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IZVORNI ZNANSTVENI RAD
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Elektroliti u slini pacijenata s metalnim i keramičkim ortodontskim bravicama

Salivary Electrolytes in Patients with Metallic and Ceramic Orthodontic Brackets

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Sažetak

Svrha: Iz postojeće literature poznato je da metalni ioni iz ortodontskih naprava mogu korodirati zbog djelovanja sline i bakterija u usnoj šupljini. Rezultati većine studija upućuju na to da se razina nikla i kroma u slini ne povisuje nakon postavljanja ortodontskih naprava. No nema istraživanja o razini titanija, kobalta, bakra i cinka u slini ortodontskih pacijenata. **Ispitanici i postupci:** Razina nikla (Ni), titanija (Ti), kroma (Cr), kobalta (Co), bakra (Cu) i cinka (Zn) mjerena je u slini četrdeset i dvoje pacijenta s keramičkim metalnim bravicama i isto toliko njih s konvencionalnima i to prije postavljanja ortodontskih naprava s pomoću induktivne spregnute plazme/masene spektrometrije i šest mjeseci poslije toga. U statističkoj analizi korištena su dva testa – Wilcoxonov signed rank i Mann-Whitneyev s razinom značajnosti od 0,05. **Rezultati:** Rezultati su pokazali da se razina titana u slini povisila šest mjeseci nakon postavljanja ortodontskih naprava. Razina kroma i cinka, pak, značajno se snizila nakon postavljanja ortodonskih naprava. Nije bilo statistički značajne razlike u razini nikla, titanija, kroma, bakra, kobalta i cinka u slini između pacijenata s metalnim i keramičkim ortotontskim bravicama. **Zaključak:** Možemo zaključiti da se razina titanija u slini značajno povisila šest mjeseci nakon postavljanja ortodontskih naprava za razliku od razine kroma i cinka koja se značajno snizila šest mjeseci poslije njihova postavljanja, bez obzira na vrstu korištenih bravica.

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Ključne riječi
ortodontske naprave; slina; elektroliti; titanij; krom; cink

Uvod

Pokazalo se da postava fiksnih ortodontskih naprava može utjecati na promjenu razine elektrolita u slini (1), tj. na povišenu koncentracije nikla i kroma. No većina autora (2 – 9) nije isticala povišenu razinu nikla i kroma u slini nakon postavljanja ortodontskih naprava.

Poznato je da je usna šupljina ekosustav za koji se zna da uzrokuje biorazgradnju metala koja se obično pojavljuje tijekom procesa elektrokemijskog raspada. Nadalje, zna se da različite sastavnice ortodontskih naprava kao što su nikal i krom, mogu uzrokovati reakcije preosjetljivosti u usnoj šupljini, citotoksičnost i dermatitis. Također mogu imati značajan mutageni, pa možda i kancerogeni potencijal (4). Srećom, većina ortodontskih pacijenata na sluznici usta nema vidljive reakcije na ortodontske materijale, vjerojatno zbog samog utjecaja sline.

Introduction

It has been reported that installment of fixed orthodontic appliances might lead to the alteration of the salivary electrolytes (1), i.e. increase in salivary nickel or chromium concentrations. However, most of the authors (2-9) reported no increase in salivary levels of nickel and chromium in patients after installment of orthodontic appliances.

It is well known that oral cavity is an ecosystem which is known to cause biodegradation of metals which usually occurrs through the process of electrochemical breakdown. Besides, it is known that various orthodontic components such as nickel and chromium can cause hypersensitivity reactions in the oral cavity, cytotoxicity, and dermatitis. Furthermore, they might have significant mutagenic and possibly carcinogenic potential (4). Luckily, most of the orthodontic patients do not have visible reactions on the oral mucosa caused by

Staffolani i suradnici (10) izvijestili su da je dnevno otpuštanje nikla, bakra i kroma u uvjetima *in vitro* u kiselom pH niže od dnevnoga unosa hranom, što podupire sigurnost upotrebe ortodontskih naprava.

Gürsoy i suradnici (11) izvijestili su da je u 4. grupi (pacijenti s recikliranim ortodontskim bravicama i lukovima) otpuštanje kroma, željeza i titanija u slini bilo veće nego u ostalim trima grupama. Otpuštanje nikla bilo je slično u 1. grupi (nove bravice i novi lukovi) i 2. grupi (nove bravice i reciklirani lukovi), zatim u 2. i 3. (reciklirane bravice i novi lukovi) te u 4. grupi. Nadalje, količina iona bakra, kroma i titanija otpuštena u 3. i 4. grupi bila je značajno viša od one otpuštene u ostalim dvjema kombinacijama.

Kuhta i suradnici (12) istaknuli su da su sve ispitivane naprave (nehrđajući čelik, nikal-titanij i termo nikal-titanij) otpustile mjerljive količine svih ispitivanih iona, promjena pH-a snažno je utjecala (do 100 puta) na otpuštanje iona i njihovo otpuštanje ovisilo je o sastavu žice, ali nije bio proporcionalno sadržaju metala u njoj. Najveći broj iona otpušten je tijekom prvog tjedna uranjanja naprave. Isti autori (12) zaključili su da su razine otpuštenih iona dovoljne da uzrokuju odgođene alergijske reakcije.

Zato je svrha ovoga rada bila usporediti razine nikla (Ni), titanija (Ti), kroma (Cr), kobalta (Co), bakra (Cu) i cinka (Zn) u slini prije postavljanja metalnih ili keramičkih bravica i šest mjeseci poslije.

Ispitanici i postupci

Istraživanje je odobrilo Etičko povjerenstvo Stomatološkog fakulteta Sveučilišta u Zagrebu (br. 36/2014.).

Svi pacijenti bili su upućeni u privatnu ordinaciju dentalne medicine *Fiziodent,* Zagreb, Hrvatska. Svaki je potpisao informirani pristanak prema Helsinškoj deklaraciji WMA. Inkluzijski kriteriji za istraživanje bili su: pacijenti koji ne boluju od sustavnih bolesti i ne uzimaju nikakve lijekove, trajna denticija, nemaju amalgamskih ispuna i metalnih krunica, prije toga nisu ortodontski liječeni i nisu lokalno liječili usta (fluoridima, probioticima i otopinama za ispiranje usta). U istraživanje su bila uključena 33 muškarca i 51 žena u dobi između 16 i 35 godina. Četrdeset i dva ispitanika imala su metalne bravice (Mini Sprint Bracker, Forestadent Bernard Forster GmbH, Pforzheim, Njemačka), a 42 keramičke (Pure, Ortho Technology Inc., Tampa, FL, SAD). Korišteni su nikal-titanijevi četvrtasti ili okrugli lukovi čiji je promjer mijenjan redovito nakon 4 do 6 tjedana. Sve su ligature bile gumene. Ortodontske naprave u obje su čeljusti postavljene od prvog kutnjaka obostrano i nije bilo pacijenata s izvađenim zubima.

Svim je pacijentima prije postavljanja ortodontskih naprava uzet uzorak sline kako bi im se odredili ispitivani elektroliti, a to je ponovljeno i šest mjeseci poslije. Svi ispitanici isprali su usta destiliranom vodom i skupili 5 ml nestimulirane sline između 8 i 11 sati prijepodne, nakon čega je uzorak podijeljen na šest dijelova. Dane su im upute da dva sata prije

orthodontic materials, probably due to the influence of saliva.

Staffolani et al. (10) reported that a daily release of Ni, Cu and Cr *in vitro* conditions in acid pH was lower than a daily dietary intake of these metals and that this findings support the use of orthodontic appliances by patients.

Gürsoy et al. (11) reported that group 4 with recycled brackets and recycled archwires released higher amounts of Cr, Fe and Ti compared to other three groups. Ni release was simmilar in groups 1 (new brackets and new archwires) and 2 (new brackets and recycled archwires) and in groups 2,3 (recyled brackets and new archwire) and 4. Furthermore, the amounts of Cu, Cr and Ti ions released from groups 3 and 4 were significantly greater than the amounts released from other two combinations.

Kuhta et al. (12) reported that all investigated appliances (stainless steel, nickel-titanium and thermo NiTi) released measurable quantities of all ions examined and the change in pH had a very strong effect (up to 100 fold) on the release of ions. Also, the release of ions was dependent on wire composition, but it was not proportional to the content of metal in the wire. The largest number of ions was released during the first week of appliance insertion. The same authors (12) concluded that levels of released ions were sufficient to cause delayed allergic reactions.

Therefore, the aim of this study was to compare salivary levels of nickel (Ni), titanium (Ti), chromium (Cr), cobalt (Co), copper (Cu) and zinc (Zn) prior to and six months after the installment metallic or ceramic brackets.

Materials and methods

This study has been approved by The Ethics Committee of the School of Dental Medicine, University of Zagreb, Croatia (No 36/2014). All patients were referred to the private dental practice Fiziodent, Zagreb, Croatia. Informed consent was collected according to guidelines from the WMA Declaration of Helsinki. Inclusion criteria were as follows: patients without systemic diseases who were not taking any medications, permanent dentition, no amalgam or metallic crowns in the oral cavity, no prior orthodontic treatment and no local therapy (fluoride, probiotic, and mouthwash). Study group included 33 males and 51 females. Forty two patients had metallic braces (Mini Sprint Bracket, Forestadent Bernard Forster GmbH, Pforzheim, Germany) and 42 had ceramic ones (Pure, Ortho Technology Inc., Tampa, FL, USA). We used NiTi squared or round archwires whose diameter was changed every 4 to 6 weeks. All ligatures were made of rubber. Orthodontic appliances were set from first to first molar in both jaws and there were not any patients with extracted teeth.

Orthodontic appliances have been inserted into oral cavities of all the patients and six months after that, salivary samples were taken and studied. Subsequently, salivary electrolytes were determined. All participants rinsed their mouth with distilled water and each subject gave 5mL of unstimulated saliva sample between 8AM and 11AM, which was then divided into 6 parts. All participants were instructed

je skupljanja sline ne jedu, ne piju (osim vode) i ne peru zube. Uzorci sline do analize čuvani su na -20° C u plastičnim epruvetama. Obrađeni su u masenom spektrometru visoke rezolucije s induktivno spregnutom plazmom radi analize razine nikla, kroma, titanija, kobalta, bakra i cinka. Prije toga postupka uzorci su zagrijani na sobnu temperaturu i razrijeđeni deset puta. Kalibracijska krivulja izrađena je iz standardne otopine pripremljene s istim reagensima kao u uzorcima. Svaki je uzorak u prosjeku je mjeren tri puta.

Statistička analiza

Normalnost distribucije testirana je Kolmogorov-Smirnovljevim testom. S obzirom na to da koncentracije svih elektrolita nisu bile normalno distribuirane, u daljnjoj analizi korištene su metode neparametrijske statistike. Razlike u koncentraciji elektrolita u slini prije ortodontskog liječenja i poslije ispitane su *Wilcoxonovim signed rank* testom. Razlike u koncentraciji elektrolita u slini između različitih materijala bravica ispitane su *Mann Whitneyjevim* testom. Rezultati su prikazani medijanom i rasponom. P vrijednost manja od 0,05 ($p < 0,05$) smatrana je statistički značajnom.

Rezultati

Nisu pronađene razlike između bazičnih koncentracija ispitivanih elektrolita u slini između pacijenata s metalnim i nemetalnim bravicama. Koncentracije titanija u slini bile su značajno veće nakon liječenja i u pacijenata s metalnim i nemetalnim bravicama. Koncentracije kroma i cinka u slini bile su značajno veće prije liječenja i u pacijenata s metalnim i nemetalnim bravicama (tablica 1.).

to refrain from eating, drinking (except water) and brushing their teeth two hours prior to saliva collection. Salivary samples were kept at -20°C until assayed in plastic containers. Samples were analyzed with high-resolution mass spectrometer with inductively coupled plasma in order to analyze Ni, Cr, Ti, Co, Cu and Zn levels. Before analysis, samples were warmed at room temperature and diluted ten-fold. A calibration curve was made from the standard solution which was made with the same reagents as in the samples. The average of three measurements was used for each sample.

Statistical analysis

Normality of distribution was tested by the Kolmogorov-Smirnov test. Since salivary concentrations of all electrolytes were not normally distributed, non-parametric methods were used in further analysis. Difference in salivary concentrations of electrolytes before and after orthodontic therapy was assessed by the related samples Wilcoxon signed rank test. A difference in salivary concentrations of electrolytes between different brace materials was assessed by the Mann Whitney test. The results were expressed as median (range) and p value lower than 0.05 ($p<0.05$) was considered statistically significant.

Results

No difference in baseline salivary concentrations of any of the studied electrolyte between patients with metallic and non-metallic braces was found. Salivary concentrations of titanium were significantly higher after the treatment in patients with metallic and non-metallic braces, respectively. Salivary concentrations of chromium and zinc were significantly higher before the treatment in patients with metallic and non-metallic braces, respectively (Table 1.).

Table 1 Salivary electrolyte concentration before and after treatment

Concentration (μg/L) median (min – max)	Metallic			Non-metallic		
	Before	After	p	Before	After	p
Nickel	4.24 (0.63–59.94)	5.04 (0.85-17.58)	0.520	5.53 (0.58-18.24)	4.39 (0.52-416.90)	0.811
Titanium	1.68 (0.42-47.93)	9.29 (0.44-1067.06)	≤0.001*	2.60 (0.26-639.86)	9.30 (0.22.1938.26)	≤0.001*
Chromium	1.95 (0.58-32.99)	1.01 (0.41-6.73)	0.004*	2.77 (0.42-61.96)	1.00 (0.39-35.05)	0.001*
Cobalt	0.46 (0.04-4.77)	0.32 (0.01-3.81)	0.129	0.33 (0.05-4.5)	0.44 (0.03-2.47)	0.613
Copper	23.31 (2.74-2461.77)	22.19 (8.16-162.56)	0.694	25.07 (7.16-164.44)	19.88 (0.62-380.87)	0.915
Zinc	220.67 (32.46-1675.17)	168.45 (21.61-3590.89)	0.031*	208.85 (19.91-868.89)	126.1 (2.07-2269.04)	0.008*

*Wilcoxon signed rank test

Rasprava

Lages i suradnici (13) mjerili su koncentraciju nikla, kroma, bakra i željeza u slini 90 ortodontskih pacijenata s metalnim i estetskim bravicama. Isti autori (13) izvijestili su o statistički značajno povišenoj razini nikla i kroma u slini pacijenata s metalnim bravicama u odnosu na grupu s estetskima. No nije bilo značajne razlike u koncentraciji željeza i bakra u pacijenata s metalnim i keramičkim bravicama. Ovaj nalaz u

Discussion

Lages et al. (13) have measured salivary levels of nickel, chromium, copper and iron in 90 orthodontic patients with metal and esthetic brackets. The same authors (13) reported a significant increase in salivary levels of nickel and chromium in patients with metallic brackets compared to the group with esthetic brackets. However, there were no significant differences in the salivary iron and copper levels between the

suprotnosti je s našim – u našem istraživanju nismo pronašli razlike u koncentraciji elektrolita u slini pacijenata s metalnim i keramičkim bravicama.

Talic i suradnici (14) istaknuli su da postavljanje fiksnih ortodontskih naprava rezultira netoksičnim povišenjem koncentracije nikla u slini tijekom liječenja, za razliku od koncentracije kroma koja ostaje stabilna. Ovaj rezultat nije u skladu s našim – naime, mi smo pronašli sniženu razinu kroma i nepromijenjenu razinu nikla šest mjeseci nakon postavljanja ortodontske naprave.

Buczko i njegovi kolege (15) pronašli su u 37 pacijenata povišene vrijednosti nikla u slini nakon postavljanja ortodontskih bravica. Amini i suradnici (16) zaključili su da se koncentracija nikla može povisiti pacijentima liječenima konvencionalnim i MIM (*metal-injection molding*) bravicama, ali je povećanje veće u slučaju konvencionalnih. Ovaj rezultat suprotan je našemu. Khaneh Masjedi i suradnici (17) usporedili su konvencionalne i nove NiTi lukove (premazane epoksidom i bakar NiTi-jem) 42 ortodontska pacijenta i zaključili da mogu povisiti razinu nikla u slini. Nadalje, NiTi lukovi premazani epoksidom, praćeni bakar NiTi lukovima mogu otpustiti manje nikla u odnosu na konvencionalne NiTi lukove. Nayak i suradnici (18) izvijestili su o značajnom povećanju kroma i malom smanjenju nikla u slini nakon postavljanja ortodontske naprave. Ova spoznaja o povećanju kroma u slini suprotna je našoj. Nayak i suradnici (18) istaknuli su da se, iako su ove vrijednosti ispod preporučene dnevne doze, mora uzeti u obzir alergijski potencijal ovih metala.

Singh i suradnici (19) izvijestili su o značajnim razlikama u razini nikla i kroma u slini prije postavljanja ortodontske naprave te jedan i tri tjedna poslije tog postupka. Najviša razina uočena je nakon jednog tjedna, no razine kroma i nikla stabilizirale su se tri tjedna poslije i bile su više od bazičnih. Ovaj nalaz u suprotnosti je s našim – u ovom našem istraživanju nije zabilježeno povećanje nikla i kroma u slini pacijenata.

Elektroliti u slini služe kao komponenta antimikrobnih svojstava sline. Bakar je sastavnica histatina, antimikrobnog peptida iz sline i antimikrobnog enzima superoksidne dizmutaze i lizilne oksidaze koja sudjeluje u sintezi kolagena. Cink je sastavnica superoksidne dizmutaze, poznatog antioksidansa. Možda je razina cinka bila značajno snižena zbog povećane antimikrobne aktivnosti sline (20, 21). No tada bi se mogla očekivati snižena razina bakra u slini, što nije pronađeno u ovom radu.

Trenutačno nemamo objašnjenje zašto se razina kroma u slini snizila nakon postavljanja ortodontskih naprava. Značajno povećanje razine titanija može upućivati na povećano otpuštanje iz lukova, bez obzira na vrstu bravica koja je korištena.

Zaključak

Razina titanija u slini značajno se povisila šest mjeseci nakon postavljanja ortodontskih naprava, za razliku od kroma i cinka čija se razina značajno snizila nakon njihova postavljanja, bez obzira na vrstu korištenih bravica.

patients with metallic and those with ceramic brackets. This finding is contrary to ours as we found no differences in salivary electrolytes with metallic and ceramic brackets. Talic et al. (14) reported that installment of fixed orthodontic appliances lead to non-toxic salivary nickel level increase during the therapy, unlike salivary chromium level which remained stable. This finding is not in concordance with our results as we found decreased chromium levels and no change in salivary nickel concentration 6 month after the insertion of orthodontic appliance. Buczko et al. (15) found out that increased salivary nickel levels were noticed in 37 patients after bracket installment. Amini et al. (16) concluded that salivary nickel level might increase in patients treated with conventional and metal-injection molding (MIM) brackets, but that the increase is higher in those having conventional brackets. This finding is also in contrast to ours. Furthermore, Khaneh Masjedi et al. (17) compared conventional and new NiTi arches (epoxy coated and copper NiTi) in 42 orthodontic patients and concluded that NiTi arches might increase salivary nickel levels. Furthermore, epoxy-coated NiTi followed by copper NiTi archwires might release less nickel compared to conventional NiTi ones. Nayak et al. (18) reported a significant increase in salivary chromium and an insignificant decrease in salivary nickel after insertion of orthodontic appliances. This finding of an increase in salivary chromium level is completely opposite to our finding. Nayak et. al (18) stated that although these levels were below recommended daily doses, allergenic potential of these metals might be taken into account. Singh et al. (19) found significant differences in salivary nickel and chromium levels before, one week and three weeks after fixed orthodontic appliance installment. The highest level was noticed after one week; however, salivary levels of chromium and nickel have become stable after three weeks and were higher than initial levels. This finding is in contrast with ours as there was no increase in salivary nickel and chromium in our patients.

Salivary electrolytes serve as component of antimicrobial properties of saliva. Copper is a part of histatine, antimicrobial salivary peptide as well as part of superoxide dismutase (antimicrobial enzyme) as well as lysyl oxidase which takes part in collagen synthesis. Zinc is part of superoxide dismutase which is known antioxidant. It is possible that zinc levels might be significantly decreased due to the increased antimicrobial salivary activity (20, 21). Therefore, decreased salivary copper levels would be expected, which was not found in this study. At this point, we do not have any explanation why salivary chromium levels decreased after the insertion of orthodontic appliances. Significantly increased titanium levels might point to a higher release of titanium from archwires regardless of bracket type that has been inserted.

Conclusion

Salivary level of titanium increased significantly six months after installment of orthodontic appliances unlike salivary levels of chromium and zinc which significantly decreased after installment of orthodontic appliances, regardless of bracket type that was used.

Sukob interesa

Autori nisu bili u sukobu interesa.

Conflict of interest

None declared

Abstract

Objectives: It is known from the existing literature that metal ions within orthodontic appliances are prone to corrosion due to the salivary and bacterial interplay in the oral cavity. The results from the most studies show that levels of salivary nickel and chromium do not increase after the installment of orthodontic appliances. **Material and methods:** However, there are no studies on salivary levels of titanium, cobalt, copper and zinc in these patients. Salivary levels of nickel (Ni), titanium (Ti), chromium (Cr), cobalt (Co), copper (Cu) and zinc (Zn) were measured in 42 patients with ceramic brackets and in 42 patients with metal conventional brackets prior to insertion of orthodontic appliances and six months after insertion of orthodontic appliances by means of inductive coupled plasma/mass spectrometry. Statistical analysis was performed by use of Wilcoxon signed rank test and Mann Whitney test with level of significance set at 0.05. **Results:** The results showed that salivary level of titanium increased significantly six months after installment of orthodontic appliances. Salivary level of chromium and zinc significantly decreased after installment of orthodontic appliances. There were no significant differences in salivary levels of nickel, titanium, chromium, copper, cobalt and zinc between the patients with metallic and those with ceramic brackets. **Conclusion:** We might conclude that the salivary level of titanium increased significantly six months after installment of orthodontic appliances unlike salivary levels of chromium and zinc which significantly decreased after installment of orthodontic appliances, regardless of bracket type which was used.

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Orthodontic Appliances; Saliva; Electrolytes; Titanium; Chromium; Zinc

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