Urinary excretion levels of nickel in orthodontic patients

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Introduction: Nickel, a primary component of orthodontic appliances, causes more allergic reactions than all other metals combined and can initiate a wide range of hypersensitivity reactions in susceptible subjects. The purpose of this study was to compare pretreatment and treatment levels of nickel in the urine of orthodontic patients wearing fixed appliances. Methods: Urine specimens were collected from 21 orthodontic patients (12 female, 9 male) before placement of orthodontic appliances and 2 months after placement. Nickel ion analysis was carried out with atomic absorption spectrophotometry. The results were submitted to descriptive analyses, the Student t test, and ANOVA for repeated measurements (P < .05). Results and Conclusions: Urinary nickel levels increased significantly 2 months after the placement of orthodontic appliances. The results were similar in both sexes. Continued follow-up is needed to determine the patterns and the long-term significance of nickel release. (Am J Orthod Dentofacial Orthop 2007;131:635-8)

Nickel, a primary component of orthodontic brackets, bands, and wires, is a potential allergen and a common cause of allergic contact dermatitis. Epidemiological data indicate that about 20% of subjects are hypersensitive to nickel. Many objects in our environment contain nickel, and it is virtually impossible to avoid exposure.

Nickel is an essential trace element and is supplied at the rate of 0.3 to 0.6 mg per day by the diet. The metal or its compounds are absorbed after inhalation or ingestion. Nickel in the plasma of healthy subjects averages 2.1 μg/L, with a range of 1.4 to 3.4 μg/L. More than 90% of the nickel ingested is excreted unabsorbed in the feces. Absorbed nickel tends to localize in connective tissues, kidneys, and lungs. Most of the absorbed nickel is believed to be excreted in urine, with an average of 4.5 μg/L (range 1.9-9.6 μg/L) in the urine of unexposed people.

The literature includes some studies in which patch tests were used to evaluate hypersensitivity reactions to nickel. Jones et al attempted to determine the incidence of nickel hypersensitivity with patch tests in 100 patients (50 men, 50 women). They found associations of sex and age with hypersensitivity in patients previously reported to be allergic to jewelry containing nickel. Alterations in blood pressure, pulse, or temperature in patients with nickel hypersensitivity were also found. After placing removable appliances, the authors observed that nickel-hypersensitive patients often showed signs of hypersensitivity at the area of contact and at distant ones. They found incidences of hypersensitivity to nickel with the patch test of 20% for women and 2% for men. Menezes et al evaluated hypersensitivity to 8 antigens, including nickel, in 38 orthodontic patients. Patch tests were carried out before and 2 months after the placement of fixed orthodontic appliances. The authors found no statistically significant difference in relation to orthodontic appliances, indicating that the appliance did not sensitize the patients or induce tolerance to the evaluated metals during the study period.

Nickel released from metallic appliances was observed in several in-vitro studies. However, it is not known whether the release of these ions from dental alloys is high enough to be clinically significant. The aim of this study was to evaluate systemic changes in nickel levels after the placement of fixed orthodontic appliance in 21 patients.

MATERIAL AND METHODS

Thirty patients in need of orthodontic treatment were selected from the postgraduate clinics for urinary nickel release evaluation. All patients or their guardians received information on the tests. Those who agreed to participate in the study signed a consent form. From this initial sample, 21 patients (12 female, 9 male) aged...
9 to 25 years were included. Evaluation comprised assessing the urinary nickel levels before and 2 months after the placement of fixed orthodontic appliances. Urine specimens were collected from the patients and shipped to a medical laboratory for analysis by atomic absorption spectrophotometry. Urine collection was achieved by using sterile 50-mL plastic containers. The patients were asked to collect the urine in the morning, after discarding the first flush. The patients were instructed to avoid contaminating the collection vessels by rinsing or wiping the surfaces. Thus, the baseline urine samples were obtained before fitting or cementing any bands and bonds. They were identified and stored in a low-temperature freezer until the atomic absorption spectrophotometry was carried on.

After the first urine collection, the patients were referred for placement of fixed orthodontic appliances (standard edgewise stainless steel appliances, 20 bonded brackets [3M Unitek, Monrovia, Calif] and 4 bands [Dental Morelli, Piracicaba, Brazil]). Two months later, urine samples were collected in the same manner.

The results were submitted to ANOVA for repeated measurements, Student t tests, and descriptive statistics.

**RESULTS**

Descriptive statistics of urinary nickel concentrations according to sex, before and after placement of the orthodontic appliances, are given in Table I.

A statistically significant difference ($P < .05$) in the amount of nickel excreted was observed before and after placement of the appliances (Table II). The Student t test (paired t test) showed a statistically significant difference between the 2 evaluated periods. Increases in urinary excretion were found after placing the orthodontic appliances ($t = -2.52, P = .02$) in 19 patients (90.4%). No statistically significant differences were seen between the sexes in urinary nickel levels (Table II) before and after the placement of the orthodontic appliances.

**DISCUSSION**

There is increasing concern about the biocompatibility of dental materials. Particularly in orthodontics, there is interest in investigating reactions secondary to the use of metals that are known allergens.

An alloy’s ability to induce a dermatitis appears to be related to its pattern and mode of corrosion. Variations in manufacturing technique and postmanufacturing finishing and polishing operations might affect the corrosion behavior of orthodontic appliances.

The resulting products might trigger inflammatory responses of the soft tissues and cause irritation or dermatitis. However, some questions remain to be answered. How much of the corrosion products is actually absorbed by the organism? Is the amount of metal released sufficient to sensitize a person or to maintain a reaction in a previously sensitized person?

The administration and elimination routes are important aspects for understanding the reactions to metals. Nickel is not a cumulative toxin; it is absorbed in the gastrointestinal tract and eliminated by its metabolic route. The main route for elimination of nickel is through the kidneys; nearly 90% is quickly excreted in urine. For patients with no occupational exposure to nickel, the mean urinary nickel level is about 4.5 µg/L (range, 1.9-9.6 µg/L) or, according to other authors, up to 50 µg/L. Nickel can also be eliminated in saliva and sweat; this might contribute to increased excretion in high-temperatures areas. Urinary and blood concentrations usually indicate recent exposure and are better correlated with acute effects.

Blood, urine, and hair are the most accessible tissues for measurement of exposure or dose to a product or substance, and are sometimes mentioned as indicator tissues. The critical determinant of the metabolism and toxic action of metals is their biological half-life—ie, the time spent by the organism to excrete half of an accumulated amount.

Smith-Sivertsen et al investigated the exposure to nickel in Norwegian and Russian populations living near 2 nickel refineries by measuring urinary nickel levels with atomic absorption spectrophotometry; 2333

<table>
<thead>
<tr>
<th>Period</th>
<th>Sex</th>
<th>n</th>
<th>Mean (µg/L)</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>Male</td>
<td>9</td>
<td>17.00</td>
<td>7.30</td>
</tr>
<tr>
<td>Female</td>
<td>12</td>
<td>18.17</td>
<td>3.87</td>
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</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>17.67</td>
<td>5.47</td>
<td></td>
</tr>
<tr>
<td>After</td>
<td>Male</td>
<td>9</td>
<td>19.04</td>
<td>3.71</td>
</tr>
<tr>
<td>Female</td>
<td>12</td>
<td>20.52</td>
<td>3.23</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>19.89</td>
<td>3.43</td>
<td></td>
</tr>
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</table>
samples were analyzed. The Russian group had a higher mean level of urinary nickel, suggesting that an isolated industrial population might not explain this finding. Differences in the lifestyles, dietary habits, and socioeconomic conditions should be evaluated to explain the nickel levels in these 2 countries.

In this study, urine samples have been monitored by atomic absorption spectrophotometry before and after orthodontic appliance placement in order to detect the systemic response to potential corrosion products of orthodontic appliances. Collection and analysis of urine samples offer the advantages of ease of collection and minimum discomfort to the patient. For these reasons, volunteers for the evaluation of urine specimens before and 2 months after placing orthodontic appliances were enlisted. There is an increased risk of specimen contamination during collection of urine samples; however, care was taken to minimize possible contamination by supplying uncontaminated containers to each patient and by telling each patient the possible sources of contamination. The results showed statistically significant differences between the 2 evaluated periods (Tables I and II), with

### Table II. Nickel levels shown by ANOVA for repeated measurements

<table>
<thead>
<tr>
<th>Factors</th>
<th>df</th>
<th>SQ</th>
<th>MS</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Period (before × after)</td>
<td>1</td>
<td>49.657</td>
<td>49.657</td>
<td>5.785</td>
<td>.027*</td>
</tr>
<tr>
<td>Sex (female × male)</td>
<td>1</td>
<td>17.907</td>
<td>17.907</td>
<td>0.521</td>
<td>.479</td>
</tr>
<tr>
<td>Interaction (period × sex)</td>
<td>1</td>
<td>0.240</td>
<td>0.240</td>
<td>0.028</td>
<td>.869</td>
</tr>
</tbody>
</table>

P ≤ .05.

df, Degrees of freedom; SQ, sums of squares; MS, mean square.

Fig 1. Urinary nickel levels before and after placement of orthodontic appliances in male subjects.

Fig 2. Urinary nickel levels before and after placement of orthodontic appliances in female subjects.
increased urinary excretion after placing the orthodontic appliances in 19 patients (90.4%), as shown in Figures 1 and 2.

Few studies have addressed the actual effects of nickel in patients wearing orthodontic appliances. Jensen et al19 studied dose-response dependency of oral exposure to nickel in a double-blind, placebo-controlled oral exposure trial; 40 nickel-sensitive persons and 20 healthy (non-nickel-sensitive) controls were given nickel sulfate hexahydrate in doses similar to and greater than the amount of nickel ingested in the normal Danish daily diet. The nickel content in urine and serum before and after oral exposure was measured to determine nickel uptake and excretion. The influence of the amount of nickel ingested on the clinical reactions to oral exposure and on nickel concentrations in serum and urine was evaluated. Among nickel-sensitive subjects, a definite dose-response dependency was seen after oral exposure to nickel. Seven of the 10 nickel-sensitive subjects had cutaneous reactions to oral exposure of 4.0 mg of nickel, an amount approximately 10 times greater than the estimated normal daily dietary intake of nickel. Four of the 10 nickel-sensitive subjects had cutaneous reactions to 1.0 mg of nickel, a dose that is close to the estimated maximum amount of nickel in the daily diet. Four of the 10 nickel-sensitive subjects reacted to 0.3 mg of nickel, an amount equivalent to that in a normal daily diet, and 1 subject reacted to the placebo. None of the 20 controls had cutaneous reactions to 4.0 mg of nickel or the placebo. Before oral exposure, there was no measurable difference in the amount of nickel in the urine or the serum of the nickel-sensitive persons and the controls. After the oral challenge, the nickel content in the urine and the serum of both groups was directly related to the dose of nickel ingested.

The biologic effect of a systemic increase in nickel levels is unknown. There is a lack of information on abnormal accumulation of nickel in specific tissues of the body. The increase of nickel in the patients, despite the low amounts in the composition of orthodontic appliances, is not easily explained. The differences in the changes of excretion of these metal ions might be due to differences in corrosion processes, solubility coefficients, or excretion mechanisms.

Although increases in metal ion levels have been detected in most patients after placement of orthodontic appliances, the levels are not sufficient to cause alarm; however, additional in-vitro and in-vivo studies should be done to determine safe levels of nickel.

CONCLUSIONS

Our findings indicate that nickel increases significantly in patients’ urine 2 months after the placement of fixed orthodontic appliances. The biologic effect of a systemic increase in urinary nickel is unknown. Long-term follow-ups and larger samples of patients are needed to validate these results and to determine the implications of these findings.

REFERENCES