. Right from the first dental visit to every post-operative follow-up recall, these visual prints will provide appropriate credentials for both the patients and clinician. Following are the uses of dental photography at every step of clinical practice.

1. Preoperative
    a. Diagnosis
    b. Treatment planning
    c. Patient education
2. Operative
    a. Progress monitoring by recording step.
    b. Self-criticism
    c. Shade matching
    d. Lab communication
    e. Smile designing
    f. Interdisciplinary communication
3. Postoperative
    a. Medicolegal proof
    b. Record keeping
    c. Research/Thesis
    d. Discussions/Presentations
    e. Publications
    f. Sharing on social network
    g. Dental insurance

4. Drugo

a. poređenje preoperativnih očekivanja i postoperativnih rezultata;

b. edukacija stomatološke pomoći;

c. održavanje stomatoloških kurseva;

d. forenzička odontologija.

Slično svakoj stručnoj inovaciji u stomatologiji, odlična obuka, kao i posvećena praksa neophodni su elementi za efikasno uključivanje fotografije kao svakodnevne komponente postojeće brige o pacijenatu.

Parodontologija je grana stomatologije koja se bavi proučavanjem potpornih struktura zuba. Značaj dokumentacije u parodontologiji ogleda se u sledećem[3]:

1. praćenju parodontalnih pregleda i dijagnostike;
2. manifestaciji etioloških fakotra ili faktora rizika;
3. objašnjenju gingivitisa, parodontitisa, BOP, CAL i zahvaćenosti furkacije;
4. dokumentovanju akutnih parodontalnih stanja (apsces, nekrotizirajući ulcerozni parodontitis itd.);
5. dokumentovanju najvažnijeg kliničkog parametra, tj. nivoa kliničkog pripoja (CAL) pre i posle tretmana, koji određuje prognozu oboljenja;
6. snimanju zarastanje parodonta, edukovanju i motivaciji pacijenta da održava dobru oralnu higijenu.

***Opšte smernice za kliničku fotografiju[3]*:**

1. Uvek imajte pri ruci foto-aparat i dodatke;
2. postavite glavu pacijenta na naslon za glavu;
3. visinu i ugao stomatološke stolice treba postaviti na pogodan nivo, tako da se pozicioniranje kamere može lako omogućiti,
4. pacijent treba da ostane u ležećem položaju za nekoliko pristupa;
5. za pružanje dobre dijagnostičke informacije zubi treba da budu suvi;
6. za kontrolu vlage i povlačenje polja predmeta i površine ogledala potražite pomoć od saradnika;
7. kamera treba da stoji mirno dok snimate fotografiju;
8. kako bi se smanjio uticaj tokom operacije, vežbati fotografske veštine.

***Pribor koji se koristi u intraoralnoj fotografiji[2,4]*:**

1. *Retraktor obraza*

Kada je reč o dobroj intraoralnoj fotografiji, značajan doprinos boljem rezultatu imaju retraktori obraza.

4. Others

a. Comparing preoperative and post-operative results

b. Educating dental assistance

c. Conducting dental courses

d. Forensic odontology

Similar to all innovative expertise in dentistry, excellent training as well as dedicated practice are indispensable elements for the effective incorporation of photography as an everyday constituent of existing patient care.

Periodontology is a branch of dentistry which deals with supporting structures of the tooth. The importance of documentation in Periodontology is as follows[3]:

1. To accompany periodontal examination and diagnosis
2. Manifestation of etiological or risk factors
3. Explanation of gingivitis, periodontitis, BOP, CAL, and furcation involvement
4. Documenting acute periodontal conditions (Abscess, Necrotizing ulcerative periodontitis etc)
5. Documenting the most important clinical parameter, i.e, clinical attachment levels (CAL) pre and post treatment which determines the prognosis of the case.
6. Record periodontal healing; thereby educating and motivating the patient to maintain good oral hygiene.

General guidelines for clinical photography[3]:

1. Always have camera apparatus and supplements handy.
2. Stabilize the patient’s head on the headrest.
3. Height and the angle of the dental chair should be set at a comfortable level so that camera positioning can be easily enabled.
4. The patient should remain in supine position for several views.
5. To enhance the diagnostic information teeth should be dry.
6. For moisture control and retraction of the subject field and the mirror surface take help from an assistant.
7. The camera should be held steady while taking the photo.
8. To reduce the influence during surgery time, practice photographic skills.

Accessories to be used in intraoral photography[2,4]:

1. Cheek Retractor

For the intraoral photography, cheek retractors have a greater contribution to the outcome.

Koriste se za uvlačenje usne, labijalne i bukalne sluzokože iz vidnog polja, zbog čega velika količina svetlosti može ući u usnu duplju i poboljšati vidljivost. Osim toga, retraktori eliminišu različite strukture mekog tkiva iz oblasti interesovanja. Retraktori obraza izrađeni su od prozirne plastike ili metala i imaju jednostruki ili dvokraki kraj. Predlažu se plastični retraktori, jer su manje primetljivi na slikama.

2. ***Intraoralna ogledala***

Intraoralna ogledala su od neprocenjivog značaja, kada se snimaju fotografije okluzalne i bukalne regije jer direktno snimanje ovih regija nije moguće. Dostupna su u različitim veličinama. Osnovni set uključuje okluzalna i bukalna ogledala. Intraoralna ogledala korisna su za fotografisanje teško dostupnih područja i predstavljaju reflektovane slike. Da biste izbegli zamagljivanje ogledala, zagrejte ogledalo u vodenom kupatilu ili zatražite od pomoćnika da lagano izduva vazduh trosmernim špricem preko ogledala. Kako bi se pojednostavilo bukalno i okluzalno snimanje, ogledala su dostupna i sa ručkama. Korišćenje ogledala pomaže da se verovatnoća vidljivosti prstiju na fotografijama svede na najmanju moguću meru. Da bi se reflektujuće površine zaštitile od mogućih oštećenja, strogo se nalaže da se ogledala pokriju pojedinačno tokom sterilizacije, a ne da se direktno mešaju sa drugim instrumentima.

3. ***Drugi pribor za intraoralno fotografisanje:***

- Trake od gaze;
- Stomatološka ogledala;
- Plastične kašike za jednokratnu upotrebu;
- Plastične lopatice;

Predlaže se DRJS kamera (digitalna refleksna kamera sa jednim sočivom) za snimanje visokog kvaliteta, predvidljive, efikasne i prijatne kliničke fotografije tokom operacije (Slika 1,2 i 3).

They are used for the retraction of the lips, labial, and buccal mucosa from the field of view, because of which greatest amount of light can enter the oral cavity and enhance the visibility. Moreover, retractors eliminate various soft tissue structures from the area of interest. Cheek retractors are available in clear plastic or metal and are either single- or double-ended. Plastic retractors are suggested because it is less noticeable in images.

2. ***Intraoral Mirrors***

Intraoral mirrors are in-valuable when taking occlusal- and buccal-view photos as capturing these pictures from direct view is not possible with the photographic angle. They are available in various sizes. A basic set includes occlusal and buccal mirrors. Intraoral mirrors are useful for taking pictures in the areas that are difficult to access and they present reflected images. To avoid fogging of the mirror, warm the mirror in a water bath, or request an assistant to blow air gently using three-way syringe across the mirror. To simplify buccal and occlusal imaging, mirrors are available with handles too. Use of mirrors help to minimize the probability of fingers being shown in the photos. To shield the reflective surfaces from possible harm, it is firmly instructed to cover the mirrors individually for sterilization purposes, and not mix them with other instruments.

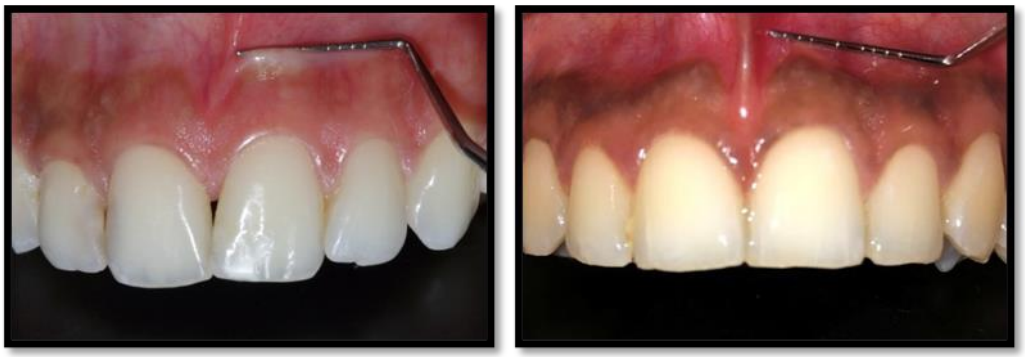
3. ***Other Accessories for Intraoral Photography:***

- Gauze strips
- Dental mirrors
- Disposable plastic spoons.
- Plastic spatulas

A DSLR (Digital Single Lens Interchangeable Reflex mirror system) camera is suggested to take high quality, predictable, effective, and pleasant clinical photography during surgery (Image 1, 2 and 3).

Uporedna vizuelna procena slika snimljenih DRJS kamerom i kamerom mobilnog telefona

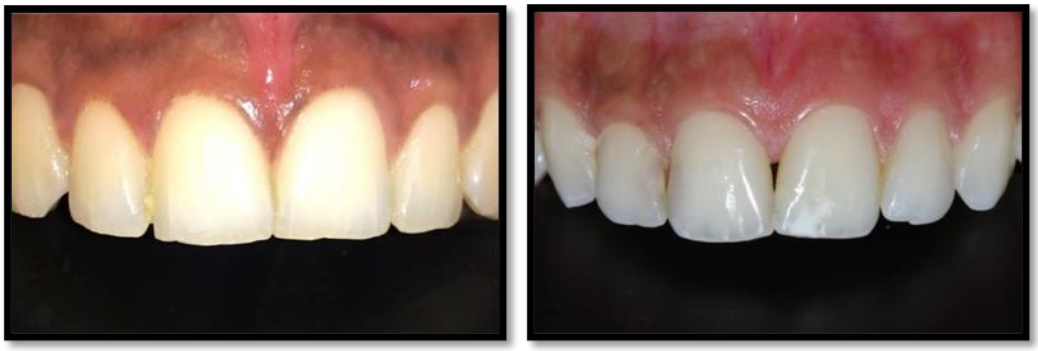
Comparative visual assessment of images taken by DSLR camera and camera of mobile phone



DRJS fotografija
DSLR Photo

Fotografija telefona sa kamerom
Camera Phone Photo

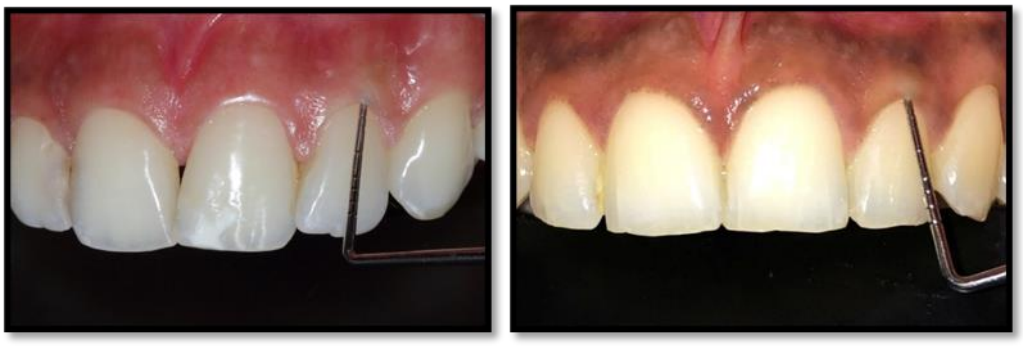
***Slika 1*:** Procena mukogingivalnog nabora
Image 1: Assessment of mucogingival fold



DRJS fotografija
DSLR Photo

Fotografija telefonskom kamerom
Camera Phone Photo

***Slika 2*:** Evaluacija roze i bele estetike
Image 2: Evaluation of pink and white aesthetics



DJRS fotografija
DSLR Photo

Fotografija telefona sa kamerom
Camera Phone Photo

***Slika 3*:** Procena biotipa gingive
Image 3: Assessment of gingival biotype

Prednosti DJLR fotoaparata za kliničku fotografiju[3]:

1. Konstantan kvalitet slike;
2. mogućnost da se trenutno i bez napora fokusira na određeno vidno polje;
3. očekivana ekspozicija, uvećanje i boja;
4. nema izobličenja slike;
5. standardizovani pogledi dozvoljavaju precizne konsultacije sa pacijentima i stomatološkim stručnjacima drugih oblasti.

Nedostaci kompaktnih fotoaparata i telefona sa kamerama za kliničku fotografiju[3]:

1. Ovi fotoaparati nisu namenjeni za određene fotografije izbliza;
2. slike snimljene kamerom telefona nisu visokog kvaliteta, jer nisu namenske kamere;
3. izazov je stalno se fokusirati na zube;
4. nedovoljna ekspozicija je uobičajena, jer postoji ograničena količina svetlosti intraoralno i veoma ograničena svetlost dospeće do senzora male kamere, a slike mogu biti previše tamne kako bi se na osnovu njih postavila dijagnoza;
5. senčenje je uobičajeno, zbog ugrađenog položaja blica;
6. neadekvatno uvećanje;
7. loša reprodukcija boja je uobičajena;
8. distorzija je uobičajena;
9. povećanje postavke ekspozicije kamere može da preeksponira slike (previše svetle kako bi se na osnovu njih uspostavila dijagnozu);
10. bočne zube je teško dugotrajno fotografisati i može zahtevati dodatno osvetljenje.

Advantages of DSLR cameras for clinical photography[3]

1. Constantly high-quality images
2. Capability to focus instantly and effortlessly on the exact field of view
3. Expectable exposure, magnification, and colour
4. No image distortion
5. Standardized views permit precise consultation with patients and other dental professionals

Disadvantages of compact cameras and camera phones for clinical photography[3]

1. These cameras are not intended for specified close-up photography
2. Images taken by camera phones are not high quality because they are not dedicated cameras
3. It is challenging to focus on the teeth constantly
4. Underexposure is common as there is restricted amount of light intraorally and very limited light will reach the small camera sensor and images may be too dark to be diagnosed
5. Shadowing is the common because of in-built flash position
6. Inconsistent magnification
7. Poor colour reproduction is common
8. Distortion is common
9. Increasing the camera's exposure setting may over-expose images (too bright for diagnosis)
10. Posterior teeth are difficult and time-consuming to photograph and may require additional lighting.

Zaključak

Intraoralna fotografija igra veoma važnu ulogu u interakciji sa pacijentom u vezi sa njihovim statusom zuba. Ovaj kratak pregled daje informacije kliničaru o neophodnosti dentalne fotografije u opštoj stomatološkoj i/ili parodontalnoj praksi. Izbor najpogodnije kamere za ekstraoralnu ili intraoralnu fotografiju zahteva obuku u oblasti digitalne fotografije. Trenutno je digitalna refleksna kamera sa jednim sočivom (DRJS kamera) najprikladniji sistem izbora za stomatološku fotografiju, koji se može koristiti za dijagnozu i planiranje lečenja, dokumentaciju, objavljivanje u časopisima, korišćenje na društvenim mrežama itd. Uvođenje fotografske obuke u nastavni plan i program biće korisno za sve koji se bave stomatologijom.

Conclusion

Intraoral photography is a vital source of communication with patients regarding their dental status. This concise overview informs a clinician regarding the necessities of dental photography in a general dental and/or periodontal practice. The choice of the most suitable camera for extraoral or intraoral photography requires advanced training in digital photography. Currently, the digital single lens reflex (DSLR) camera is the most appropriate system of choice for dental photography which can be used for diagnosis and treatment planning, documentation journal publication, use of social media etc. Introducing photographic training within the curriculum will be beneficial topic for all pursuing dentistry.

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Conflict of Interest: Nil
Financial Support: Nil
Acnowlegments:Nil

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UPUTSTVA AUTORIMA

Acta Stomatologica Naissi je naučni časopis Klinike za dentalnu medicinu, Medicinskog fakulteta Univerziteta u Nišu, koji publikuje radove iz svih oblasti stomatologije i srodnih medicinskih grana.

Ljubazno molimo autore da pažljivo pročitaju sledeće informacije o pripremi rada i podnošenju istog za štampanje. Radovi koji nisu napisani u skladu sa ovim instrukcijama biće vraćeni autorima sa zahtevom da isprave korekcije pre slanja istog na recenziju. Odbijeni radovi se ne vraćaju sem slika.

UREĐIVAČKA POLITIKA

Časopis publikuje uvodnik, originalne naučne ili stručne radove, klinički relevantne studije, preglede, prikaz slučaja, preliminarna saopštenja, tehničke inovacije, pisma uredniku, članke iz moderne literature, izveštaj o knjigama, novosti i izveštaje sa nacionalnih i internacionalnih kongresa, simpozijuma i ostalih aktuelnih sastanaka, koji nisu prethodno publikovani ili predati za publikovanje na nekom drugom mestu. Svi primljeni radovi biće recenzirani od dva anonimna recenzenta, i kada je to potrebno od statističara. Autori će biti obavešteni o prijemu, odbijanju, ili potrebnoj reviziji za najkasnije 6 nedelja od podnošenja rada. Radovi se ne plaćaju.

JEZIK

Svi predati radovi za štampanje moraju biti napisani na srpskom i engleskom jeziku. Apstrakti treba da budu pripremljeni pored srpskog i na preciznom i gramatički ispravnom engleskom jeziku (US engleski stil) (videti niže). Izbegavati korišćenje latinskih izraza; ako su potrebni staviti ih u zagrade.

ETIKA

Kada se radi o eksperimentima na humanom materijalu ili pacijentima, ukazati da li je primenjeni postupak u skladu sa etičkim standardima odgovornog komiteta za ljudske eksperimente ili sa Deklaracijom iz Helsinkija (1964, amandmani iz 1975 i 1983) Svetske medicinske asocijacije.

GENERALNE INSTRUKCIJE

PRIPREMA RADA

Radovi treba da budu napisani na A4 formatu sa duplim proredom, obezbeđujući 25 mm margine. Samo jedna kopija rada treba da sadrži prezime i prvo slovo autorovog imena u gornjem desnom uglu. Broj stranica rada počinje sa naslovnom stranom kao strana 1 i nastavlja se saređanjem.

NASLOVNA STRANA

Gornji deo naslovne strane treba da sadrži: a) puni naslov rada (velikim slovima), b) puna imena (prvo ime, srednje slovo ako je primenljivo i poslednje ime) svih autora bez akademskih titula, c) nazivi institucija i d) radni naslov od ne više od 10 reči. Na dnu naslovne strane molimo da ukažete na ime autora odgovornog za korespondenciju, sa akademskim zvanjem, poštanskom adresom, telefonskim i fax brojevima i E-mail adresom.

Sledeća strana počinje samo sa naslovom, i dalje se nastavlja sa tekstom. Tekst treba da bude podeljen u delove sa naslovima: uvod, pacijenti/materijal i metod rada, rezultati, diskusija, zaključci, zahvalnost i literatura. Za tabele, figure (slike) i legende vidi deo Tabele i Figure.

Poželjno je da se koriste reči prikladne za indeksiranje i pretraživanje. Ako takvih reči nema u naslovu, poželjno je da se naslovu doda podnaslov.

Ako je članak u prethodnoj verziji bio izložen na skupu u vidu usmenog saopštenja (pod istim ili sličnim naslovom) podatak o tome treba da bude naveden u posebnoj napomeni pri dnu prve strane članka.

APSTRAKT I KLJUČNE REČI

Originalni radovi moraju da sadrže strukturni apstrakt od 250 reči, podeljenih na sledeća 4 paragrafa:

Uvod: opisuje problem o kome se radi u radu

Materijali i metode: opisuje kako je istraživanje sprovedeno

Rezultati: opisuje primarno rezultate

Zaključak(ci): saopštenje autora o zaključcima proisteklim iz rezultata, i implicira njihovu kliničku primenljivost.

Strukturni apstrakti nisu potrebni kod uvodnika i pisma. Ispod apstrakta stoje ključne reci i to tri do pet. Ključne reči mogu biti uzete samo iz Medical Subjects Headings (MeSH).

Apstrakt treba da bude preveden i na engleski jezik (US style), sa naslovom, imenima autora, institucija i ključnim recima.

Za pisanje radova u formi prikaza slučaja, treba uraditi strukturirani apstrakt, na sledeći način:

Osnova problema: (opisati problem ili pojavu u nekoliko rečenica),

Metode rada: (opisati kako je obrađen i dijagnostikovan pacijent i koja bolest ili poremećaj je u pitanju),

Rezultati: (opisati rezultate rada i krajnji ishod),

Zaključak: (1-3 rečenice koja može da služi i kao opis celog postupka koji je rađen i napisan u radu).

TABELE I FIGURE

Svaka tabela sa jasnim naslovom na srpskom i engleskom treba da bude otkucana sa duplim proredom na odvojenom papiru. Obeležiti brojevima tabele jednu za drugom kako nailaze posle prvog navođenja u tekstu (obeležavaju se arapskim brojevima). Dati svakoj kolumni kratko ili skraćeno zaglavlje. Staviti objašnjenja u legendama svih nestandardnih skraćenica korišćenih u tabeli. Za jedinice i merenja vidi odeljak niže. Ne koristiti unutrašnje horizontalne i vertikalne linije. Staviti sve tabele na kraju vaseg fajla. Uvek odvojiti posebne kolumne upotrebom tabulatora, a ne upotrebom razmaknice, tabele moraju biti u tekst formatu.

Linijski prikazani dijagrami i ilustracije (fotografije, fotomikrografije itd.), trebaju biti osmišljene kao figure. Oni takođe treba da budu smešteni na odvojenom listu papira i numerisani jedan za drugim arapskim brojevima u saglasnosti sa prvim koji je citiran u tekstu. Figure treba da budu profesionalno nacrtane i fotografisane. Svaka figura treba da bude etiketirana pozadi ukazujući broj figure, prezime i prvo slovo imena autora, i vrh figure. Fotografije treba da se daju u dva primerka. Kolor fotografije ce se štampati samo u dogovoru sa urednikom ili ako autor sam snosi troškove. Fotomikrografije moraju imati obeleženu unutrasnju razmeru, i simbole, i strelice ili slova treba da su u kontrastu sa pozadinom. Na fotografijama pacijenata mora se sakriti identitet, osim ako se pacijenti u pismenoj formi slože sa objavljivanjem njihovih fotografija sa identitetom. Ukoliko ste pozajmili ili već publikovali negde fotografije priložite i pismenu dozvolu za reprodukovanje. Naslovi i detaljna objašnjenja fotografija treba da budu data u legendama. Ako su korišćeni simboli, strelice, brojevi ili slova za identifikaciju delova slike objasniti svaku jasno u legendi.

ZAHVALNOSTI

Priznanja i zahvalnosti prethode literaturi specificirajući generalnu podršku kao i odeljenje i ime šefa odeljenja, priznanja tehničkoj pomoći i konačno finansijskoj i materijalnoj pomoći. Navesti naziv i broj projekta, odnosno naziv programa u okviru koga je nastao članak i naziv institucije koja je finansirala projekat, u posebnoj napomeni pri dnu prve strane članka.

LITERATURA

Autori su odgovorni za tačnost literaturnih podataka. Reference treba da budu na posebnom listu i delu odmah iza teksta. Samo reference bitne za studiju mogu biti citirane. Kada je citiranje literature neophodno primeniti Vankuver stil. Na posebnom listu se navode citati referenci koji su označeni rednim brojevima po redosledu u kome se pojavljuju u tekstu i svaki citat odgovara brojevima koji sadrži navedenu referencu. Primeri tačnih oblika referenci :

RADOVI U ČASOPISIMA

1. Standardni članak u časopisu (lista svih autora, ali ako je broj veći od šest citirati tri i dodati et al): Glass DA, Mellonig JT, Towle HJ. Histologic evaluation of bone inductive proteins complexed with coralline hydroxyapatite in an extraskeletal site of the rat. J Periodontol 1989; 60:121-125.

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JEDINICE MERE

Sva merenja treba da budu izražena u terminima Internacionalnog Sistema Jedinica (Si).

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Ako se koriste nestandardne skraćenice potrebno je prilikom prvog korišćenja celog izraza u tekstu dati njegov puni naziv, a zatim u daljem tekstu koristiti skraćenicu. Nazivi simptoma, znakova i bolesti, kao i anatomski i histološki detalji ne mogu se skraćivati.

OFFPRINTS

Korespondirajući autori svih tipova radova izuzev pisama, novosti i pregleda knjiga primiće 1 broj časopisa oslobođena plaćanja.

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Mogu se koristiti samo za identifikaciju zapošljenja autora, za objašnjenje simbola u tabelama i ilustracijama itd. Koristite sledeće fusnote: *,&, #,**, itd.

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Poslati 3 kopije rada i elektronsku verziju (CD-ROM, E-mail). Kopije rada i sav sadržaj treba spakovati u tvrdu kovertu kako bi se sprecilo oštećenje za vreme poštanskog saobraćaja. Radovi moraju biti potkrepljeni sa zatvorenim pismom potpisanim od svih autora. Ono mora da sadrži: a) izjavu da je rad pročitan i odobren od svih autora; b) informaciju o prethodnoj ili dupliciranoj publikaciji ili davanju rada na drugom mestu ili nekog njenog dela ranije; c) izjavu o finansijskim ili drugim vezama koje mogu dovesti do sukoba interesa; d) ime, adresu i broj telefona autora za korespondenciju koji je odgovoran za komunikaciju i korespondenciju; e) izjavu da su klinička i eksperimentalna istraživanja sprovedena u skladu sa institucijskim etičkim komitetom ili sa Helsinskom deklaracijom. Sem ovoga, pismo treba da sadrži i obaveštenje o vrsti rada i da li autori plaćaju ekstra cenu za kolor reprodukcije.

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Sekretari: Asist. Simona Stojanović, Mr. sci dr Miloš Tijanić

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Skladištenje informacije: CD-ROM u Windows XP ili veći format. Software: radovi na disku treba da budu u Word-u za Windows. Etiketa: Napišite prvo ime autora na nalepnici CD-a, zajedno sa imenom i verzijom korišćenog word procesora. Oznaciti sve CD sadržajem figura, dijagrama itd, sa imenom prvog autora, imenom fajla, formatom i sabijenim šemama ako su korišćeni. Fajlovi: priložiti tekst i tabele svakog rada kao pojedinacni fajl, ali stavite sve figure, grafikone itd., u odvojenim fajlovima. Dozvoljeni grafički formati su EPS i TIF. Veličina figura treba da bude 8,5 cm ili 18,0 cm u rezoluciji od minimalno 300 dpi. Molimo Vas da pošaljete originalne fotografije, ne šaljite foto-kopije. Format: unosite svoj tekst besprekidno, samo umetnuti hard return na kraju paragrafa ili poglavlja, podnaslova, lista itd. Ne upotrebljavajte softwareski plan stranica. Molimo Vas da koristite Times New Roman 12 font za Word za Windows. Neku reč ili frazu u tekstu koju želite da izdvojite označite kroz rad u italic pismu. Boldirajte ono što se koristi uzastopno u tekstu za određene matematicke simbole, na primer, vektori. Molimo da proverite disk na virus i verifikujte da on sadrži ispravan fajl.

PODNOŠENJE REVIDIRANIH ČLANAKA

Autori mogu predati svoje revidirane radove uključujući tabele i figure na CD-u sa PC ili Mac fajlom. Vratiti revidirane radove sa celokupnim materijalom na istu adresu sekretarijat.

INSTRUCTIONS TO AUTHORS

Acta Stomatologica Naissi is a scientific journal of the University of Niš, Faculty of Medicine and Clinic of Dental Medicine, which publishes articles relevant to the science and practice of Dentistry in general and related areas.

Please read carefully the following instructions to authors prior to manuscript preparation and submission. Papers which are not prepared according to the propositions and instructions will be returned to authors for corrections before forwarding them to reviewers. In case of unacceptable articles only illustrations will be returned.

EDITORIAL POLICY

Acta Stomatologica Naissi publishes editorials, original scientific or clinical articles, review articles, preliminary reports, case reports, technical innovations, letters to the editor, articles from up-to-date literature, book reviews, reports and presentations from national and international congresses and symposiums which have not been previously submitted for publication elsewhere. All submitted articles will be reviewed by at least 2 reviewers, and when appropriate, by a statistical reviewer. Authors will be notified of acceptance, rejection, or need for revision within 6 weeks of submission. Articles are not paid for.

LANGUAGE

All submitted articles should be written in bilingual (Serbian and English) language. Abstracts should be written in Serbian and precise and grammatically correct English language, preferably US English. Avoid using Latin terms; however if necessary, put them in parentheses.

ETHICS

When reporting experiments on human subjects, indicate whether the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) or with the Helsinki Declaration (1964, amended in 1975 and 1983) ofthe World Medical Association.

GENERAL INSTRUCTIONS

PREPARATION

Articles should be written on A4 white bond paper size (21x29.5cm) on one side of the paper only, and double-spaced (including illustration legends and references) providing 25 mm ample margins all around. Only one copy of the manuscript should contain the surname and the author's first name initial in the upper right corner. Manuscripts should be organized as follows: Title Page, Abstract and Key words, Introduction, Patients/Materials and Methods, Results, Discussion, Conclusions, Acknowledgments, References, Figure Legends, Tables, Figures. Title page is numbered as page 1, and all other pages should be numbered conse-quently.

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Abstract and Key words

All original abstracts should be submitted with a structured abstract, consisting of no more than 250 words, and the following 4 paragraphs:

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Conclusion: Reports what authors have concluded from these results, and notes their clinical implications.

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Results: (describe the results of the work and the final outcome),

Conclusion: (1-3 sentences that can also serve as a description of the whole procedure that was done and written in the paper).

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Results: (describe the results of the work and the final outcome),

Conclusion: (1-3 sentences that can also serve as a description of the whole procedure that was done and written in the paper).

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ACKNOWLEDGEMENTS

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Journals:

1. Standard journal reference. (Note: list all authors if six or less; when seven or more, list only first three and add et al): Glass DA, Mellonig JT, Towle HJ. Histologic evaluation of bone inductive proteins complexed with coralline hydroxyapatite in an extraskeletal site of the rat. J Periodontol 1989;60:121-125.

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 ofthe brain. The Washington Post 1989Ang 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.

10. Online journals with volume and page information. Fowler EB, Breault LG. Ridge augmentation with a folded acellular dermal matrix allograft: A case Report. J Contemp Dent Pract (serial online). 2001;2(3):31-40. Available from: Procter&Gamble Company, Cincinnat, OH. Accessed December 15, 2001.

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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