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# Metal Ion Released from Old Prostheses May Affect Oral Lesions: A Pilot Study

Hye-Min Ju[1,2], Ji-Su Kim[2], Yong-Woo Ahn[2], Soo-Min Ok[2], Sung-Hee Jeong[2]

[1]Department of Oral Medicine, Dental Research Institute, Pusan National University Dental Hospital, Yangsan, Korea
[2]Department of Oral Medicine, Dental Research Institute, Pusan National University School of Dentistry, Yangsan, Korea

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**Correspondence to:**
Sung-Hee Jeong
Department of Oral Medicine, Dental Research Institute, Pusan National University School of Dentistry, 49 Busandaehak-ro, Mulgeum-eup, Yangsan 50612, Korea
Tel: +82-55-360-5242
Fax: +82-55-360-5238
E-mail: drcookie@pusan.ac.kr

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**Purpose:** To investigate the correlation between the amount of salivary metal ions released from fixed prostheses and the period of restoration insertion, and to evaluate the correlation between the type and amount of metal ions in saliva and oral lesions (OL).

**Methods:** Based on the oldest prosthesis, we divided patients into two groups: more than 5 years (n=19) and less than 5 years (n=10). Patients were also divided into two groups by another criteria: the one with the presence (n=15), and the one with absence (n=14) of OL, and the amounts of metal ions were examined. Metal ions—gold (Au), copper, cobalt (Co), chromium (Cr), nickel, zinc, aluminum, palladium (Pd), tin, and platinum (Pt)—were measured using laser ablation microprobe inductively coupled plasma mass spectrometry.

**Results:** Significantly higher quantities of Co, Pt, and Pd ions were released in patients with fixed prosthesis of more than 5 years ($p<0.05$). Measurement of the average amount of salivary metal ions was performed on patients with and without OL - Significantly higher amounts of Cr, Pd and Au ions were released in patients with OL ($p<0.05$).

**Conclusions:** Old prostheses (≥5 years) released metal ions, and among them were Co, Pt and Pd ions more than others. Patients with OL showed significantly higher levels of ion release, especially Cr, Pd and Au. There was a positive correlation between the amount of a certain kind of released metal ions, especially Pd, and the development of OL. Salivary Pd ion released from old prostheses could affect the pathogenesis of OL; therefore, long-term follow-up is important.

**Key Words:** Metals; Old prosthesis; Oral lesion; Saliva

## INTRODUCTION

Artificial teeth made of various dental materials,including ceramics, acrylates, composites and metal alloys, are used to replace natural teeth when recovery of oral health and aesthetic improvement are needed.[1)] The oral cavity is exposed to several environments in which metal alloys corrode over time. Factors which are inherent in the metals used include microstructure, chemical composition, construction technique, and galvanizing properties because of interactions among existing metallic restorations. Factors that may initiate corrosion include secreted saliva, the reflux of organic acids, temperature fluctuations because of food and drink intake, and the accumulation of plaque. In particular, saliva is affected by diet and medication intake. Studies of metal ion detection in saliva have reported that initially, fixed prostheses mainly release metal ions; however, the amount of released metal ions is not consistent and declines over time. However, these results were derived from short-term studies (duration of less than 6 months).[1,2)] There is a lack of studies on the long-term effects of fixed prostheses.

Previous studies on human exposure to metal ions and inflammation primarily depended upon patch testing on skin or serum tests. Previous studies have shown that particles released from orthopedic implants, used in surgeries such as hip arthroplasty, cause chronic inflammation when they are locally accumulated, leading to osteolysis in the long run. Furthermore, there have been a number of studies on dental material patch testing targeted for patients with oral lesions, the result of which showed that dental material caused allergic reactions.[3-8] Nevertheless, there is a lack of research on the correlation between salivary metal ions and oral lesions in patients with fixed prostheses in contact with mucosa.

Therefore in this study, we investigated correlation between the amount of traditional dental material metal ions—gold (Au), copper, cobalt (Co), chromium (Cr), nickel (Ni), zinc (Zn), aluminum (Al), palladium (Pd), tin (Sn) and platinum (Pt)—released from fixed prostheses in saliva and the period of restoration insertion, and studied the correlation between the amount of released metal ions in saliva and oral mucosal lesions.

## MATERIALS AND METHODS

### 1. Patients

This study included 29 patients who visited the Department of Oral Medicine, Pusan University Dental Hospital from March to September in 2013. Out of 29 patients, 28 were female with an average age of 52.96±16.16. Only one male patient, 43 years old, was included.

For patients with more than one restoration in the mouth, the duration of prosthesis restoration was examined based on the oldest prosthesis. Oral prostheses were divided into two groups: more than 5 years and less than 5 years.

Table 1 shows the distribution of subjects by diagnosis. Patients were classified as having oral lichen planus (OLP), burning mouth syndrome (BMS), recurrent aphthous stomatitis (RAS) or miscellaneous (MISC). The miscellaneous group included xerostomia, temporomandibular disorder, paresthesia and hyperkeratosis. OLP group was diagnosed with the modified WHO clinical criteria proposed by van der Meij and van der Waal in 2003.[9] OLP has a lace-like white lesion (reticular pattern), erosive, atrophic, bullous, and plaque- type lesions bilaterally on the oral mucosa. The inclusion criteria for BMS group were a burning sensation in the mouth, consistent for more than 3 months. The patients have normal salivary flow rate (unstimulated whole saliva >0.1 mL/min and stimulated whole saliva >0.5-0.7 mL/min), and normal results in laboratory tests of complete blood counts, liver and renal function, thyroid function (T3, T4, and thyroid stimulating hormone), folate, serum iron, ferritin, vitamin B12, and zinc levels. And also, candidiasis was not found in oral swab and culture. Lesions such as OLP and RAS were classified as oral lesions that show oral mucosal defects; lesions except OLP and RAS were classified as non-oral lesions. The study protocol was approved by the Institutional Review Board of Pusan National University Dental Hospital (IRB no. PNUDH-2013-029).

### 2. Collection of Saliva Sample

Unstimulated whole saliva was collected from patients with or without oral lesions at their first visit. A polypropylene tube was used for 3 minutes to collect saliva. The saliva samples were kept in a −80°C freezer until analysis.

### 3. Analysis of Metal Ion

Metal ions—gold (Au), copper (Cu), cobalt (Co), chromium (Cr), nickel (Ni), zinc (Zn), aluminum (Al), palladium (Pd), tin (Sn), platinum (Pt)—were measured using a laser ablation microprobe inductively coupled plasma mass spectrometer (LAM-ICP-MS, PerkinElmer, Optima 3000, USA).

To evaluate the levels of metal ions in saliva, samples were diluted directly with nitric acid, as described by Kim et al.[10] Operating conditions for instruments recommended by the manufacturer were met.

**Table 1.** Distribution of subjects

| | Patients (n=29) |
|---|---|
| OLP | 11 (37.93) |
| BMS | 3 (10.35) |
| RAS | 1 (3.45) |
| MISC | 14 (48.28) |

Values are presented as number (%).
OLP, oral lichen planus; BMS, burning mouth syndrome; RAS, recurrent aphthous stomatitis; MISC, miscellaneous.

### 4. Statistical Analysis

The Mann-Whitney U test was used to determine significant difference in mean values of salivary metal ions, depending on the difference in period of restoration insertion and the presence/absence of oral lesions. p-values less than 0.05 were considered statistically significant. Statistical analyses were performed using SPSS Statistics ver. 20.0 (IBM Co., Armonk, NY, USA).

## RESULTS

### 1. Proportion by Restoration Type

The highest proportion of prostheses in patients consisted of gold crowns, inlay and onlay (46.7%), followed by porcelain-fused metal crowns (28.9%). Oral restorations included more than one kind. The relative proportion(s) among restorations for each diagnosis was the same with that among the restorations for overall diagnoses (Table 2).

### 2. Amounts of Metal Ions in Saliva Depending on the Period of Restoration Insertion

Among 29 patients, when they were divided according to the period of insertion of the oldest restorations, the control group (<5 years) size was n=10 and study group (≥5 years) size was n=19. In both groups, Zn, Al and Cu were observed in terms of amounts of metal ions in saliva, with first (Zn) being the highest. There were no significant differences in metal ion contents except for Co, Pt and Pd. These three ions showed significantly higher levels in the study group (≥5 years) (Mann-Whitney U-test). Co was 0.72±0.38 ppb in the control group, 1.61±2.77 ppb in the study group and was 2 times higher in the study group (p=0.048). Pt was 0.04±0.02 ppb in the control group, 0.25±0.46 ppb in the study group, showing the difference of more than 6 times in the study group (p=0.011). Pd was 0.27±0.36 ppb in the control group, 0.74±0.94 ppb in the study group and was 2 times higher in the study group (p=0.004) (Table 3).

### 3. Difference of the Amounts of Salivary Metal Ions With or Without Oral Lesions

Among the 29 total patients, 14 were in the OL (oral lesion=OLP+RAS) and 15 were in the non-OL group. In most cases, no statistically significant difference was observed between the two groups, but statistically significant difference in the amount of metal ions of Cr, Pt, Pd and Au was observed. Significantly higher amounts of Cr, Pd and Au ions were released in patients with oral lesions, with the average amount of 29.68±5.46 ppb (p=0.039), 1.06±1.17 ppb (p=0.008) and 56.51±20.18 ppb (p=0.012) respectively. By contrast, significantly higher amounts of Pt ions were released in patients without oral lesions (ppb) (Table 4).

## DISCUSSION

Over time, metal interacts with various elements in various environments and becomes corroded. Released ions and particles accumulate in the human body. In recent studies, orthopedic alloys were reported to increase the metal ion content of serum and urine in vitro and in vivo. In cases of total hip arthroplasty with metal-on-metal, it was reported

**Table 2.** Number of dental restorations in patients

| Restoration | OLP | BMS | RAS | MISC | Total |
|---|---|---|---|---|---|
| Amalgam filling | 2 | 0 | 0 | 3 | 5 |
| Gold crown, inlay, onlay | 9 | 3 | 1 | 8 | 21 |
| Metal crown, inlay | 1 | 0 | 0 | 0 | 1 |
| Porcelain fused metal crown | 4 | 3 | 1 | 5 | 13 |
| Resin filling | 1 | 0 | 0 | 1 | 2 |
| Implant | 1 | 0 | 0 | 2 | 3 |
| Total | 18 | 6 | 2 | 19 | 45 |

OLP, oral lichen planus; BMS, burning mouth syndrome; RAS, recurrent aphthous stomatitis; MISC, miscellaneous.

**Table 3.** Mean value of salivary metal ions evaluated when patients were classified with prosthesis placement period based on 5 years (ppb)

| | <5 y (n=10) | ≥5 y (n=19) | p-value |
|---|---|---|---|
| Cu | 52.94±48.25 | 52.18±32.73 | 0.714 |
| Cr | 24.32±7.10 | 29.12±9.12 | 0.169 |
| Ni | 38.39±35.11 | 28.37±30.41 | 0.680 |
| Zn | 284.75±225.95 | 658.67±1120.27 | 0.551 |
| Co | 0.72±0.38 | 1.61±2.77 | 0.048* |
| Al | 103.54±84.25 | 152.01±274.87 | 0.714 |
| Pt | 0.04±0.02 | 0.25±0.46 | 0.011* |
| Sn | 0.13±0.25 | 0.31±0.42 | 0.105 |
| Pd | 0.27±0.36 | 0.74±0.94 | 0.004* |
| Au | 22.31±37.88 | 42.74±67.25 | 0.233 |

Values are presented as mean±standard deviation.
Statistical significance test was done by Mann-Whitney U-test.
*p<0.05.

**Table 4.** Mean value of salivary metal ions with or without oral lesion (ppb)

| | OL (n=15) | Non-OL (n=14) | p-value |
|---|---|---|---|
| Cu | 51.44±30.76 | 53.07±42.54 | 0.822 |
| Cr | 29.68±5.46 | 26.11±10.05 | 0.039* |
| Ni | 34.55±29.15 | 30.16±34.11 | 0.281 |
| Zn | 859.55±1439.53 | 328.17±278.14 | 0.822 |
| Co | 1.07±0.43 | 1.45±2.88 | 0.111 |
| Al | 120.31±76.86 | 144.45±284.52 | 0.116 |
| Pt | 0.11±0.11 | 0.21±0.48 | 0.038* |
| Sn | 0.37±0.49 | 0.17±0.28 | 0.066 |
| Pd | 1.06±1.17 | 0.29±0.23 | 0.008* |
| Au | 56.51±20.18 | 22.98±12.07 | 0.012* |

OL, oral lesions.
Values are presented as mean±standard deviation.
Statistical significance test was done by Mann-Whitney U-test.
*p<0.05.

that metal ions accumulate at a high level of 0.1-100 ng/mL in serum.[4] Fixed dental prostheses for dental treatment are also often made of metal alloys with various alloy components. The oral cavity environment is particularly prone to corrosion due to saliva, microorganisms and pH variations. Studies on the metal ion release in artificial saliva in various pH and bacterial plaque conditions have been conducted in vitro. Furthermore, in in vivo studies, metal ions were present in the saliva of patients without metal restorations; however, studies have shown that the metal ion concentration in saliva was significantly higher in patients with metal dental prostheses.

However, most of these studies examined the prosthesis within 6 months. In previous studies, metal ions increased immediately after restoration of prostheses, and the amounts of ions decreased with time. Nevertheless, in clinical practice, oral lesions were often observed around prolonged prostheses of more than 5 years. Therefore, we investigated the relationship between metal ion release and oral lesions in patients with prolonged placement of prostheses.[11,12] In this study, we focused on the restoration period of prostheses; therefore, we divided the subjects into two groups according to the restoration period - less than 5 years, and more than 5 years. In previous studies, primarily Ni, Cr, and Co showed increased levels in saliva after prosthetic restoration. Because Co-Cr is a traditional dental cast alloy, much research has been done on these metal ions.[13-16] The concentration of these ions in saliva was higher in Co, Pt, and Pd in the study group, although there was no statistically significant difference in the concentration of Cu, Cr, Ni, Zn or Al (Table 3). Table 4 shows the correlation between the amount of metal ions in the oral lesion group (OL) and the non-OL group (Non-OL). In the OL group, the amounts of released Cr, Pd, and Au were greater.

When we investigate the results in Tables 3 and 4 synthetically, we note that more amounts of Pd were released in the study group than in control group, and Pd was also found in statistically significantly higher amounts in the saliva of the subjects in the group with OL.

Pd is an alloy commonly used in fixed dental prostheses such as crowns and bridges.

Therefore, the oral mucosa of many people is exposed to Pd; however, it has not been proven to cause allergic contact dermatitis unlike Ni, and has not been studied as often as Co-Cr. Pd allergy is not well documented. However, recently, the response of Th2-mediated cytokines due to Pd exposure has attracted attention. Recent studies have reported that exposure to Pd stimulates various cytokines in rat serum and human skin tests.[17-19] In this study, most of the diagnoses in patients with OL (78.57%) was OLP. OLP is a T-cell mediated disease; further studies on the correlation between Pd and OLP are needed.

In this study, there are several limitations: first, the period of restoration insertion was only based on the patient's report; second, the proportion of the alloy composition of the prostheses in the patients was varied and uncontrollable. There was also a lack of baseline metal ions for patients without prostheses. Nevertheless, this is one of the rare studies to investigate the distribution of metal ions in saliva with long-term prostheses (over 5 years) as well as the distribution of metal ions depending on the presence or absence of OL. Further studies should be conducted regarding the proportion of metal ions in prostheses, investigating the exact insertion period of the prostheses with larger sample sizes, as well as measuring secreted cytokines.

In conclusion, in this pilot study, we examined the distribution of metal ions in the saliva of patients with fixed prostheses. Old prosthesis (≥5 years) continues to release more metal ions, especially Co, Pt, and Pd. Plus, patients with oral lesions showed significantly higher levels of ion release, especially Cr, Pd and Au. Therefore, there was a positive correlation between the amount of released metal

ions, especially Pd, and the development of oral lesions. Salivary Pd ion released from old prostheses may affect the pathogenesis of oral lesions; therefore, long-term follow-up is important.

## CONFLICT OF INTEREST

No potential conflicts of interest relevant to this article arereported.

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