Salivary Concentrations of Nickel and Chromium in Patients with Burning Mouth Syndrome

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SUMMARY It has been documented *in vitro* and *in vivo* that metal dental appliances release metal ions due to corrosion. Dentists must choose among many dental casting alloys available, often without knowledge of their biological properties and effect on oral mucosa. The aim of this study was to measure metal content of nickel (Ni) and chromium (Cr) in whole saliva of 85 patients with and without metal dental appliances. Unstimulated whole saliva was collected and analyzed by using electrothermal atomic absorption spectrometry. History data, subjective complaints and objective findings on oral mucosa were recorded. The concentration of metal ions was investigated in correlation to burning mouth syndrome, erythema of oral mucosa, pH and smoking habit. Results showed a higher Ni concentration in patients with metal restorations, especially wearers of predominantly base metal appliances. The concentration of Cr showed no difference between patient groups. Although burning mouth syndrome was more frequent in the group with dental casting alloys, there was no correlation between higher Ni and Cr concentrations and burning mouth syndrome. Erythema of oral mucosa was a common finding in study patients, but did not correlate with salivary Ni and Cr ion concentrations. Salivary Ni and Cr concentrations were not related to either pH or smoking habit.

KEY WORDS: dental casting alloys, saliva, electrothermal atomic absorption spectrometry, burning mouth syndrome, corrosion

INTRODUCTION

Dental casting alloys placed in the oral cavity for a period of time may cause adverse effects as a consequence of corrosion (1,2). *In vitro* corrosion tests do not necessarily reflect the *in vivo* situation. Biological factors such as bacteria, saliva composition, food, and wear may contribute to corrosion of dental casting alloys (2,3). While clinically patients adapt well to nickel-chromium (Ni-Cr) appliances, corrosion products and components of these alloys are known to cause contact hypersensitivity and other tissue reactions (4,5). There are many concerns regarding the biocompatibility of metal ions released from these alloys to surrounding tissue (2,6). Metal ions released from metal appliances in dentistry or in other medical fields can cause adverse effects that are manifested from mild disturbances to severe toxic reactions (7). Some current reports suggest the link between oral symptoms and contact hypersensitivity to metal ions (6).

Therefore, the aim of the present study was to measure the concentration of Ni and Cr ions in saliva of patients with and without metal restorations and appliances in relation to the presence of oral symptoms, pH of saliva and influence of smoking.

MATERIALS AND METHODS

Subjects

The patients included in the study were referred to Department of Oral Medicine, School of Dental Medicine, University of Zagreb, for treatment of intraoral complaints or symptoms. A total of 85 patients were enrolled in the study and divided into three groups: (a) study group (n=54) included wearers of metal prosthodontic appliances having worn appliances for more than 5 years; (b) control group 1 (n=14) with amalgam restorations placed in the mouth for no less than 5 years; and (c) control group 2 (n=17) without metal restorations and appliances. Data included patient history and clinical findings that were recorded in a questionnaire created for this study. Distribution of patients according to age, sex, saliva pH and smoking habits is shown in Table 1.

In the study group, 25 patients were wearers of predominantly base metal appliances, 18 patients were wearers of noble appliances, and 11 patients were wearers of high noble appliances.

The institutional Ethics Committee approved the study and an informed consent was obtained from each patient enrolled in the study.

Saliva analysis

Three milliliters of whole unstimulated saliva were collected from each patient by the spitting method into graduated tube. Clinical examination of patients was performed in the morning at the same time from 10 to 11 am. Patients were instructed not to eat or drink for at least two hours before each saliva collection. The samples were immediately stored at -20 ^{0}C and on the next day transported to the laboratory for electrothermal atomic absorption spectrometry (EAAS).

After thawing, an aliquot of the saliva sample was dried and ashed in quartz crucibles at 450 ^{0}C overnight. The residue was dissolved in 0.5% nitric acid solution and adjusted to 5 mL. Elements were measured in prepared solutions by EAAS on a Varian Instrument model SpectrAA 300 (Springvale, Victoria, Australia) equipped with D_2 background correction and using pyrolytically coated partitioned tubes. At least two replicates were measured from each saliva sample. Detection limits were calculated as B + 3 SD, where B is the mean of at least 10 replicate measurements of the lowest standard solution and SD is standard deviation of these measurements. Detection limits obtained for nickel (Ni) and chromium (Cr) were 1.44 and 0.09 μg/L, respectively. Internal quality control of the method was tested by measuring Certified Reference Material for Trace Metals DORM-2 dogfish muscle (National Research Council, Canada). Values obtained for Ni and Cr were within 10% of the reference value.

Statistical analysis

Data were processed using descriptive statistical methods. The χ^2-test with a statistical significance level of 0.05 (p=0.05) was used for testing the significance of association. In case of low frequencies, the exact Fisher test was applied.

Table 1. Distribution of patients according to age, sex, salivary pH and smoking habit

Patient group	Age (yrs) mean (range)	Sex (F/M)	Salivary pH (mean ± SD)	Smokers	Nonsmokers
Study group with dental casting alloys (n=54)	58.5 (27-76)	43 F 11 M	6.60±0.52	13	41
Control group 1 with amalgam restorations (n=14)	45.8 (24-74)	10 F 4 M	6.66±0.47	2	12
Control group 2 without metal restorations (n=17)	60.3 (14-80)	16 F 1 M	6.39±0.61	5	12

RESULTS

The Ni content in saliva was significantly higher in study group, especially in wearers of predominantly base metal when compared to noble and high noble appliance wearers (p=0.004). There was no salivary Cr concentration increase in study group as compared to controls. Mean values, standard deviations and range between minimum and maximum concentration values for Ni and Cr in saliva of patient groups are shown in Table 2. Burning mouth syndrome (BMS) and erythema of oral mucosa were the most common findings in all patient groups. No significantly higher concentration of Ni and Cr were found in patients with BMS and erythema of oral mucosa (p=0.7 for Ni and p=0.2 for Cr). BMS was more common in the study group and in the control group without metal restorations and appliances (p=0.02). Regarding salivary pH, there were no significant differences among patients. The mean pH value in all three groups was 6.7 and slightly below neutral pH (5). Salivary pH was not significantly different between smokers and nonsmokers. At determined pH values, there were no significant between-group differences in the concentration of Ni and Cr ions.

DISCUSSION

The results of this study showed the salivary concentration of Ni to be significantly higher in subjects with metal dental appliances, especially wearers of predominantly base metal appliances, which is in agreement with previous studies (8). Nickel ion concentration was also elevated in patients without metal restorations and appliances (4.55 µg/L), although not significantly, probably due to daily dietary intake (9). The mean value of Ni in saliva from parotid gland is 2.2 µg/L and in serum 2.6 µg/L (10). The available data on the mean values of Cr in serum range from 0.01 to 0.3 µg/L (11).

Although there was no statistically significant between-group difference in Cr concentration, a slightly higher Cr concentration (10.83 µg/L) was found in the study group. However, these values were by far below the determined dietary intake levels, which are 23-29 mcg Cr and 39-54 mcg Cr *per* day for adult women and adult men, respectively (12). Sfondrini *et al*. (13) found the amount of Cr released to artificial saliva at various acidities (pH 4.2, 6.5, and 7.6) from several orthodontic brackets to be by far below the daily dietary intake level of Cr. Greater resistance of Cr to corrosion is due to the formation of stable chromium-oxide film on the surface of dental Co/Cr alloys (6,8,14). Lower release of Cr in comparison to Ni in this study could be explained by the formation of chromium-oxide film, which increased corrosion resistance. Also, it was found that the increasing amount of Cr in Ni-Cr commercial alloys reduced the amount of Ni release, but not linearly (15). In our study, there was no significant correlation between the concentrations of Ni and Cr ions in saliva and BMS, although BMS was the most common oral finding. This is in agreement with a previous study, in which burning mouth sensations were attributed to allergy, but only 10% of these patients had skin tested positive to relevant metal ion (16). BMS was also attributed to other dental materials (acrylates), but in 90% of patients allergy was not proved (6). In our study, BMS was more common in older patients and wearers of complete acrylate dentures. Therefore, it can be concluded that BMS is not correlated with higher metal ion concentration in saliva. Clinical appearance of erythema was the second most common finding in our patients, but

Table 2. Mean, standard deviation (SD) and range (min-max) of nickel and chromium salivary concentrations according to patient groups

Patient group	Nickel (µg/L)					Chromium (µg/L)				
	n	Mean	SD	Min	Max	n	Mean	SD	Min	Max
Study group (n=54)	54	19.18	56.52	0.34	364.5	54	10.83	48.18	0.09	353.3
Control group 1 (n=14)	14	4.19	4.71	0.40	17.50	14	2.85	2.85	0.09	8.30
Control group 2 (n=17)	17	4.55	4.76	0.85	18.10	17	2.51	2.42	0.09	10.80

its occurrence did not correlate with higher salivary concentrations of Ni and Cr either. The occurrence of mucosal erythema due to contact allergies to metal ions, errors in manufacturing dental appliances or as a consequence of microbial adherence on oral mucosa (2) is well documented in the literature; however, the effect of metal ions on cell metabolism and DNA damage of oral epithelial cells still remains a concern and is a subject of research (17).

In this study, the mean salivary pH was 6.7. This slightly acid salivary pH was not associated with greater release of metal ions. Previous studies have shown that corrosion was more present at lower pH from predominantly base metal alloys, especially Ni-based alloys. After storage at pH 1 or 4, significantly increased corrosion and release of Ni ions was revealed (2).

Some studies demonstrated a decreased salivary pH in smokers (18). We did not find significant differences in pH between smokers and nonsmokers, probably due to a small number of patient smokers. This finding may also explain why there were no significant differences in the concentration of metal ions, Ni and Cr, between smokers and nonsmokers.

The results of the present study indicated significantly higher concentrations of nickel in oral cavity in wearers of predominantly base metal appliances. Given that nickel has already been documented as both highly allergenic (2) and cytotoxic (17), it is of utmost importance to choose dental materials that will ensure the lowest release of harmful metal ions as to prevent allergic and cytotoxic reactions.

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References

1. Garhammer P, Schmalz G, Hiller KA, Reitinger T. Metal content of biopsies adjacent to dental cast alloys. Clin Oral Investig 2003;7:92-7.
2. Geurtsen W. Biocompatibility of dental casting alloys. Crit Rev Oral Biol Med 2002;13:71-84.
3. Bumgardner JD, Johansson BI. Effects of titanium-dental restorative alloy galvanic couples on cultured cells. J Biomed Mater Res 1998;43:184-91.
4. Setcos JC, Babaei-Mahani A, Silvio LD, Mjör IA, Wilson NH. The safety of nickel containing dental alloys. Dent Mater 2006;22:1163-8.
5. Moneret-Vautrin DA, Burnel D, Sainte-Laudy J, Beaudouin E, Croizier A. Allergy to nickel in dental alloys. Eur Ann Allergy Clin Immunol 2004;36:311-2.
6. Schmalz G, Garhammer P. Biological interactions of dental cast alloys with oral tissues. Dent Mater 2002;18:396-406.
7. Steens W, von Foerster G, Katzer A. Severe cobalt poisoning with loss of sight after ceramic-metal pairing in a hip – case report. Acta Orthop 2006;77:830-2.
8. Wataha JC. Alloys for prosthodontic restorations. Review. J Prosthet Dent 2002;87:351-63.
9. Eliades T, Trapalis C, Eliades G, Katsavrias E. Salivary metal levels of orthodontic patients: a novel methodological and analytical approach. Eur J Orthod 2003;25:103-6.
10. Nielsen FH. Nickel. In: Mertz W (ed). Trace Elements in Human and Animal Nutrition. 5th ed. New York: Academic Press, Inc.; 1988. pp. 245-66.
11. Anderson RA. Chromium. In: Mertz W (ed) Trace Elements in Human and Animal Nutrition. 5th ed. New York: Academic Press, Inc.; 1988. pp. 225-40.
12. Institute of Medicine, Food and Nutrition Board Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. Washington, DC: National Academy Press; 2001.
13. Sfondrini MF, Cacciafesta V, Maffia E, Massironi S, Scribante A, Alberti G, *et al.* Chromium release from new stainless steel, recycled and nickel-free orthodontic brackets. Angle Orthod 2009;79:361-7.
14. Lygre H. Prosthodontic biomaterials and adverse reactions: a critical review of the clinical and research literature. Review. Acta Odontol Scand 2002;60:1-9.
15. Jones SB, Taylor RL, Colligon JS, Johnson D. Effect of element concentration on nickel release from dental alloys using a novel ion beam method. Dent Mater 2010;26:249-56.
16. Schmalz G, Hiller KA, Garhammer P, Reitinger T. Patients with (claimed) local adverse effects to dental alloys. Transactions of the Academy of Dental Materials 1999;13:138. Abstract No.22.
17. Faccioni F, Franceschetti P, Cerpelloni M, Fracasso ME. *In vivo* study on metal release from fixed orthodontic appliances and DNA damage in oral mucosa cells. Am J Orthod Dentofacial Orthop 2003;124:687-94.
18. Parvinen T. Stimulated salivary low rate, pH, and lactobacillus and yeast concentrations in nonsmokers and smokers. Scand J Dent Res 1984;92:315-8.