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ORIGINAL ARTICLE

Comparison Between Nickel and Chromium Levels in Serum and Urine in Patients Treated with Fixed Orthodontic Appliances: A Longitudinal Study

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Abstract

Objective: To compare levels of nickel and chromium in serum and urine in orthodontic patients treated with fixed orthodontic appliances. **Material and Methods:** Nickel and chromium ion concentration were measured in serum and urine of twenty patients (12 females and 8 males, aged 17-28 years old) who had fixed orthodontic treatment using Coupled Plasma-Atomic Emission Spectroscopy. The samples were taken before treatment (Baseline), two months, and six months later during treatment. Data were analyzed using repeated ANOVA, Bonferroni post-hoc test, and paired t-tests. The level of significance was set at 5%. **Results:** Average serum nickel level changed from 6.420 ppb to 6.855 ppb. Average serum chromium level changed from 5.305 ppb to 5.505 ppb in 6 months. Average urinary nickel level changed from 5.320 ppb to 5.610 ppb. Average urinary chromium level changed from 5.370 ppb to 5.520 ppb in 6 months. There was a statistically significant difference in serum ($p<0.001$) and urinary chromium ($p=0.007$) levels between observation times. **Conclusion:** Orthodontic treatment might raise both urinary and serum nickel levels, but the differences were not statistically significant; the alterations in chromium levels were not consistent; nickel levels were higher in serum than in urine; chromium levels were higher in urine than in serum.

Keywords: Orthodontic Appliances; Serum; Orthodontic Brackets.

Introduction

Metal is the main component of fixed orthodontic appliances. Due to various pressure (force), temperature fluctuation, a variety of food, and electrochemical reactions, the metal ion can release into the saliva, which is acting as a medium for continuous erosion over time [1,2]. The conditions like lowered salivary pH, high salt diet, soft drinks, fluoride-containing toothpaste and mouthwashes, can influence the ion release of metal [3].

The stainless steel as a major component of brackets, wires, and bands, is resistant to stain and corrosion, however, they are not resistant to temperature, or the microbiological and enzymatic environments in the oral cavity. It contains approximately 18% chromium (Cr), 8% nickel (Ni), iron, and carbon, which can be absorbed by the body. A high percentage of nickel (50%) can be found in NiTi (nickel-titanium) wire [3,4].

The release of metal ions into the body has been studied in various conditions. Nickel and chromium levels in saliva [5-7], in serum [8,9], and in urine [10,11] have been evaluated by previous researchers, after periods of treatment with fixed orthodontic appliances, but the results were not consistent. The nickel and chromium levels on saliva of fixed orthodontic wearers were increase [12,13] after certain period of treatment, however the levels were not significantly different after a period of 30-90 day [14]. Nickel and chromium levels in serum increased significantly two years after insertion of orthodontic appliance [15], however, the levels decreased gradually after the initial increase [8]. Nickel level in urine increased significantly two months after placement of orthodontic appliance [11] while a long-term retrospective study showed a significant difference between treatment and control group [10].

The most common cause of metal-induced contact dermatitis is nickel and chromium [16]. Moreover, they might cause breast cancer, miscarriage, birth defect, lung and kidney diseases, neurological disorders, and cardiovascular collapse [17,18]. Urine and serum are the body fluids commonly analyzed for a nickel ion level. Moreover, urine collection is painless, noninvasive, and convenient, so urine is more practical than serum for the biological monitoring of nickel-exposed workers [19].

Different with previous researchers, we tried to compare the levels of nickel and chromium in serum with those in the urine of the same subject. It has not been investigated so far. Therefore, the aim of the study was to compare the nickel and chromium levels in serum and urine of patients having fixed orthodontic treatment.

Material and Methods

Study Design and Sampling

This longitudinal study was conducted on twenty patients (12 females and 8 males) who visited to Hasanuddin University Dental Hospital in Makassar, Indonesia, between the months of April 2017 to October 2017. Their age ranged from 17 to 28 years (mean 19.2 ± 3.3 years). The inclusion criteria were: patients were willing to be part of the study and needed fixed orthodontic treatment in both arches. The exclusion criteria were: any systemic diseases, syndromes, allergies, metal restorations, piercing, and previous orthodontic treatment.

Data Collection

The fixed appliance consisted of bonded 0.018 inch slot preadjusted Roth prescription stainless steel brackets (Zhejiang Protect Medical Equipment Co., Zhejiang, China) on all teeth except the molars, stainless steel orthodontic bands (Zhejiang Protect Medical Equipment Co., Zhejiang, China), NiTi wires (Nitinol; Ormco Corp., Orange, CA, USA), and stainless steel arch wires (Remantium; Dentaurum GmbH & Co., Ispringen, Germany).

The blood samples (6 mL) were collected from the antecubital fossa of either hand, and centrifuged at 3000 rpm for 10 minutes, to produce 2 mL of serum. The serum was divided into two, one portion for nickel, and the other for chromium analysis. The blood was collected from each individual at different periods during the study: before appliance insertion (Baseline), then two months (T_2), and six months (T_6) after appliance insertion. The samples were kept in a freezer until they were analyzed.

The urine samples were collected in the morning from the same subjects using sterile nickel-free 50-mL plastic containers. Patients were asked to collect the urine after discarding the first flush. They were also instructed to avoid contaminating the vessels by wiping or rinsing the surfaces. The specimens were stored in a low-temperature freezer until they were analyzed.

The measurement of nickel and chromium levels (ppb - part per billion) in serum and urine were performed using Inductively Couple Plasma Atomic Emission (ICP-AES/Mass Spectroscopy).

Data Analysis

The results were analyzed using the Statistical Package for Social Science (SPSS) for Windows, version 11 (SPSS Inc., Chicago, IL, USA). Statistical analysis was performed using repeated ANOVA, Bonferroni post hoc test, and paired t-test. P-value <0.05 was considered to be statistically significant.

Ethical Aspects

The objectives of the study were explained to the participants and written informed consent was obtained before starting the study. The research was approved by the ethics committee of the Medical Faculty, Hasanuddin University.

Results

Average serum nickel and chromium levels during the experimental period are shown in Table 1. There was no statistically significant difference in serum and urinary nickel levels between observation times. However, there was a statistically significant difference in serum ($p<0.001$) and urinary chromium ($p=0.007$) levels between observation times (Table 1).

Table 1. Nickel and chromium ion levels in serum and urine at different treatment time.

Body Fluids	Ion	Ion Level (ppb) Baseline Mean ± SD	2 Months Mean ± SD	6 Months Mean ± SD	**p-value**
Serum (n=20)	Nickel	6.420± 0.727	6.610± 0.682	6.855± 0.751	0.154
	Chromium	5.305± 0.440	4.810± 0.341	5.505± 0.328	<0.001*
Urine (n=20)	Nickel	5.320± 0.742	5.585± 0.938	5.610± 0.994	0.581
	Chromium	5.370± 0.337	5.065± 0.482	5.520± 0.356	0.007*

ppb = part per billion; *Repeated Anova test: p<0.05; significant.

The Bonferroni post-hoc test results are shown in Table 2. There are statistically significant differences between serum chromium levels at baseline and 2-month observation (p=0.001), as well as between 2-month- and 6-month observations (p<0.001). A significant difference was also found in between 2-month- and 6-month observations in the urine (p=0.005). In the serum, T0 was higher than T2 (decrease), but T2 was lower than T6 (increase). In the urine, T2 was also lower than T6 (increase).

Table 2. Multi-comparison test of chromium ion levels by orthodontic treatment period.

Chromium Level	**Group Compared**	**Mean Difference**	**95% CI**	**p-value**
Serum	T0 vs. T2	0.495	0.189 – 0.801	0.001*
	T0 vs. T6	-0.200	-0.553 – 0.153	0.461
	T2 vs. T6	-0.695	-0.990 – 0.400	<0.001*
Urine	T0 vs. T2	0.305	-0.058 – 0.668	0.119
	T0 vs. T6	-0.150	-0.391 – 0.091	0.354
	T2 vs. T6	-0.455	-0.781 – 0.129	0.005*

*Bonferroni post hoc test; p<0.05: significant; T0 = mean of the level before insertion of the appliance; T2 = mean of the level at the end of the second month; T6 = mean of the level at the end of the sixth month.

The difference between serum and urinary nickel and chromium levels are shown in Table 3. There were statistically significant differences between serum and urinary nickel level at all observation times (p<0.05).

Table 3. Mean differences between serum and urinary nickel ion levels at different period of orthodontic treatment time.

Body Fluid	**Baseline** Mean ± SD	**p-value**	**2 Months** Mean ± SD	**p-value**	**6 Months** Mean ± SD	**p-value**
Serum	6.420 ± 0.727		6.610 ± 0.682		6.855 ± 0.751	
Urine	5.320 ± 0.742	0.001*	5.585 ± 0.938	0.002*	5.610 ± 0.994	<0.001*
Difference	1.100 ± 1.209		1.025 ± 1.273		1.245 ± 1.141	
(95% CI)	(0.534–1.665)		(0.429–1.620)		(0.710–1.779)	

[a]Normality test, Shapiro-Wilk test: p>0.05; data distribution normal; *Paired sample t-test: p<0.05; significant.

Table 4 shows that urinary chromium levels at all observation times were higher than those in serum, however, the difference was only statistically significant for the 2-month observation (p=0.010). Unlike the chromium values, changes in nickel values were not statistically significant either in serum and urine. Serum nickel levels were higher than those in urine at all observation times, and the differences were statistically significant.

Table 4. Mean differences between serum and urinary chromium ion levels at different period of orthodontic treatment times.

Body Fluid	Baseline		2 Months		6 Months	
	Mean ± SD	p-value	Mean ± SD	p-value	Mean ± SD	p-value
Serum	5.305 ± 0.440		4.810 ± 0.341		5.505 ± 0.328	
Urine	5.370 ± 0.337	0.604	5.065 ± 0.482	0.010*	5.520 ± 0.356	0.813
Difference	-0.065±0.551		-0.255±0.396		-0.015±0.279	
(95% CI)	(-0.323–0.193)		(-0.440-0.069)		(-0.145-0.115)	

[a]Normality test, Shapiro-Wilk test: p>0.05; data distribution normal; *Paired sample t-test: p<0.05; significant.

Discussion

The majority of previous studies regarding the metal ion concentration on patients having fixed orthodontic treatment used saliva rather than serum and urine. Although saliva has a relationship with serum, the content of metal ion levels might not be the same. Fixed orthodontic appliances, which contain variable amounts of nickel and chromium, can release these metals into the saliva. Nonetheless, it is not clearly identified how much released nickel and chromium are absorbed by the organism. However, previous studies have not explored the amount of nickel and chromium leached into saliva over an extended period of time. In this study, we attempted to evaluate and compare nickel and chromium levels in the serum and urine during 6 months observation.

Several researchers examined the levels of nickel and chromium in the saliva of patients having fixed orthodontic treatment [12,13]. They showed an increase in nickel and chromium ions immediately after the appliance insertion, but the difference was not significant. We consider that the increased levels were most likely due to the newly leached metal ions being present in the saliva before they were absorbed by the body. In human serum, nickel is bound to albumin, alpha-2 macroglobulin, and ultrafiltrable ligands (eg, histidine). Urinary excretion is the major route for the elimination of absorbed nickel [20].

Previous authors have observed that the urinary nickel concentrations in males and females were not different [10]. Moreover, this study used a time-series design so that we could observe the alteration of Ni and Cr ion concentrations over time in the same subjects.

The current study result (Table1) showed that there was an increase in the mean of serum nickel level from 6.420 ppb (baseline) to 6.610 ppb (2-month observation) and then to 6.855 ppb (6-month observation). These increases were not statistically significant and were likely due to the presence of dissolved nickel ions from fixed orthodontic appliances being absorbed through the gastrointestinal tract into the blood. However, the numbers were low. This result does not agree with the previous findings [8]. The results indicate that, although nickel level in the serum was significant initially in the samples when compared to the controls, there was a gradual decrease of serum nickel level when the appliance was present for a longer duration. However, our findings agreed with those described by some authors who showed that there was no statistically significant difference in mean of nickel ion concentration overtime between pre-appliance insertion and the end of sixth month's period [15]. However, they did find a statistically significant difference in mean of nickel ion concentration between pre-insertion and the end of a year period.

Average urinary nickel level increased from 5.320 ppb (baseline) to 5.585 ppb (2-month observation) and then to 5.610 ppb (6-month observation); however, the increases were not statistically significant (Table 1). One interesting finding was that when nickel levels in the serum rose, so did nickel levels in the urine. We consider that there is a balance between nickel concentration in serum and in urine. It has been previously shown that urinary nickel level increased significantly 2 months after the placement of orthodontic appliances [11]. A retrospective cohort study developed to evaluate systemic nickel in patients undergoing orthodontic therapy for a minimum period of one year concluded that orthodontic therapy for longer durations with stainless-steel arch wires might slightly, but significantly, elevate urinary nickel levels [10].

Some of our findings were inconsistent with previous findings, might possibly be due to different study methodology. Our study was a longitudinal study, while the previous studies were retrospective cohort or cross-sectional studies. In addition, the variation in results could be due to one or more of following reasons: there may have been differences in fixed appliance types, in the accuracy of measuring devices utilized, in sampling methods and analysis of data collected, and the studies were performed on different races.

Occupational exposure to chromium generally occurs through inhalation and dermal contact, whereas the general population is exposed most often by ingestion through chromium content in soil, food, and water [17]. It is not easy to identify how much released nickel is absorbed by the organism [7,11,15]. Nickel ions can be discharged into the saliva via several mechanisms including galvanic corrosion of orthodontic appliances. Urinary excretion is the major route for the elimination of absorbed nickel [2]. Approximately, 90% of blood nickel is quickly excreted through urine with an elimination half-time of 28 hours. Therefore, renal elimination rate might reflect well the systemic nickel level as well as its acute changes [2,11].

In this study, we attempted to compare serum nickel and chromium levels with urinary nickel and chromium levels. It was found that serum nickel levels were higher compared with those in urine at all observation times (Table 3). It might be caused by food sources rich in nickel absorbed by the digestive system. One shortcoming of our study was that we did not investigate the dietary intake of nickel and chromium of the participants. However, urinary chromium levels were higher than those in serum (Table 4). The mechanisms of absorption and transport of the chromium ion are still uncertain. Little is known of the fate of the chromium ions that are taken orally or in the digestive tract. Chromium ions from the orthodontic appliance, like chromium supplementation of the diet, resulting in an increase in urinary chromium loss, and most absorbed chromium is rapidly excreted. That is probably the reason why the urinary chromium level in the second month declined, then rose again at the time of the sixth-month observation.

Another interesting finding of this study was the similarity of the patterns of the serum and urinary chromium levels; when the serum chromium levels decreased/increased, so did the urinary chromium levels (Table 2). Our finding for serum chromium values was in accordance with the study by the previous researchers [8,21] who also did not find significant differences in serum chromium levels over 4 –6 month periods of time.

In this study, the maximum value of serum and urinary nickels were 6.855 ppb and 5.610 ppb, respectively. The values were far below the average dietary intake. Oral daily intake of nickel by food is estimated to be between 300 and 600 μg [23], while the average daily intake of chromium is between 50 and 200 μg. Although the orthodontic appliances did not have any effect on the general level of nickel and chromium concentrations both in serum and urine, it cannot be excluded that minor amounts of nickel and chromium dissolved from appliances could be important in cases of hypersensitivity to those metal ion. The release of nickel from orthodontic appliance may be correlated with clinical abnormalities, such as gingivitis, gingival hyperplasia, lip desquamation, and burning sensation in the mouth. In addition, a low concentration of nickel ion has a potential effect on biological cells, such as DNA alterations mainly through base damage and DNA strand scission [19,22,24].

The limitations of the study were difficulty in controlling eating habits of the participants. Secondly, the nickel and chromium contents of food were vary, this might be able to confound their levels in the body fluid.

Conclusion

Orthodontic treatment could increase both serum- and urinary nickel levels after two- and six months, although the differences were not statistically significant. The chromium levels in both serum and urine initially declined and then rose again. Serum nickel levels were higher than those in urine, however urinary chromium levels were higher than those in serum. By understanding the nickel and chromium ions release to the body, alternative materials without metal ion release could be developed to reduce or overcome the negative effect of the fixed metal orthodontic appliance.

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