

Ivona Bago¹, Andrija Bošnjak²

Odnos razine glikoliziranoga hemoglobina (HbA1c) i pušenja prema parodontalnom statusu kod pacijenata s dijabetesom melitusom ovisnih o inzulinu

Relationship of HbA1c Level and Smoking to Periodontal Status in Insulin-Dependent Diabetic Patients

¹ Stomatološki odjel, Dom zdravlja Zagrebačke županije, Zaprešić, Hrvatska
Dental Medicine Unit, Zagreb County Health Center, Zaprešić, Croatia

² Zavod za parodontologiju, Stomatološki fakultet, Zagreb, Hrvatska
Department of Periodontology, School of Dental Medicine, Zagreb, Croatia

Sažetak

Svrha istraživanja bila je ispitati učinak trajanja dijabetesa melitusa (DM-a) i razine glikoliziranoga hemoglobina (HbA1c) na parodontalni status pacijenata s inzulinski ovisnim DM-om, ali i kombinirani učinak pušenja i razine glikoliziranog hemoglobina parodontalni status. Ispitanici su slučajno odabrani među pacijentima s inzulinski ovisnim DM-om, a liječe se u Zavodu za endokrinologiju Opće bolnice "Sveti Duh". Podaci su dobiveni razgovorom, kliničkim parodontološkim pregledom te iz kartona pacijenata arhiviranih u Zavodu. Kao mjesta s parodontitisom odabrana su ona s dubinom sondiranja od 5 i više mm. Modelom Poissonove regresije izračunat je relativni rizik s 95 postotnim intervalom pouzdanosti, korigiran za dob ispitanika. Razmjerni rizik da izgubi pričvrstak kod pušača je bio 12,805, a za dubinu sondiranja 7,99. Relativni rizik kod pušača za razinu glikoliziranog hemoglobina (HbA1c) veću od 8,5 iznosio je 10,681 ($p = 0,002$), a za razinu od 8,5 i manju - 8,214 ($p = 0,006$). Relativni rizik za gubitak pričvrstka kod nepušača bio je 4,891 ($p = 0,031$). Kod pušača s inzulinski ovisnim DM-om i lošom glikemičkom kontrolom najveći je rizik za razvoj i progresiju parodontalne bolesti.

Zaprimljen: 18. srpnja 2006.

Prihvaćen: 4. rujna 2006.

Adresa za dopisivanje

Andrija Bošnjak
Sveučilište u Zagrebu
Stomatološki fakultet
Zavod za parodontologiju
Gundulićeva 5
10000 Zagreb
Tel. +38514802155
Fax +38514802159
bosnjak@sfdzg.hr

Ključne riječi

parodontitis; dijabetes melitus;
pušenje

Uvod

Utjecaj dijabetesa melitusa (DM-a) kao rizičnog čimbenika za parodontitis već se duže potanko istražuje. No, općeniti zaključci teško se mogu dobiti, jer su objavljena istraživanja kontradiktorna. Dok neki autori tvrde kako nema utjecaja DM-a na parodontalna tkiva (1 do 3), suvremena epidemiološka istraživanja smatraju DM pravim rizičnim čimbenikom kad je riječ o parodontitisu. Još godine 1993. parodontitis je spomenut kao šesta komplikacija DM-a (4), a tu je tvrdnju kasnije potvrdio i Reesov pregledni rad (5).

Prema mišljenju Grossija i suradnika DM je jedina sistemska bolest koja je jasno povezana s gubitkom pričvrstka (ALa-) (6). Dijabetes melitus ne samo da utječe na prevalenciju i težinu parodontitisa, nego može djelovati i na njegovu progresiju. Mnoga istraživanja potvrdila su teži oblik parodontitisa kod dijabetičara s inzulinski ovisnim DM-om (7 do 10).

Dijagnostika i praćenje DM-a uključuje mjerenje razine glukoze i glikoliziranog hemoglobina (HbA1c) u krvi. Istraživanja kontrole i komplikacija DM-a pokazala su da redovito i kvalitativno praćenje bolesti smanjuje komplikacije 50 do 75 posto. (11). Metoda odabira je određivanje razine glikoliziranog hemoglobina u krvi. Kod pacijenata s visokom razinom glukoze, ona se ireverzibilno veže za hemoglobin. Zato je koncentracija glikoliziranog hemoglobina (HbA1c) linearno ovisna o koncentraciji glukoze u krvi, što omogućuje glikemičku kontrolu tijekom 6 do 12 tjedana, budući da je prosječni životni vijek eritrocita 120 dana. Smatra se da je metabolička kontrola bolesti vrlo važna u parodontalnom statusu inzulinski ovisnih dijabetičara, jer oni kod kojih je loša imaju i veću incidenciju parodontitisa (12). Slično tome, loša glikemička kontrola povezana je s težim oblicima parodontitisa (13), njegovom progresijom (14) te većom resorpcijom kosti (15). Takvi dijabetičari češće imaju gingivitis i AL (16), no ako poboljšaju glikemičku kontrolu to neće popraviti njihov parodontalni status. Neka istraživanja nisu potvrdila korelaciju metaboličke kontrole i težine parodontitisa (17 do 19). Razlog za kontradiktorne rezultate vjerojatno je različita klasifikacija metaboličke kontrole i različite dijagnostičke metode. Glavind i suradnici istaknuli su da pacijenti koji dulje od 10 godina boluju od DM-a imaju veći AL od onih s kratkotrajnim DM-om (20). Rosenthal i suradnici povezali su DM s AL-om, ali ne i s glikemičkom kontrolom (21), a Thorstensson i suradnici istaknuli su trajanje DM-a i parodontitisa (22).

Introduction

The influence of diabetes mellitus (DM) as a risk factor for periodontitis has been widely discussed for a long time. Still, it is with much difficulty that one can obtain some general conclusions, since the published studies are contradictory. Some of the authors claim there is no influence of DM on periodontal tissues (1-3), while modern epidemiological studies consider DM as a true risk factor for periodontitis. Back in 1993 periodontitis was mentioned as the sixth complication of DM (4), a statement that was further supported by Rees' review (5). According to Grossi et al. DM is the only systemic disease clearly correlated to attachment loss (AL) (6). DM not only influences the prevalence and severity of periodontitis, but also has some effect on its progression. A number of studies have shown a more severe periodontitis in insulin-dependent diabetics (7-10).

The diagnosis and follow-up of DM include measuring of glucose levels and HbA1c values in blood. The investigations of control and complications of DM have shown that regular and qualitative disease follow-up reduces the complications to 50-75% (11). The method of choice is determining the concentration of glycolized hemoglobin (HbA1c). In patients with high levels of glucose in blood, glucose binds irreversibly to hemoglobin. Thus, the concentration of HbA1c is linearly dependent on blood concentration of glucose. This enables glycemic control during 6-12 weeks, lifespan of erythrocytes being around 120 days.

It is considered that the metabolic control of the disease has an important role in the periodontal status of insulin-dependent diabetics. Insulin-dependent patients with poor control show a greater incidence of periodontitis (12). Similarly, poor glycemic control is associated with more severe periodontitis (13), progression of periodontitis (14), and greater bone resorption (15). Diabetics with poor glycemic control have gingivitis and AL more frequently (16), but improvement in glycemic control does not improve their periodontal status. Some studies did not confirm the correlation between metabolic control and severity of periodontitis (17-19). The reason for these contradictory results is probably based in the variations of classification of metabolic control and different diagnostic methods used. One study showed that patients with DM for more than 10 years have greater AL than those with short-term DM (20). Rosenthal et al. have associated DM with AL, but not with glycemic control (21), and Thorstensson et al. have associated duration of DM and periodontitis (22).

Pušenje je rizični čimbenik za razvoj parodontitisa (23), a nekoliko je istraživanja pokazalo da je i dodatni faktor u razvoju te bolesti kod pacijenata s DM-om. To se može objasniti sličnostima mehanizama djelovanja duhana i DM-a. Duhan utječe na upalne procese i povećava produkciju upalnih citokina te smanjuje koncentraciju IgG-a i IgA-a u serumu (24, 25). Čini se da su teži parodontitis i pušenje povezani s lošom glikemičkom kontrolom (26).

Svrha ovog istraživanja bila je ispitati utjecaj trajanja DM-a i razine glikoliziranog hemoglobina (HbA1c) na parodontalni status pacijenata s DM-om te ispitati utjecaj pušenja i razine glikoliziranog hemoglobina na parodontalni status, ali i procijeniti kako pušenje kao modificirajući čimbenik utječe na pacijenta s DM-om.

Materijal i metode

Ispitanici

Ispitanici su slučajnom metodom odabrani među pacijentima koji boluju od inzulinski ovisnog DM-a, a liječe se u Zavodu za endokrinologiju Opće bolnice "Sveti Duh" u Zagrebu (Hrvatska). Uporabljeni su sljedeći kriteriji: informirani pristanak, dijagnoza inzulinski ovisnog DM-a i najmanje 10 zuba u ustima (po 5 u svakoj čeljusti). Način istraživanja i protokol potvrdilo je bolničko Etičko povjerenstvo. Podaci su dobiveni razgovorom (intervjuom) s odabranim ispitanicima, kliničkim parodontološkim pregledom te iz kartona pacijenata arhiviranih u Zavodu.

Ispitna skupina sastojala se od 60 pacijenata od 34 godine pa prema višoj dobi, i to 32 žene (u dobi od 34 do 81 godine) te 28 muškaraca (u dobi od 34 do 79 godina). Razine srednje vrijednosti glikoliziranog hemoglobina tijekom posljednjih godinu dana (HbA1c) uzete su iz kartona pacijenata i iznosile su između 5,9 i 15,7. Vrijednosti su dihotomizirane na 8,5, s tim da one od 8,5 i manje predstavljaju dobru glikemičku kontrolu, a veće od 8,5 lošu, prema smjernicama hrvatskoga i finskog Društva za DM. Normalne vrijednosti glikoliziranog hemoglobina (HbA1c) kod osoba koje ne boluju od DM-a iznose između 4 i 6. Podaci o pušenju dobiveni su razgovorom, a uključivali su broj popušanih cigareta izraženih u broju kutija na godinu te pušački staž. Varijable u analizi bila je pušač/nepušač.

Klinički pregled

Klinički parodontološki pregled obavljala je prva autorica (IB), a on je uključivao sljedeće varijable:

Smoking is a risk factor for the development of periodontitis (23). Additionally, a number of studies have shown that smoking is an adjunctive factor for periodontitis development in patients with DM. This can be explained by similarities in the mechanisms of action between tobacco and DM. Tobacco influences the inflammatory mechanisms and increases the production of inflammatory cytokines, as well as decreases the concentration of IgG and IgA in the serum (24, 25). More severe periodontitis and smoking seem to be associated with poor diabetic control (26).

The aim of this study was to investigate the influence of DM duration and HbA1c level on periodontal status of patients with DM, and the influence of smoking and HbA1c level on periodontal status, but also to assess the importance of smoking as a modifying factor in patients with DM.

Materials and methods

Subjects

The subjects were randomly recruited from a pool of patients suffering from insulin-dependent DM of the Department of Endocrinology of the General Hospital "Sveti Duh" in Zagreb, Croatia. The used criteria were: informed consent, diagnosis of insulin-dependent DM, and presence of at least 10 teeth in the mouth (5 in each jaw). The study design and protocol were both accepted and confirmed by the Ethical committee of the hospital. The data was collected by means of an interview with the selected subjects, clinical periodontal examination, and patients' charts from the department.

The study cohort consisted of 60 patients, aged 34 years and more, 32 women (aged between 34 and 81) and 28 men (aged between 34 and 79). HbA1c levels (mean values of glycolized hemoglobin during the last year) were obtained from patients' charts, and were between 5.9 and 15.7. The value was dichotomized to 8.5, values of 8.5 and less representing good glycemic control, and values higher than 8.5 representing poor glycemic control, according to the guidelines of the Croatian and Finnish societies for DM. The normal values of HbA1c in non-diabetic patients are between 4 and 6. Data on tobacco used was gathered by interviews, and included the number of smoked cigarettes, represented by smoked packs in a year, and the duration of smoking in years. The variable in analysis was smoker/nonsmoker.

Clinical examination

Clinical periodontal examination was performed by one examiner (IB), and included the following

dubinu sondiranja (PD), gingivalnu recesiju (GR), AL te mjerenje vrijednosti Papilla Bleeding Indexa (PBI-ja). PD se mjerio na vestibularnim stranama svih prisutnih zuba kalibriranom parodontalnom sondom (DB 768, Aesculap, Tuttlingen, SR Njemačka). Zabilježena su samo mjesta s PD-om većim od 5 mm. GR se mjerio na vestibularnim stranama svih zuba, a vrijednost AL-a dobivena je zbrajanjem vrijednosti PD-a i GR-a. Mjesta s AL-om većim od 4 mm smatrana su mjestima s parodontitisom. Te su vrijednosti uporabljene kao determinante parodontitisa u nedavno objavljenim radovima (27, 28). PBI se mjerio prema originalnoj tehnici (29) te je analiziran kao kontinuirana varijabla.

Statistička analiza

Statistička analiza provedena je na temelju programa SPSS (SPSS Inc., Chicago, IL, SAD), verzijom 10.0. Relativni rizik (RR) s 95 postotnim intervalom pouzdanosti (CI) procijenjen je Poissonovim regresijskim modelima za AL između 4 i 8 mm te za PD između 5 i 9 mm, prilagođeno za broj zuba i dob. Poissonova regresija koristi se u skupnim (kohortnim) istraživanjima rijetkih (ili neodređenih) ishoda tijekom različitih vremenskih razdoblja. Za takva istraživanja u kojima se svi ispitanici prate istodobno, kao što je ovo, vrijednost vremenskog trajanja izloženosti riziku označava se s 1 za svaki subjekt (30). Korekciju je obavio statistički program, istodobno s analizom regresijskog modela.

Rezultati

U Tablici 1. su srednje vrijednosti dobi, trajanja DM-a, PBI-ja, PD-a, AL-a i pušenja (broj popušenih kutija na godinu) u odnosu prema razini glikoliziranog hemoglobina (HbA1c) i pušenja. RR za AL kod pušača iznosio je 12,802 (95 postotni CI: 5,661-15,343), a za PD 7,99 (95 postotni CI: 3,45-9,012) (Tablica 2.), nakon što je u regresijski model dodan interakcijski pojam "HbA1c > 8,5, pušenje" i usklađivanja preostalih varijabli. RR za AL kod razine HbA1c > 8,5 iznosio je 10,681 (95 postotni CI: 2,16-14,478), a za razinu ≤ 8,5 - 8,214 (95 postotni CI: 5,665-11,32). Ti podaci upućuju na izravno djelovanje pušenja i razine glikoliziranog hemoglobina (HbA1c) na napredovanje parodontitisa kod dijabetičara.

Rasprava

Rezultati ovog istraživanja jasno ističu utjecaj razine glikoliziranog hemoglobina (HbA1c) i pušenja na parodontalni status inzulinski ovisnih dijabetičara. Pušači s nereguliranom glikemičkom kontro-

variables: probing depth (PD), gingival recession (GR), AL, and Papilla Bleeding Index (PBI). PD was measured on vestibular sites of all present teeth by a calibrated periodontal probe (DB 768, Aesculap, Tuttlingen, FR Germany). Only sites with PD of 5 mm and greater were noted. GR was measured on vestibular sites of all present teeth, while AL was computed as the sum of PD and GR. Sites with AL greater than 4 mm were considered as periodontitis. These values were used recently as determinants of periodontitis (27,28). PBI was measured according to the original technique (29), and analyzed as a continuous variable.

Statistical analysis

The statistical analysis was performed using SPSS (SPSS Inc., Chicago, IL, USA), version 10.0. Relative risks (RR) with 95% confidence interval were assessed by means of Poisson regression models for AL between 4 and 8 mm and PD between 5 and 9 mm, adjusted for the number of teeth and age. Poisson regression is used in cohort studies of rare (or undetermined) outcomes conducted over variable lengths of time. For cohort studies in which all subjects were followed for the same time period, such as this one, time-at-risk value was specified as 1 for each subject (30). The correction was performed by the statistical package, at the same time as the regression model analysis.

Results

Table 1 shows mean values of age, duration of DM, PBI, PD, AL, and smoking (number of smoked packs in a year) in relation to HbA1c level and smoking. RR for AL in smokers was 12.802 (95% confidence interval (CI): 5.661-15.343), and for PD 7.99 (95% CI: 3.45-9.012) (Table 2), when the interaction term "HbA1c > 8.5, "smoking", was added into the regression analysis, after the adjustment of other variables. RR for AL at HbA1c level > 8.5 was 10.681 (95% CI: 2.16-14.478), and for the level ≤ 8.5 it was 8.214 (95% CI: 5.665-11.32).

These data suggest a direct effect of smoking and HbA1c level on further progression of periodontal disease in diabetic patients.

Discussion

The results of our study clearly show the influence of HbA1c level and smoking on periodontal status of insulin-dependent diabetics. Smokers with unregulated glycemic control (HbA1c > 8.5) have

Table 1. Mean values (standard deviation) of age, duration of DM, PBI, PD, AL, and number of cigarette packs smoked in a year in relation to HbA1c level and smoking**Tablica 1.** Srednje vrijednosti (standardna devijacija) dobi, trajanja DM-a, PBI-ja, PD-a, AL-a i broja popušanih kutija tijekom godine u odnosu prema glikoliziranom hemoglobinu (HbA1c) i pušenju

	Dob (god) • Age (yrs)	Broj zuba • Number of teeth	Trajanje DM-a (god) • Duration of DM (yrs)	PBI	PD (mm)	AL (mm)	Broj kutija (god) • Number of packs (yrs)
HbA1c > 8,5, pušači • HbA1c > 8,5, smokers	51 (9,8)	17,2 (6,51)	9,6 (9,03)	31,88 (19,03)	3,35 (1,6)	6,72 (2,44)	16,88 (9,11)
HbA1c ≤ 8,5, pušači • HbA1c ≤ 8,5, smokers	63 (13,8)	19,8 (8,27)	5,9 (6,75)	18 (16,43)	2,14 (0,71)	5,99 (1,89)	32,03 (24,4)
HbA1c > 8,5, nepušači • HbA1c > 8,5, nonsmokers	67,4 (9,3)	24,2 (7,55)	14,7 (11)	9,2 (10,25)	2,51 (0,88)	5,48 (2,49)	-
HbA1c ≤ 8,5, nepušači • HbA1c ≤ 8,5, nonsmokers	61 (13,2)	31,9 (10,11)	12,6 (8,4)	12,05 (11,04)	1,64 (0,61)	3,11 (1,25)	-

DM - Dijabetes melitus • Diabetes mellitus; PBI - Indeks krvarenja • Papilla bleeding index; PD - Dubina sondiranja • Probing depth; AL - Gubitak pričvrška • Attachment loss

Table 2. Results of Poisson regression analysis for the number of sites with AL 4-8 mm and PD 5-9 mm**Tablica 2.** Rezultati Poissonove regresijske analize za broj mjesta s AL-om 4 - 8 mm i PD-om 5 - 9 mm

	AL			PD		
	RR	(95% CI)	p	RR	(95% CI)	P
Pušenje • Smoking	12,805	5,76-31,1	0,001	7,99	3,35-9,08	0,007
Nepušenje • Not smoking	4,891	1,43-6,67	0,031	0,621	0,37-0,84	0,434
HbA1c > 8,5	10,681	6,2-17,32	0,002	12,36	4,82-27,2	0,001
HbA1c ≤ 8,5	1	-	-	1	-	-
HbA1c > 8,5, pušači • smoker	8,214	5,7-11,98	0,006	3,789	2,11-4,38	0,057
HbA1c ≤ 8,5, nepušači • nonsmoker	1	-	-	1	-	-
PBI	2,111	0,91-3,32	0,152	2,668	1,93-3,27	0,108
Broj zuba • Number of teeth	1,215	0,9-1,97	0,0115			
Dob • Age	0,185	0,12-0,26	0,669	0,237	0,18-0,35	0,628
Trajanje DM-a (god) • Duration of DM (yrs)						
0-15	1,219	1,1-1,7	0,274	1,392	0,98-2,65	0,243
15+	2,289	1,3-3,35	0,136	2,696	1,47-3,17	0,91

CI – Interval pouzdanosti • Confidence interval; RR - Relativni rizik • Relative risk

RR je usklađen za druge varijable, a interakcija "HbA1c > 8,5, pušenje" dodana je u model

RR was adjusted for other variables, and the interaction "HbA1c > 8.5, smoking" was added into the model

lom (HbA1c > 8,5) imaju najviše vrijednosti PBI-ja, PD-a i AL-a. Nije opažena razlika između srednjih vrijednosti PD-a i AL-a kod pušača s dobrom i lošom glikemičkom kontrolom. Najniže su vrijednosti kod kontroliranih pacijenata-nepušača. Smatra se da se kod pacijenata s lošom glikemičkom kontrolom koji puše više od onih s dobrom glikemičkom kontrolom vidi izravni utjecaj na parodontalni status. No, to nije potvrđeno budući da pušači s dobrom glikemičkom kontrolom puše gotovo dvostruko manje od onih s lošom glikemičkom kontrolom (Tablica 1.). Za te rezultate vjerojatno je kriva opća loša briga za zdravlje i slaba regulacijom bolesti kod inzulinski ovisnih dijabetičara, što rezultira lošom glikemičkom kontrolom i slabijim parodontalnim statusom (31). Više plaka i ne tako česta oralna higijena također su povezani s DM-om ovi-

the highest values of PBI, PD and AL. There is no difference in mean values of PD and AL in smokers with good and poor glycemic control. The lowest values can be observed in controlled nonsmoking patients. It is considered that patients with poor glycemic control smoke more than those with good glycemic control, which is affecting their periodontal status. This has not been confirmed, since smokers with good glycemic control smoke almost twice as much as smokers with poor glycemic control (Table 1). These results are probably caused by generally poor care and poor disease regulation in insulin-dependent diabetics, leading to poor glycemic control and worse periodontal status, which has been confirmed (31). More plaque and less frequent oral hygiene have also been correlated with insulin-dependent DM and higher values of HbA1c (32). It can be

snim o inzulinu i višim vrijednostima glikoliziranog hemoglobina (32). Možemo zaključiti da loša oralna higijena kod ispitanika s nereguliranim inzulinski ovisnim DM-om utječe na njihov parodontalni status, ali istodobno je moguće i da loš parodontalni status utječe na razinu glikoliziranog hemoglobina (HbA1c). Istraživanja su potvrdila da parodontitis može djelovati na glikemičku kontrolu pacijenata s DM-om (31) te da mehanička terapija smanjuje razinu glikoliziranog hemoglobina (33). Rezultati regresijske analize (Tablica 2.) kod pušača s inzulinski ovisnim DM-om jasno pokazuju statistički povećan rizik za AL, ali ne i za PD.

Potvrđena je i korelacija između nereguliranog DM-a i parodontalnih parametara. Haffajee i Socransky povezali su dob s AL-om (34). Iako smo procjenjivali utjecaj dobi na parodontalni status, nismo pronašli statistički znatnu korelaciju između dobi, AL-a i PD-a.

Smatra se da pacijenti s DM-om imaju povećanu produkciju uznapredovalih produkata glikozilacije (AGE) (35). Njihova koncentracija u gingivalnom tkivu dijabetičara gotovo je dvostruko veća u usporedbi sa zdravim ispitanicima te uzrokuje mikrovaskularna oštećenja i zadebljanje krvnih žila (36), pojačavajući nastanak upalnih citokina (35). Čak su i potvrđene neke citokine kod pacijenata s DM-om. (37,38). Povećane razine glukoze dovode do poremećaja u ekspresivnosti fibronektinskih receptora, onemogućavajući proces cijeljenja. Esmatjes i suradnici opisali su povišene vrijednosti nekih citokina kod pušača s DM-om (39) te su zaključili da pušenje može pojačati hipoglikemiju, a i prevalenciju mikrovaskularnih komplikacija DM-a.

Naše istraživanje pokazalo je izravan utjecaj pušenja i povišene razine glikoliziranog hemoglobina (HbA1c) kod inzulinski ovisnih dijabetičara na AL i PD, što je u skladu s rezultatima dugotrajnog praćenja pacijenata s DM-om tipa I (40). Slične rezultate objavili su i Syrjälä i suradnici (41), no bez povezanosti s PD-om. U našem istraživanju nije bilo statistički znatne razlike između trajanja DM-a te AL-a i PD-a, slično kao i u istraživanju De Pommereaua i suradnika (20). Firatli i suradnici su, suprotno našem istraživanju, pronašli statistički znatnu povezanost između trajanja DM-a i parodontalnog statusa i više AL-a, ali ne i s plakom i gingivalnim indeksima kod pacijenata s DM-om (11). Budući da su oni ispitivali povezanost trajanja DM-a i parodontalni status djece i adolescenata, a naša je populacija prosječne dobi od 34 do 81 godine, radi se o potpuno različitim ciljnim skupinama, ali i o drugoj bolesti (tip I nasuprot tipa II). Mo-

concluded that poor oral hygiene in unregulated insulin-dependent subjects influences their periodontal status, but at the same time, poor periodontal condition may influence the level of HbA1c. Studies have shown that periodontitis can affect the glycemic control in DM patients (31), and that mechanical therapy results in lower values of HbA1c (33). The results of regression analysis (Table 2) clearly show statistically increased risk for AL, but not for PD, in smokers with insulin-dependent DM.

Furthermore, the correlation between unregulated DM and periodontal parameters has been confirmed. Haffajee and Socransky have correlated age with AL (34). Although we have assessed the influence of age on periodontal status, there was no statistical correlation between age, AL and PD.

It is considered that patients with DM have increased production of advanced glycosylation end-products (AGE) (35). The concentration of AGEs in the gingival tissue of diabetics is almost double when compared to healthy individuals, thus causing microvascular damage and thickening of the blood vessel walls (36), and enhancing the inflammatory cytokines production (35). Investigators have confirmed higher values of some cytokines in DM patients (37,38). Increased level of glucose leads to a deformation in expressiveness of fibronectin receptors, disabling the healing process. Esmatjes et al. have described increased levels of some cytokines in smokers with DM (39) and have concluded that smoking can increase hyperglycemia, and that it can subsequently increase the prevalence of microvascular complications in smokers with DM.

Our study shows the direct influence of smoking and increased level of HbA1c in insulin-dependent DM on AL and PD, which corroborates the results of long-term follow-up of diabetes type I patients (40). Similar results were published by Syrjälä et al. (41), who did not find the correlation with PD. There was no statistically significant correlation between duration of DM and AL and PD in our study, similarly to De Pommereau et al. (20). Firatli et al. have, contrary to our results, shown statistically significant correlation between duration of DM and periodontal status, more AL, but not with plaque and gingival indices in patients with DM (11). Since they studied the correlation between DM duration and periodontal status of children and adolescents, and the age range of our population was between 34 and 81 years, these are completely different study cohorts, as well as they have had different diseases (type I and type II). It can be said that, according to

že se reći da, na temelju ispitivanja Firatlija i suradnika (11), postoje indicije da trajanje DM-a kod djece i adolescenata utječe na pogoršanje parodontalnog statusa, što još nije potvrđeno kod odraslih osoba.

Zaključak

Pacijenti s inzulinski ovisnim DM-om, a pušači su, u najrizičnijoj su skupini za razvoj i progresiju parodontalne bolesti te zato trebaju detaljnu shemu parodontalne terapije s kraćim razmacima između posjeta. Jačina DM-a mjerena razinom glikoliziranog hemoglobina (HbA1c) i pušenje imaju izravni razorni učinak na parodontalni status ispitivane populacije.

Napomena

Prva autorica rada nagrađena je godine 2004. rektorovom nagradom Sveučilišta u Zagrebu za istraživanje koje je rezultiralo ovim radom.

the results of Firatli et al. (11), there is information that DM duration in children and adolescents directly influences periodontal status, a correlation yet to be confirmed in adult population.

Conclusion

Insulin-dependent DM patients that smoke have the greatest risk for the development and progression of periodontal disease, and therefore are in need of a detailed periodontal therapy scheme with shorter recall intervals. The severity of DM measured by HbA1c level and smoking has direct deteriorating influence on periodontal status in the studied population.

Acknowledgment

Ivona Bago, fifth-year student of dental medicine at the time, received the Rector's Award of the University of Zagreb in 2004 for the research that resulted in this article.

Abstract

Objective of work. The aim of the study was to investigate the effect of diabetes mellitus (DM) duration and HbA1c level on periodontal status of patients with insulin-dependent DM, as well as the combined effect of smoking and HbA1c level on periodontal status. Subjects were randomly selected from the patients with insulin-dependent DM that are treated at the Department of Endocrinology in the hospital "Sveti Duh". Data was gathered by means of an interview, clinical periodontal investigation and patients' charts from the department. Sites with probing depth of 5 mm and greater were selected as sites with periodontitis. By means of Poisson regression model a relative risk with 95% confidence interval was computed, corrected for age of the subjects. Relative risk for attachment loss in smokers was 12.805, and for probing depth in smokers 7.99. Relative risk of the HbA1c level > 8.5 in smokers was 10.681 ($p = 0.002$), and 8.214 ($p = 0.006$) for HbA1c level ≤ 8.5 . Relative risk for attachment loss in nonsmokers was 4.891 ($p = 0.031$). It was concluded that insulin-dependent smokers with poor glycemic control have the greatest risk for development and progression of periodontal disease.

Received: July 18, 2006

Accepted: September 4, 2006

Address for correspondence

Andrija Bošnjak
University of Zagreb
School of Dental Medicine
Department of Periodontology
Gundulićeva 5
HR-10000 Zagreb
Croatia
Tel. +38514802155
Fax +38514802159
bosnjak@sfzg.hr

Key words

periodontitis; diabetes mellitus; tobacco use disorder

References

- Rylander H, Ramberg P, Blohme G, Lindhe J. Prevalence of periodontal disease in young diabetics. *J Clin Periodontol.* 1987;14(1):38-43.
- Hayden P, Buckley LA. Diabetes mellitus and periodontal disease in an Irish population. *J Periodontol Res.* 1989;24(5):298-302.
- Katz PP, Wirthlin M, Szpunar SM, Selby JV, Showstack JA. Epidemiology and prevention of periodontal disease in individuals with diabetes. *Diabetes Care.* 1991;14(5):375-85.
- Löe H. Periodontal disease. The sixth complication of diabetes mellitus. *Diabetes Care.* 1993;16(1):329-34.
- Rees TD. The diabetic dental patient. *Dent Clin North Am.* 1994;38(3):447-63.
- Grossi SG, Zambon JJ, Ho AW, Koch G, Dunford RG, Machtei EE et al. Assessment of risk for periodontal disease. I. Risk indicators for attachment loss. *J Periodontol.* 1994;65(3):260-7..
- Oliver RC, Tervonen T. Diabetes - a risk factor for periodontitis in adults? *J Periodontol.* 1994;65(5 Suppl):S530-8.
- Novaes Junior AB, Silva MA, Batista Junior EL, dos Anjos BA, Novaes AB, Pereira AL. Manifestations of insulin-dependent diabetes mellitus in the periodontium of young Brazilian patients. A 10-year follow-up study. *J Periodontol.* 1997;68(4):328-34.
- Novaes Junior AB, Pereira AL, de Moraes N, Novaes AB. Manifestations of insulin-dependent diabetes mellitus in the periodontium of young Brazilian patients. *J Periodontol.* 1991;62(2):116-22.

10. Burket LW, Sidoni A Jr. Diabetes and the dental patient. *J Am Dent Assoc.* 1959;58(2):81-5.
11. Firatli E, Yilmaz O, Onan U. The relationship between clinical attachment loss and the duration of insulin-dependent diabetes mellitus (IDDM) in children and adolescents. *J Clin Periodontol.* 1996;23(4):362-6.
12. Patino-Marin N, Loyola-Rodríguez JP, Valadez-Castillo FJ, Hernandez-Sierra JF, Pozos-Guillen Ade J. Effect of metabolic control in type I diabetes patients and its association with periodontal disease. *Rev Invest Clin.* 2002;54(3):218-25.
13. Tsai C, Hayes C, Taylor GW. Glycemic control of type 2 diabetes and severe periodontal disease in the US adult population. *Community Dent Oral Epidemiol.* 2002;30(3):182-92.
14. Collin HL, Uusitupa M, Niskanen L, Kontturi-Närhi V. Periodontal findings in elderly patients with non-insulin dependent diabetes mellitus. *J Periodontol.* 1998;69(9):962-6.
15. Taylor GW, Burt BA, Becker MP, Genco RJ, Shlossman M. Glycemic control and alveolar bone loss progression in type 2 diabetes. *Ann Periodontol.* 1998;3(1):30-9.
16. Karjalainen KM, Knuutila ML, von Dickhoff KJ. Association of the severity of periodontal disease with organ complications in type 1 diabetic patients. *J Periodontol.* 1994;65(11):1067-72.
17. Bačić M, Plančak D, Granić M. CPITN assessment of periodontal disease in diabetic patients. *J Periodontol.* 1988;59(12):816-22.
18. de Pommereau V, Dargent-Pare C, Robert JJ, Brion M. Periodontal status in insulin-dependent diabetic adolescents. *J Clin Periodontol.* 1992;19(9 Pt 1):628-32.
19. Kawamura M, Tsurumoto A, Fukuda S, Sasahara H. Health behaviors and their relation to metabolic control and periodontal status in type 2 diabetic patients: a model tested using a linear structural relations program. *J Periodontol.* 2001;72(9):1246-53.
20. Glavind L, Lund B, Loe H. The relationship between periodontal state and diabetes duration, insulin dosage and retinal changes. *J Periodontol.* 1968;39(6):341-7.
21. Rosenthal IM, Abrams H, Kopczyk A. The relationship of inflammatory periodontal disease to diabetic status in insulin-dependent diabetes mellitus patients. *J Clin Periodontol.* 1988;15(7):425-9.
22. Thorstensson H, Hugoson A. Periodontal disease experience in adult long-duration insulin-dependent diabetics. *J Clin Periodontol.* 1993;20(5):352-8.
23. Obeid P, Bercy P. Effects of smoking on periodontal health: a review. *Adv Ther.* 2000;17(5):230-7.
24. Giannopoulou C, Cappuyns I, Mombelli A. Effect of smoking on gingival crevicular fluid cytokine profile during experimental gingivitis. *J Clin Periodontol.* 2003;30(11):996-1002.
25. Verma S, Bhat KM. Diabetes mellitus - a modifier of periodontal disease expression. *J Int Acad Periodontol.* 2004;6(1):13-20.
26. Taylor GW, Burt BA, Becker MP, Genco RJ, Shlossman M, Knowler WC, et al. Severe periodontitis and risk for poor glycemic control in patients with non-insulin-dependent diabetes mellitus. *J Periodontol.* 1996;67(10 Suppl):1085-93.
27. Bošnjak A, Relja T, Vučićević-Boras V, Plasaj H, Plančak D. Pre-term delivery and periodontal disease: a case-control study from Croatia. *J Clin Periodontol.* 2006;33(10):710-6.
28. Caton JG, Ciancio SG, Blieden TM, Bradshaw M, Crout RJ, Hefti AF, et al. Subantimicrobial dose doxycycline as an adjunct to scaling and root planing: post-treatment effects. *J Clin Periodontol.* 2001;28(8):782-9.
29. Saxer UP, Turconi B, Elsasser C. Patient motivation with the papillary bleeding index. *J Prev Dent.* 1977;4(4):20-2.
30. McNutt LA, Wu C, Xue X, Hafner JP. Estimating the relative risk in cohort studies and clinical trials of common outcomes. *Am J Epidemiol.* 2003;157(10):940-3.
31. Toljamo M, Hentinen M. Adherence to self-care and glycaemic control among people with insulin-dependent diabetes mellitus. *J Adv Nurs.* 2001;34(6):780-6.
32. Syrjala AM, Knecht MC, Knuutila ML. Dental self-efficacy as a determinant to oral health behaviour, oral hygiene and HbA1c level among diabetic patients. *J Clin Periodontol.* 1999;26(9):616-21.
33. Mealey BL, Rethman MP. Periodontal disease and diabetes mellitus. Bidirectional relationship. *Dent Today.* 2003;22(4):107-13.
34. Haffajee AD, Socransky SS. Relationship of cigarette smoking to attachment level profiles. *J Clin Periodontol.* 2001;28(4):283-95.
35. Seppälä B, Sorsa T, Ainamo J. Morphometric analysis of cellular and vascular changes in gingival connective tissue in long-term insulin-dependent diabetes. *J Periodontol.* 1997;68(12):1237-45.
36. Iacopino AM. Diabetic periodontitis: possible lipid-induced defect in tissue repair through alteration of macrophage phenotype and function. *Oral Diseases.* 1995;1(4):214-29.
37. Zhang YM, Su Y, Jin ZQ. Research on histologic changes of periodontal tissue, testification of TNF-alpha and their relationship in diabetics rats. *Shanghai Kou Qiang Yi Xue.* 2003;12(5):352-5.
38. Pucher J, Stewart J. Periodontal disease and diabetes mellitus. *Curr Diab Rep.* 2004;4(1):46-50.
39. Esmatjes E, Flores L, Lario S, Clària J, Cases A. Smoking increases serum levels of transforming growth factor-β in diabetic patients. *Diabetes Care.* 1999;22(11):1915-6.
40. Plančak D, Bošnjak A, Pavelić B. Severe periodontal condition as a result of diabetes mellitus type I - a case report. *Diabetol Croat.* 2002;31:231-5.
41. Syrjala AM, Ylostalo P, Niskanen MC, Knuutila ML. Role of smoking and HbA1c level in periodontitis among insulin-dependent diabetic patients. *J Clin Periodontol.* 2003;30(10):871-5.