Original article

eISSN 2799-8010
J Yeungnam Med Sci 2023;40(4):373-380
https://doi.org/10.12701/jyms.2022.00955

JYMS
JOURNAL OF YEUNGNAM MEDICAL SCIENCE

Association between dental amalgam restoration and urine mercury concentrations among young women: a cross-sectional study

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Background: The association between dental amalgam fillings and urine mercury concentrations was investigated in this study to assess the health risks associated with dental amalgams.
Methods: This cross-sectional study included 99 women in their 20s who visited the dental clinic in Daegu, Korea. The 99 participants were composed of 68 subjects who had dental amalgam fillings (exposure group) and 31 subjects who did not have dental amalgam fillings (nonexposure group). Oral examinations were conducted by a single dental hygienist, sociodemographic features were investigated as confounding variables, and urine mercury concentrations were measured using an automatic mercury analyzer.
Results: The mean ± standard deviation of the urine mercury concentrations of the exposure and nonexposure groups were 1.50 ± 1.78 µg/g creatinine and 0.53 ± 0.63 µg/g creatinine, respectively. The exposure group showed significantly higher levels than the nonexposure group ($p<0.01$). The urine mercury concentration significantly increased with an increase in the number of teeth filled with amalgam, cavity surfaces involved, and number of defective amalgam fillings, and according to the latest exposure time ($p<0.001$). In the multiple regression analysis of amalgam-related factors and urine mercury concentrations after correction for confounding factors, the urine mercury concentration in the group with six or more amalgam-filled teeth, 11 or more cavity surfaces, and two or more defective amalgams was significantly higher than that in the nonexposure group ($p<0.001$).
Conclusion: According to this study, exposure to dental amalgams was confirmed to significantly affect urine mercury concentrations.

Keywords: Dental amalgam; Mercury; Urine; Women

Introduction

Mercury is classified into elemental, inorganic, and organic types [1]. Elemental and inorganic mercury are used as materials for thermometers, sphygmomanometers, pesticides, preservatives, and dental amalgams, for example, with human exposure being primarily through occupational, environmental, or dental amalgams. However, eating contaminated fish is the main route of ex-

Received: December 26, 2022 • **Revised:** January 12, 2023 • **Accepted:** January 25, 2023 • **Published online:** March 21, 2023
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posure to organic mercury [2]. Chronic exposure to mercury mainly causes damage to the nervous system, which leads to neuropsychiatric symptoms, such as tremors, anxiety, forgetfulness, insomnia, nervous irritability, general fatigue, cognitive impairment, and movement disorders. It can also cause renal dysfunction, muscle atrophy, muscle spasms, and polyneuritis [3]. Dental amalgams, used as restorative materials in dental treatment, are alloys of metallic mercury (50%) and have been widely used since the 19th century because they are easy to work with, are economical, and have excellent strength [4]. However, patients receiving dental amalgam fillings may be exposed to mercury vapors generated during treatment, mercury ions generated from amalgam corrosion, or amalgam particulates generated during mastication [5]. Thus, the harmfulness of amalgams remains controversial. Some studies reported that there were no significant differences between the quantity of mercury detected in people with amalgam fillings and that in people without amalgam fillings [6,7]. The Korean Society for Conservation of Dentistry confirmed the stability of dental amalgam as a restorative material [8]. However, Nicolae et al. [9] reported that the urine mercury concentrations of women with 26 to 30 dental amalgam-filled surfaces were higher than those of the group who had no amalgam fillings. Al-Saleh and Al-Sedairi [10] reported that urine and hair mercury concentrations in children with dental amalgam fillings were significantly higher than those in the control group without amalgam fillings. Woods et al. [11] reported a high correlation between urine mercury concentrations and the dental amalgam-filled area as well as the elapsed time after filling.

In Korea, Kim and Song [12] reported that the presence of dental amalgam restorations in the mouth increased mercury levels in urine and saliva due to accumulation in the body, and Baek et al. [13] reported that urine mercury concentrations tended to increase as the number of amalgam-filled teeth increased in elementary school students. Jung et al. [14] reported that the number of amalgam-filled teeth had a significant effect on urine mercury concentrations in children. Considering the harmfulness of amalgams, some countries, such as Japan, Norway, and Sweden, have completely regulated their use [15], and the U.S. Food and Drug Administration recommends limiting its use in children and pregnant women [16]. However, in Korea, there are no recommendations for restricting the use of amalgams in dental treatment.

To accurately evaluate the effects of dental amalgams on the human body, mercury exposure must be evaluated prior to their use. Previous studies on the effect of dental amalgams on mercury concentrations in the body mainly involved children who are sensitive to mercury [14,17-21]. However, it may be difficult to determine the degree of chronic mercury exposure in children due to unstable measurements of dental amalgam fillings because children from 6 to 12 years are in the teeth exchange period. In addition, there are limitations in examining the effect of amalgam exposure on mercury in the body because the cooperation of children with oral examinations is low, and the opinions of their parents are highly likely to be involved in the investigation of confounding variables.

Mercury-exposed women of childbearing age may be at risk of stillbirth or giving birth to a baby with deformities, and children exposed to mercury through the placenta in the uterus may develop neurodevelopmental disorders, such as motor and sensory disorders during growth [22]. Therefore, it is important to investigate the association between dental amalgam exposure and mercury concentrations in the body. In addition, young women are less likely to be exposed to amalgams, both environmentally and professionally. Therefore, this study was conducted on women in their 20s to evaluate future health risks of dental amalgams by determining the relationship between dental amalgam fillings and urine mercury concentrations.

Methods

Ethical statements: This study was approved by the Institutional Review Board (IRB) of Yeungnam University Hospital (IRB No: PCR-10-136) and written informed consent was obtained from the subject.

1. Study protocol and participants

From December 2011 to December 2012, female patients in their 20s from a dental clinic located in Daegu, a metropolitan city in Korea, were selected as the study population. The objectives and methods of this study were explained to 254 subjects, and written informed consent was obtained from 130 of them. Participants with systemic diseases such as mental illness, kidney disease, hypertension, diabetes, and cognitive dysfunction; long-term drug users; those working in mercury-related workplaces; those who withdrew consent; and those with missing data were excluded. Thus, 31 participants were excluded from the study. Among the 99 included participants, 68 women with dental amalgam fillings were selected as the 'exposure group,' while 31 women who had no dental amalgam fillings were selected as the 'nonexposure group.'

2. Oral examination and interview about amalgam restoration history

A single dentist performed the oral examination and recorded information regarding the dental treatment history after an interview with the participants. For example, the amount of amalgam filling was measured by examining the number of amalgam-filled teeth and the number of amalgam-filled surfaces (mesial, distal, buccal, lingual or palatal, and occlusal surfaces) of the teeth. Defective amalgam restorations, such as restorations with corrosion, cracks on the surface of the amalgam, or secondary caries and microcracks, were examined. The date of amalgam restoration was determined through interviews with the participants or medical records.

3. Urine mercury concentrations

Approximately 15 μL of spot urine was collected in a polypropylene conical tube with no risk of heavy metal contamination and stored frozen at –20°C or colder until analysis. Urine mercury concentrations were measured by the combustion-gold amalgamation method using a direct mercury analyzer (DMA-80; Milestone, Milan, Italy). For urine concentration correction, urine creatinine was measured with an Automatic Chemistry Analyzer (ADVIA 1650; Siemens, Tarrytown, NY, USA) using colorimetric analysis.

4. Confounding variables

The following sociodemographic features were recorded through administration of a questionnaire and interviews: age, education level, income level, smoking and drinking status, amount of shellfish intake, and frequency of shark meat intake.

5. Statistical analysis

Statistical analyses were performed using IBM SPSS ver. 21.0 (IBM Corp., Armonk, NY, USA). The significance level was set at 0.05. After testing the data for normality, parametric (*t*-test, analysis of variance) and nonparametric (Mann-Whitney, Kruskal-Wallis) analyses were performed, and the Bonferroni method was used for *post hoc* testing. To adjust for the effects of confounding variables, such as age, income level, drinking status, and shellfish and shark meat intake, the corrected mercury concentration was calculated using the nonstandardized residual of the regression model, and the association between dental amalgams and urine mercury concentrations was evaluated through regression analysis.

Results

1. Sociodemographic characteristics of the study population

The majority of participants were 20 to 24 years (58 patients [58.6%]), university educated (50 [50.5%]), nonsmokers (72 [72.7%]), and nondrinkers (70 [70.7%]). There were no differences in the sociodemographic characteristics between the exposure groups (Table 1).

2. Urine mercury concentrations according to sociodemographic characteristics

The means of the urine mercury concentrations were 1.19 ± 1.57 μg/g creatinine in all subjects, 1.50 ± 1.78 μg/g creatinine in the exposure group, and 0.53 ± 0.63 μg/g creatinine in the nonexposure group. Urine mercury concentrations were significantly higher in the exposure group than in the nonexposure group ($p < 0.01$). There was a statistically significant difference in urine mercury concentrations according to income level ($p < 0.01$). Those with a higher income had lower urine mercury concentrations ($p < 0.01$). Except for income level, there were no differences in urine mercury concentrations according to sociodemographic characteristics (Table 2).

3. Urine mercury concentrations according to amalgam exposure characteristics

There were significant differences in urine mercury concentrations ($p < 0.01$) according to some amalgam restoration characteristics, such as the number of amalgam-filled teeth, cavity surfaces, defective amalgam restoration, and treatment time of the recent amalgam restoration (Table 3). Those with more amalgam-filled teeth, greater cavity surfaces, or defective amalgam restorations showed significantly higher urine mercury concentrations ($p < 0.01$). Moreover, urine mercury concentrations were significantly higher in the group receiving amalgam treatments at least 1 year prior than in the control group not receiving amalgam treatments ($p < 0.01$).

4. Association between amalgam-related variables and urine mercury concentrations

Multiple linear regression analysis was performed to evaluate the association between the amalgam-related variables and urine mercury concentrations. Adjustments for age, shellfish intake, income level, and drinking status in the second model, and age, shellfish intake, income level, drinking status, and shark meat intake frequency in the third model were made.

In all models, six or more amalgam-filled teeth, 11 or more amalgam-filled cavity surfaces, and two or more defective amalgam restorations were significantly associated with urine mercury concentrations ($p < 0.01$). In the third model, compared with the corresponding values in the nonexposure group, the urine mercury concentration was 2.337 μg/g creatinine higher in the group with six or more amalgam-filled teeth, 2.607 μg/g creatinine higher in the group with 11 or more amalgam-filled cavity surfaces, and 3.568 μg/g creatinine higher in the group with two or more defective amalgams ($p < 0.001$). However, there was no significant differ-

Table 1. Sociodemographic characteristics

Characteristic	Exposure group	Nonexposure group	Total	*p*-value
No. of patients	68	31	99	
Age (yr)				
20–24	39 (57.4)	19 (61.3)	58 (58.6)	0.827
25–29	29 (42.6)	12 (38.7)	41 (41.4)	
Education				
Graduate high school	11 (16.2)	3 (9.7)	14 (14.1)	0.552
During university	32 (47.1)	18 (58.1)	50 (50.5)	
Graduate university	25 (36.8)	10 (32.3)	35 (35.4)	
Income (million KRW/mo)				
2–2.99	14 (20.6)	3 (9.7)	17 (17.2)	< 0.001
3–3.99	32 (47.1)	5 (16.1)	37 (37.4)	
≥ 4	22 (32.4)	23 (74.2)	45 (45.5)	
Smoking				
Current/ex-smoker	18 (26.5)	9 (29.0)	27 (27.3)	0.811
None	50 (73.5)	22 (71.0)	72 (72.7)	
Drinking				
Yes	22 (32.4)	7 (22.6)	29 (29.3)	0.353
No	46 (67.6)	24 (77.4)	70 (70.7)	
Shellfish intake[a)]				
≤ 21	17 (25.0)	8 (25.8)	25 (25.3)	0.963
22–57	18 (26.5)	7 (22.6)	25 (25.3)	
58–93	16 (23.5)	9 (29.0)	25 (25.3)	
≥ 94	17 (25.0)	7 (22.6)	24 (24.2)	
Shark meat intake				
Do not eat at all	27 (39.7)	15 (48.4)	42 (42.4)	0.334
Eat very rarely[b)]	13 (19.1)	8 (25.8)	21 (21.2)	
Eat usually	28 (41.2)	8 (25.8)	36 (36.4)	

Values are presented as number only or number (%).
KRW, Korean won.
[a)]The survey subjects were divided into quartiles according to the shellfish intake measured using the food intake frequency table. [b)]Eat it but just taste it.

ence in mercury concentrations according to amalgam-filling time (Table 4).

Discussion

As concerns regarding mercury toxicity intensify, hesitance to use dental amalgam restorations is also gradually increasing in many countries. However, dental amalgams are still used because of their ease of manipulation, excellent strength, and low cost. According to the 2012 National Oral Health Survey in Korea, amalgam was used as a filling material for permanent teeth in 27.1% of patients [23]. Amalgams filling the oral cavity may leak metallic mercury in the form of vapor; thus, their adverse effects remain controversial [24]. However, in this study, a significant association between dental amalgam restorations and urine mercury concentrations was observed among women in their 20s, after adjusting for some important confounding variables.

Mercury vapor in the human body is absorbed into the alveoli and distributed to each organ. Thus, mercury concentrations in the blood, hair, and urine are often measured to evaluate exposure levels. Blood mercury concentrations are effective indicators of recent exposure, but they have the disadvantages of difficult sample collection and a short half-life of 40 to 70 days. Thus, they are not an accurate indicator of repeated chronic exposure. Hair mercury concentrations have the advantage of easy sampling, and with cooperation from the patients, long-term exposure to mercury can be assessed if the length of hair is classified and analyzed according to the growth period. However, hair mercury concentrations can be easily affected by external pollutants, and approximately 90% of the total amount of hair mercury is organic mercury, which currently has no established exposure limit [25]. Thus, in this study, urine mercury concentrations were used as an exposure index to determine the degree of mercury exposure in the human body. Urine mercury concentrations were measured using DMA-80, which operates by collecting heat-vaporized mercury on a porous surface coated with gold and analyzing at a wavelength of 253.7 nm by atomic absorption spectroscopy [26]. Inorganic mercury accumulates most in the kidneys via metabolic processes. Thus,

Table 2. Urine mercury concentrations (μg/g creatinine) according to sociodemographic characteristics

Characteristic	Urine mercury concentration (μg/g creatinine)					
	Exposure group		Nonexposure group		Total	
	Mean ± SD	*p*-value	Mean ± SD	*p*-value	Mean ± SD	*p*-value
Age (yr)						
20–24	1.40 ± 1.85	0.761	0.48 ± 0.53	0.570	1.09 ± 1.59	0.609
25–29	1.64 ± 1.71		0.62 ± 0.78		1.34 ± 1.56	
Education						
Graduate high school	1.98 ± 1.95	0.589	1.34 ± 1.41	0.273	1.84 ± 1.8	0.223
During university	1.22 ± 1.36		0.43 ± 0.50		0.94 ± 1.18	
Graduate university	1.68 ± 2.18		0.47 ± 0.40		1.32 ± 1.91	
Income (million KRW/mo)						
2–2.99	1.85 ± 1.73[a,b]	0.013	0.37 ± 0.20	0.753	1.55 ± 1.65[a,b]	< 0.001
3–3.99	1.84 ± 2.09[b]		0.78 ± 0.84		1.70 ± 1.99[b]	
≥ 4	0.82 ± 1.04[a]		0.50 ± 0.62		0.66 ± 0.86[a]	
Smoking						
Current/ex-smoker	2.53 ± 2.68	0.043	0.75 ± 0.71	0.174	1.94 ± 2.36	0.062
None	1.18 ± 1.26		0.45 ± 0.61		0.95 ± 1.15	
Drinking						
Yes	1.93 ± 1.78	0.112	1.04 ± 1.14	0.299	1.70 ± 1.66	0.020
No	1.32 ± 1.77		0.38 ± 0.28		1.00 ± 1.51	
Shellfish intake[a)]						
≤ 21	0.87 ± 0.56	0.186	0.64 ± 0.75	0.929	0.80 ± 0.62	0.819
22–57	1.23 ± 1.47		0.77 ± 1.00		1.10 ± 1.35	
58–93	1.48 ± 1.04		0.37 ± 0.31		1.06 ± 0.99	
≥ 94	2.51 ± 2.89		0.39 ± 0.21		1.86 ± 2.59	
Shark meat intake						
Do not eat at all	1.41 ± 1.52	0.995	0.57 ± 0.72	0.890	1.11 ± 1.35	0.867
Eat very rarely[b)]	1.14 ± 1.03		0.54 ± 0.74		0.91 ± 0.96	
Eat usually	1.78 ± 2.27		0.46 ± 0.32		1.47 ± 2.06	
Total	1.50 ± 1.78		0.53 ± 0.63		1.19 ± 1.57	< 0.001

SD, standard deviation.
[a)]The survey subjects were divided into quartiles according to the shellfish intake measured using the food intake frequency table. [b)]Eat it but just taste it.
[a,b]Bonferroni *post hoc* test: (a < b).

Table 3. Urine mercury concentrations (μg/g creatinine) according to amalgam exposure characteristics

Characteristic	n (%)	mean ± SD	*p*-value
No. of amalgam-filled teeth			
0[a)]	31 (32.0)	0.53 ± 0.63[a]	< 0.001
1–5	49 (50.5)	0.92 ± 0.88[b]	
≥ 6	17 (17.5)	3.19 ± 2.55[c]	
No. of amalgam-filled cavity surfaces			
0[a)]	31 (32.0)	0.53 ± 0.63[a]	< 0.001
1–5	37 (38.1)	0.71 ± 0.61[a]	
6–10	19 (19.6)	1.99 ± 1.60[b]	
≥ 11	10 (10.3)	3.52 ± 2.94[b]	
Treatment time of the recent amalgam filling (yr)			
0[a)]	31 (32.0)	0.53 ± 0.63[a]	< 0.001
< 1	7 (7.2)	1.28 ± 1.22[a,b]	
1–3	21 (21.6)	1.19 ± 1.45[b]	
≥ 3	38 (39.2)	1.72 ± 2.02[b]	
No. of defective amalgams			
0[a)]	31 (32.0)	0.53 ± 0.63[a]	< 0.001
0	35 (36.1)	0.77 ± 1.05[a]	
1	22 (22.7)	1.44 ± 0.88[b]	
≥ 2	9 (9.3)	4.49 ± 2.57[c]	
Total	97 (100)	1.19 ± 1.57	

SD, standard deviation.
[a)]Nonexposure group.
[a,b,c]Bonferroni *post hoc* test: (a < b < c).

Table 4. Regression analysis between amalgam-related variables and urine mercury concentrations

Variable	Model I		Model II		Model III	
	β[a)]	*p*-value	β[a)]	*p*-value	β[a)]	*p*-value
No. of amalgam-filled teeth[b)]						
1–5	0.385	0.192	0.238	0.449	0.087	0.773
≥6	2.654	<0.001	2.495	<0.001	2.337	<0.001
No. of amalgam-filled cavity surfaces[b)]						
1–5	0.974	0.573	0.063	0.744	0.032	0.92
6–10	1.455	<0.001	1.222	0.924	1.143	0.006
≥11	2.989	<0.001	2.807	<0.001	2.607	<0.001
Treatment time of the recent amalgam filling[b)]						
<1	0.743	0.244	0.359	0.582	0.242	0.711
1–3	0.658	0.128	0.144	0.747	0.068	0.878
≥3	1.183	0.002	0.875	0.021	0.709	0.067
No. of defective amalgams[b)]						
0	0.239	0.392	0.115	0.689	0.029	0.921
1	0.908	0.005	0.699	0.039	0.612	0.075
≥2	3.959	<0.001	3.710	<0.001	3.568	<0.001

Model I, crude model; model II, adjusted for age, shellfish intake, income level, and drinking status; model III, adjusted for age, shellfish intake, income level, drinking status, and shark meat intake frequency.
[a)]Standardized regression coefficient. [b)]Reference, nonexposure group.

urine mercury is the most accurate biomarker for long-term and chronic exposure [12]. Dental amalgams are an inorganic form of mercury that release mercury vapor, which can be inhaled [5]. However, since the amount of mercury excreted in urine varies according to the time of collection and water metabolism in the body, differences exist among individuals, and the daily excretion amount fluctuates greatly [27]. Thus, mercury concentrations were normalized to urine creatinine levels [28].

Dutton et al. [29] reported that the urine mercury concentrations of subjects with dental amalgam fillings were significantly higher than those of a control group without fillings. Al-Saleh and Al-Sedairi [10] reported that the urine mercury concentrations of women with amalgam fillings were significantly higher than those of women in the control group. In Korea, Jin et al. [21] reported that there was a significant difference in urinary mercury concentrations between children with amalgam-treated teeth (1.69 ± 2.85 μg/g creatinine) and children without amalgam-treated teeth (1.11 ± 1.42 μg/g creatinine). In the present study, the urine mercury concentration was 1.50 ± 1.78 μg/g creatinine in the exposure group and 0.53 ± 0.63 μg/g creatinine in the control group, which were significantly different ($p < 0.01$) and consistent with the results of previous studies. It might be observed that exposure to dental amalgam fillings affected the mercury concentration in the body.

Dunn et al. [19] reported that the number of dental amalgam fillings exhibited a dose-response relationship with urine mercury concentrations. Factor-Litvak et al. [30] and Nicolae et al. [9] reported a linear relationship between the number of dental amalgam surfaces and urine mercury concentrations. In the results of the present study, as the number of teeth and cavity surfaces filled with amalgam increased, the urine mercury concentration significantly increased ($p < 0.001$), which is consistent with the results of previous studies. Furthermore, even after adjusting for the effects of shellfish intake, income level, drinking status, and shark meat intake frequency, which may affect mercury exposure, the urine mercury concentration was 2.337 μg/g creatinine higher in the group with six or more amalgam-filled teeth and 2.607 μg/g creatinine higher in the group with 11 or more amalgam-filled cavity surfaces than in the group without dental amalgam fillings. The results of this study showed that urine mercury concentrations increased significantly as the number of amalgam-filled teeth and cavities increased ($p < 0.001$).

Levy et al. [17] reported that amalgams had a large effect in the multiple regression analysis of urinary mercury concentrations in children, and Jung et al. [14] reported that the urinary mercury concentration was 1.951 μg/g creatinine higher in children in the 7-to-9-year age group and 1.517 μg/g creatinine higher in children in the ≥11-year age group than in the group without amalgam-filled teeth, which is consistent with the results of our study. As the number of defective amalgams increased, urine mercury concentrations significantly increased. Dental amalgam, which has a heterogeneous multiphase structure, can easily corrode and is affected by its composition and mechanical properties [31]. Therefore, defective amalgams seem to have a lower risk of mercury particle leakage into the human body compared to fully reacted and sound normal amalgams, which is a novel finding of this study.

However, this study has several limitations. Since the study subjects were recruited from the same regions, it was not possible to fully represent the level of human mercury exposure due to amalgam fillings in young Korean women. In addition, to check the degree of mercury exposure in the body, it is necessary to collect and examine not only urine but also blood, hair, and other samples simultaneously. A detailed investigation of the type of filled amalgam is also required, as there is a difference in mercury exposure depending on the properties of the filled amalgam. Nevertheless, this study has the advantage of examining the intake frequency and amount of shellfish to adjust for the effect of dietary habits on urine mercury concentrations. In addition, there was a significant correlation between the quantitative level of dental amalgam exposure and urinary mercury concentrations by examining not only the number of teeth filled with amalgam but also the number of cavity surfaces and defective restorations.

As a result of this study, exposure to dental amalgams had a significant effect on mercury concentrations in the human body; therefore, caution should be exercised regarding amalgam use in certain populations, such as pregnant women, lactating women, and children. In addition, in the case of defective amalgam fillings, it is recommended that they be removed and replaced because their health risks have been confirmed in this study.

Notes

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

Funding

None.

Author contributions

Conceptualization, Data curation, Formal analysis: SBP, JS; Methodology: SBP, EKK, JS; Project administration: EYP; Visualization: EKK; Writing-original draft: EKK, EYP; Writing-review & editing: EKK, EYP.

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