Original Article

Nickel and Chromium Levels in the Saliva and Serum of Patients With Fixed Orthodontic Appliances

Günseli Ağaoğlu, DDS, PhD[a]; Tülin Arun, DDS, PhD[b]; Belgin İzgü, MD[c]; Ayşen Yarat, MD[d]

Abstract: The aim of this study was to evaluate the concentrations of nickel and chromium ions in salivary and serum samples from patients treated with fixed orthodontic appliances. A second aim of this study was to determine any significant changes in these concentrations during any period of the treatment time. Saliva and blood samples were collected from 100 patients ranging in age from 12 to 33 years. Twenty samples from each group were obtained. The groups were as follows: In the first group, saliva and blood samples were collected before insertion of the fixed appliances. In the second, third, fourth, and fifth groups, samples were collected at 1 week, 1 month, 1 year, and 2 years after appliance insertion. The serum was prepared by centrifuging the blood samples at 3000 rpm for 10 minutes. The fixed appliances consisted of an average of 4 bands and 20 bonded brackets. No palatal or lingual appliances welded to bands or extraoral auxiliary appliances were used. The spectrophotometric determinations were carried out using electrothermal atomic absorption spectrophotometry. The results indicated certain differences in the amounts of nickel and chromium released from fixed orthodontic appliances during different periods of treatment. The Mann-Whitney *U*-test from the SPSS statistics program was used to analyze the significance of the differences between no-appliance samples and those obtained with the appliances present. In the serum, there were statistically significant increases in ion concentration in the second-year groups. In saliva samples, nickel and chromium reached their highest levels in the first month and decreased to their initial level in the rest of the groups. It can be concluded that fixed orthodontic appliances release measurable amount of nickel and chromium when placed in the mouth, but this increase doesn't reach toxic levels for nickel and chromium in the saliva and serum. (*Angle Orthod* 2001;71:375–379.)

Key Words: Trace elements; Nickel; Chromium; In vivo; Atomic absorption spectrophotometry

INTRODUCTION

The stainless steel used for orthodontic brackets, bands, and wires contains approximately 18% chromium (Cr) and 8% nickel (Ni). Nickel and chromium have dermatological, toxicological, and possibly mutagenic effects. Nickel is the most common cause of metal-induced allergic contact dermatitis.[1–6] Chromium allergy is estimated at 10% in male subjects and 3% in female subjects.[7] Blanco-Dalmau et al[8] found 31.9% of the women and 20.7% of the men in a population of 403 showed a positive reaction to a patch test with nickel sulfate. Jones et al[9] reported a positive skin patch test to nickel sulfate in 20% of the female patients and 2% of the male patients in a population of 100 dental patients. Therefore, there is the possibility that nickel and chromium released from stainless steel orthodontic bands, brackets, and wires might elicit an allergic reaction. Nickel allergy reactions to orthodontic appliances have been reported after the use of facebow and neck straps[10,11] and also after the insertion of orthodontic arch wires.[12,13]

The most significant human exposure to nickel and chromium occurs through the diet. The average dietary intake for these metals has been estimated to be 200–300 μg/d for nickel[3] and 50–200 μg/d for chromium.[14] The known cancer risk presented by nickel, chromium, and their compounds has been documented in the literature.[3,7]

In the oral environment, biodegradation of metals occurs usually by electrochemical breakdown.[15–19] The in vitro release rate from full-mouth orthodontic appliances was reported to be 40 μg/d for nickel and 36 μg/d for chromium.[20] Kerousuo et al[2] found that, during the first month of

[a]Reseach Assistant, Department of Orthodontics, Faculty of Dentistry, Marmara University, İstanbul, Turkey.
[b]Associate Professor, Department of Orthodontics, Faculty of Dentistry, Yeditepe University, İstanbul, Turkey.
[c]Research Assistant, Department of Basic Sciences, Faculty of Medicine, Uludağ University, Bursa, Turkey.
[d]Professor, Department of Basic Sciences, Faculty of Dentistry, Marmara University, İstanbul, Turkey.
Corresponding author: Tülin Arun, DDS, PhD, Yeditepe Üniversitesi, Dişhekimliği Fakültesi, Bağdat Cad. No. 238, Göztepe, İstanbul, Turkey.
(e-mail: tarun@mail.koc.net).

Accepted: January 2001. Submitted: November 2000.

treatment, fixed orthodontic appliances did not significantly affect nickel and chromium concentrations of saliva. The release of nickel from fixed orthodontic appliances was reported to be related to both the composition and the method of manufacture of the appliances but not to be proportional to the nickel content.[21] Barrett et al[22] concluded that the release rates of nickel or chromium from stainless steel and nickel-titanium arch wires were not significantly different.

The purpose of this study was to determine if there was a significant increase in serum and salivary levels of nickel and chromium in patients having fixed orthodontic treatment and to evaluate the concentrations of nickel and chromium ions present following different durations of orthodontic treatment time.

MATERIALS AND METHODS

The patients in this study were treated in the Department of Orthodontics, Faculty of Dentistry, University of Marmara. Saliva and blood samples were collected from 100 patients (67 females and 33 males) ranging from 12 to 33 years of age, with an average age of 19.5 years. Salivary and blood samples were taken from patients who were treated using fixed orthodontic appliances. Orthodontic appliances consisted of an average of 4 bands and 20 bonded brackets manufactured by Unitek (Monrovia, California), nickel titanium wires manufactured by Ormco (Glendora, California), and stainless steel wires manufactured by Unitek.

Criteria of patient inclusion were as follows:

- Patients were in the permanent dentition period,
- Patients did not have any amalgam fillings and metal restorations, which could any galvanic corrosion in the mouth,
- Patients had standard edgewise brackets on the incisors, canines, and premolars and standard edgewise bands on the first molars,
- Patients did not have any palatal or lingual appliances welded to the bands (ie, rapid maxillary expansion appliance) or extraoral auxiliary orthodontic appliances (ie, headgear).

In order to determine salivary and serum nickel and chromium levels during different periods of treatment, 20 samples from each group were obtained. The groups were as follows: In the first group, saliva and blood samples were collected before insertion of the fixed appliances. In the second, third, fourth, and fifth groups, samples were collected 1 week, 1 month, 1 year, and 2 years after appliance insertion, respectively.

All saliva samples were collected in the morning before breakfast. The patients rinsed their mouths thoroughly with deionized and distilled water before the collection. Saliva was sampled for 5 minutes with the mouth closed without stimulation and transferred to plastic test tubes. Blood was obtained from the antecubital fossa of the arm and centrifuged at 3000 rpm for 10 minutes in order to prepare the serum. Acid-washed plastic containers were used for storage of saliva and serum samples. The samples were kept at −20°C until they were processed.

TABLE 1. Salivary Cr and Ni Levels in Different Periods of Fixed Treatment Time (ppb)

Groups[a]	Mean	SD
Cr 1	0.76	1.43
Cr 2	0.53	0.57
Cr 3	1.53	3.31
Cr 4	0.91	1.03
Cr 5	0.54	0.67
Ni 1	4.45	2.87
Ni 2	4.12	2.65
Ni 3	11.53	9.24
Ni 4	7.01	7.15
Ni 5	4.44	4.00

[a] Cr 1 and Ni 1, mean collection before insertion of the appliance; C2 and Ni 2, mean collection at end of the first week; C3 and Ni 3, mean collection at end of the first month; C4 and Ni 4, mean collection at end of the first year; and C5 and Ni 5, mean collection at end of the second year.

The spectrophotometric determinations were carried out using an electrothermal atomic absorption spectrophotometer in Uludağ University Faculty of Medicine (Unicam 90 Graphite Furnace, ATI Unicam 929 AAS). Before the analysis, samples were centrifuged at 3000 rpm for 10 minutes to settle particulate matter. A calibration curve was made from the results obtained with standard solutions prepared with the same reagents as those used for the serum samples. Synthetic saliva was used for the calibration curve made for the salivary analysis. Each test was analyzed 3 times and the average was used as the result. Before each test, 1 distilled water sample was processed in order to prevent possible contamination. The insoluble precipitate was not included in the analysis because of the problem of particles causing variation in the results.

The Mann-Whitney *U*-test from the SPSS statistics program was used for statistical analysis of the results. The statistically significant differences were analyzed in 5 different periods of treatment time for the 4 main groups, which included chromium in saliva, nickel in saliva, chromium in serum, and nickel in serum.

RESULTS

The results indicate certain differences in the amounts of nickel and chromium in saliva and serum of the patients with fixed orthodontic appliances during different periods of treatment time. In our study, release of chromium in saliva was 0.53–1.53 ppb and nickel in saliva was between 4.12 and 11.53 ppb (Table 1). Levels of nickel serum were found to be between 7.87 and 10.27 ppb, while levels of chromium serum were found to be between 6.16 and 10.98 ppb (Table 2).

TABLE 2. Serum Cr and Ni Levels in Different Periods of Fixed Treatment Time (ppb)

Groups[a]	Mean	SD
Cr 1	6.21	21.30
Cr 2	6.23	21.62
Cr 3	7.02	21.43
Cr 4	6.16	20.76
Cr 5	10.98	29.28
Ni 1	8.36	11.20
Ni 2	9.03	10.45
Ni 3	8.53	10.81
Ni 4	7.87	12.08
Ni 5	10.27	14.17

[a] Cr 1 and Ni 1, mean collection before insertion of the appliance; C2 and Ni 2, mean collection at end of the first week; C3 and Ni 3, mean collection at end of the first month; C4 and Ni 4, mean collection at end of the first year; and C5 and Ni 5, mean collection at end of the second year.

TABLE 3. Mann-Whitney *U*-Test for Salivary Cr and Ni Levels

Parameter (Cr)	Test (*P*)	Parameter (Ni)	Test (*P*)
Group 1–2	.7319	Group 1–2	.8190
Group 1–3	.0220*	Group 1–3	.0531*
Group 1–4	.1423	Group 1–4	.5400
Group 1–5	.2608	Group 1–5	.5723
Group 2–3	.0356*	Group 2–3	.0564*
Group 2–4	.1416	Group 2–4	.6336
Group 2–5	.5625	Group 2–5	.5947
Group 3–4	.8085	Group 3–4	.1760
Group 3–5	.0115*	Group 3–5	.0454*
Group 4–5	.0463*	Group 4–5	.3954

* $P < .05$, ** $P < .01$, *** $P < .001$.

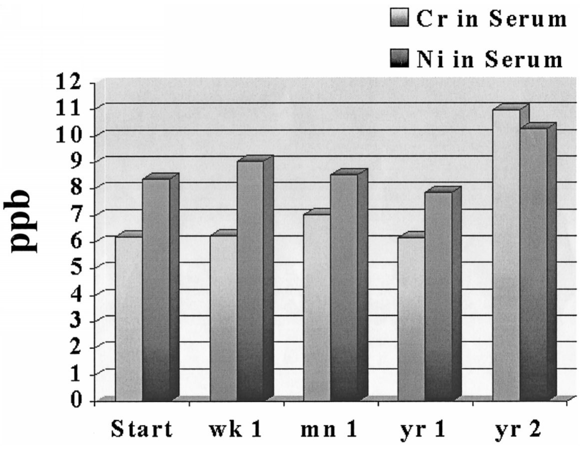

FIGURE 1. Cr and Ni levels in serum during different periods of treatment time.

In salivary samples, Ni and Cr values increased in the first-month group compared with the initial and the first-week groups. The decrease in the values of the second-year group was also statistically significant when compared with the first-month group (Table 3, Figure 1).

In serum samples, there was a statistically significant increase in the amount of chromium in the second-year group in comparison with the other groups (Table 4, Figure 2). There was no relationship between serum and salivary nickel levels in different periods of fixed orthodontic treatment. In the first month of fixed orthodontic treatment, salivary and serum Cr levels were found to be increased in comparison with the values of the first-week group.

TABLE 4. Mann-Whitney *U*-Test for Serum Cr and Ni Levels

Parameter (Cr)	Test (*P*)	Parameter (Ni)	Test (*P*)
Group 1–2	.1086	Group 1–2	.1563
Group 1–3	.9514	Group 1–3	.8554
Group 1–4	.8721	Group 1–4	.0432*
Group 1–5	.0071**	Group 1–5	.5634
Group 2–3	.0414*	Group 2–3	.1961
Group 2–4	.1889	Group 2–4	.0018**
Group 2–5	.0007***	Group 2–5	.3367
Group 3–4	.8547	Group 3–4	.0230*
Group 3–5	.0327*	Group 3–5	.7679
Group 4–5	.0138*	Group 4–5	.0093**

* $P < .05$, ** $P < .01$, *** $P < .001$.

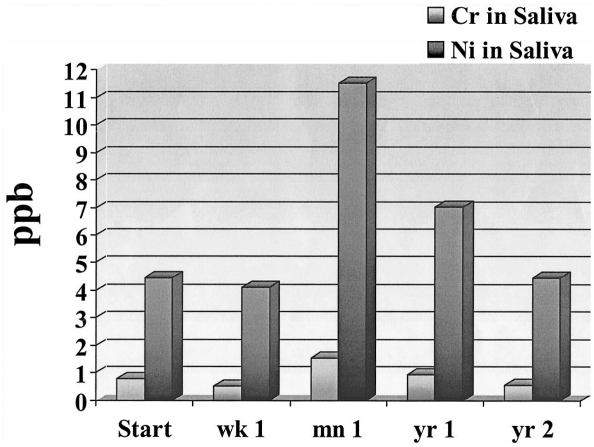

FIGURE 2. Cr and Ni levels in saliva during different periods of treatment time.

DISCUSSION

Most of the metals used in the oral cavity can be expected to undergo some type of corrosion. Several previous studies have reported on the corrosive behavior of orthodontic wires, brackets, bands, or appliances separately. In our study, we didn't separate the appliance components under in vitro conditions because, in orthodontic treatment, wires, brackets, and bands are used together in the oral environment. In this investigation, the aim was to determine the corrosion during different periods of standard fixed orthodontic treatment. The main reason for choosing cross-sectional material was to analyze many patients. The criteria would limit the material if the patients were included longitudinally.

Previous studies have not investigated the corrosion caused by fixed orthodontic appliances in the oral cavity over the long term. Most studies have also used artificial salivary solutions. Saliva has a dynamic composition that may be affected by many physiologic variables such as diet, salivary pH, health conditions, and salivary flow rate.[23] In order to standardize the material, the saliva was collected from patients who did not have any health problems or any caries in the mouth. All the samples were taken in the morning before breakfast and the patients rinsed their mouths thoroughly with deionized and distilled water before the collection.

In this study, we preferred to use saliva samples obtained from orthodontic patients in order to analyze the release in the dynamic oral cavity environment. Artificial salivary solutions are not commonly used in long-term studies based on their precipitation disadvantage. Fixed orthodontic treatment generally lasts about 2 years, so there was a necessity for long-term research of the release from the fixed orthodontic appliances. The purpose of this study was to determine if there was a significant increase in the amounts of nickel and chromium in the serum and saliva of patients having fixed orthodontic treatment over 5 different periods of treatment time.

The spectrophotometric determinations were carried out using electrothermal atomic absorption spectrophotometry with a graphite furnace. This is a common method used for trace element analysis in the literature.[2,15,20–22,24–31]

The concentrations of salivary nickel and chromium show large variations in the literature. According to the different reports, the mean concentration of chromium is between 1 and 61 ppb[2,24,25] and the mean concentration of nickel is between 1 and 55 ppb.[2,24,26] In our study, the release of chromium in saliva was between 0.53 and 1.53 ppb and the release of nickel in saliva was between 4.12 and 11.53 ppb. These levels are within the normal ranges and are far below the average daily dietary intake of 300 μg nickel and 50–200 μg chromium.[3,14]

In the literature, the levels of nickel and chromium in serum were found to be approximately 0.2 ppb.[27–30] In our study, the levels of nickel in serum were between 7.87 and 10.27 ppb and the levels of chromium in serum were between 6.16 and 10.98 ppb. The higher values found in serum might be the result of contamination from the stainless steel venipuncture needle.

In serum samples, there was a statistically significant increase of chromium values in the second-year group in comparison with the other groups. No data are available in the literature to compare with our results for long periods of treatment. Our short-term findings for serum values are in accordance with the study by Bishara et al,[31] who also did not find any differences of blood nickel amounts in 4–5 month periods of time.

In the salivary samples, Ni and Cr values were increased in the first-month group in comparison with the initial and the first-week groups. The decrease in the values of the second-year group was also statistically significant when compared with the first-month group. Our findings for the first-week group are consistent with the findings reported by Kerousuo et al[2] but are in contrast with the first-month results of the same study. There are no data available with which to compare our results for long periods of treatment, as our data related to serum samples.

CONCLUSION

Our findings indicate that measurable amounts of nickel and chromium can be found in the serum and saliva of the patients wearing fixed orthodontic appliances but that these values might change during different periods of orthodontic treatment. It can be concluded that there could be a release from the fixed appliances when placed in the mouth but that the values in any period of the treatment don't reach toxic levels of salivary and serum nickel and chromium and are similar to those found in healthy individuals.

REFERENCES

1. Platt J, Guzman A, Zuccari A, Thornburg DW, Rhodes BF, Oshida Y, Moore BK. Corrosion behavior of 2205 duplex stainless steel. *Am J Orthod Dentofac Orthop.* 1997;112:69–79.
2. Kerousuo H, Moe G, Hensten-Pettersen A. Salivary nickel and chromium in subjects with different types of fixed orthodontic appliances. *Am J Orthod Dentofac Orthop.* 1997;111:595–598.
3. Barceloux DG. Nickel. *J Clin Toxicol.* 1999;37:239–258.
4. Leonard A, Gerber GB, Jacquet P. Carcinogenicity, mutagenicity and teratogenicity of nickel. *Mutat Res.* 1981;87:1–15.
5. Savolainen H. Biochemical and clinical aspects of nickel toxicity. *Rev Environ Health.* 1996;11(4):167–173.
6. Kerousuo H, Kullaa A, Kerousuo E, Kanerva L, Hensten-Pettersen A. Nickel allergy in adolescents in relation to orthodontic treatment and piercing of ears. *Am J Orthod Dentofac Orthop.* 1996;109:148–154.
7. Norseth T. The carcinogenicity of chromium. *Environ Health Perspect.* 1981;40:121–130.
8. Blanco-Dalmau L, Carrasquillo-Alberty H, Silva-Parra J. A study of nickel allergy. *J Prosthet Dent.* 1984;52:116–119.
9. Jones TK, Hansen CA, Singer MT, Kessler HP. Dental implications of nickel hypersensitivity. *J Prosthet Dent.* 1986;56:507–509.
10. Greig DGM. Contact dermatitis reaction to a metal buckle on a cervical headgear. *Br Dent J.* 1983;155:61–62.
11. Bass JK, Fine H, Cisneros GJ. Nickel hypersensitivity in the orthodontic patient. *Am J Orthod Dentofac Orthop.* 1993;103:280–285.
12. Dunlap CL, Vincent K, Barker F. Allergic reaction to orthodontic wire: report of a case. *J Am Dent Assoc.* 1989;118:449–450.
13. Al-Waheidi EMH. Allergic reaction to nickel orthodontic wires: a case report. *Quintessence Int.* 1995;26:385–387.
14. Anderson RA. *Essential and Toxic Trace Elements in Human Health and Disease.* New York, NY: Alan R. Liss; 1986:190–197.
15. Toms AP. The corrosion of orthodontic wire. *Eur J Orthod.* 1988; 10:87–97.

16. Maijer R, Smith DC. Biodegration of the orthodontic bracket system. *Am J Orthod Dentofac Orthop.* 1986;90:195–198.
17. Council on Dental Materials, Instruments, and Equipment. American Dental Association status report on the occurrence of galvanic corrosion in the mouth and its potential effects. *J Am Dent Assoc.* 1987;115:783–787.
18. Bergman M. Corrosion in the oral cavity—potential local and systemic effects. *Int Dent J.* 1986;36:41–44.
19. Kim H, Johnson JW. Corrosion of stainless steel, nickel-titanium, coated nickel-titanium, and titanium orthodontic wires. *Angle Orthod.* 1999;69:39–44.
20. Park HY, Shearer TR. In vitro release of nickel and chromium from simulated orthodontic appliances. *Am J Orthod Dentofac Orthop.* 1983ğ:156–159.
21. Grimsdottir MR, Gjerdet NR, Hensten-Pettersen A. Composition and in vitro corrosion of orthodontic appliances. *Am J Orthod Dentofac Orthop.* 1992;101:525–532.
22. Barrett R, Bishara SE, Quinn JK. Biodegradation of orthodontic appliances. Part I. Biodegradation of nickel and chromium in vitro. *Am J Orthod Dentofac Orthop.* 1993;103:8–14.
23. Crossner CG. Salivary flow rate in children and adolescents. *Swed Dent J.* 1984;8:271–276.
24. Berge M, Gjerdet NR, Erichsen ES. Corrosion of silver soldered orthodontic wires. *Acta Odontol Scand.* 1982;40:75–79.
25. deMelo JF, Gjerdet NR, Erichsen ES. Metal release from cobalt-chromium partial dentures in the mouth. *Acta Odontol Scand.* 1983;41:71–74.
26. Gjerdet NR, Erichsen ES, Remlo HE, Evjen G. Nickel and iron in saliva of patients with fixed orthodontic appliances. *Acta Odontol Scand.* 1991;49:73–78.
27. Sunderman FW Jr. Biological monitoring of nickel in humans. *Scand J Work Environ Health.* 1993;19:34–38.
28. Sunderman FW, Aitio A, Morgan LG, Norseth T. Biological monitoring of nickel. *Toxicol Ind Health.* 1986;2:17–78.
29. Sunderman FW Jr, Crisostomo MC, Reid MC, Hopfer SM, Nomoto S. Rapid analysis of nickel in serum and whole blood by electrothermal atomic absorption spectrophotometry. *Ann Clin Lab Sci.* 1984;14:232–241.
30. Nomoto S, Sunderman FW Jr. Atomic absorption spectrometry of nickel in serum urine and other biological materials. *Clin Chem.* 1970;16:477–485.
31. Bishara S, Barrett RD, Selim M. Biodegradation of orthodontic appliances. Part II. Changes in the blood level of nickel. *Am J Orthod Dentofac Orthop.* 1993;103:115–119.