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Association between Amalgam Tooth Fillings and Blood Mercury Levels in Children

Joon Sakong[1], Youn-Hee Choi[2,4]*, Sun-Young Chung[2], Hojang Kwon[3], Wilfried Karmaus[4], Anwar T. Merchant[4], Mina Ha[3], Yun-Chul Hong[5], Dongmug Kang[6], and Keun-Bae Song[2]

[1]*Department of Preventive Medicine and Public Health, College of Medicine, Yeungnam University, Daegu 705-717, Korea*
[2]*Department of Preventive Dentistry, School of Dentistry, Kyungpook National University, Daegu 700-412, Korea*
[3]*Department of Preventive Medicine and Public Health, College of Medicine, Dankook University, Choognam 330-714, Korea*
[4]*Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, SC 29208, USA*
[5]*Institute of Environmental Medicine, College of Medicine, Seoul National University, Seoul 110-799, Korea*
[6]*Department of Preventive and Occupational Medicine, Pusan National University, Yangsan 626-870, Korea*

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The notion that dental amalgam is a potential source of mercury exposure remains a controversial issue. However, there are few epidemiological analyses that have addressed whether this occurs in children. We aimed in our current study to identify the relationship between dental amalgam filling surfaces and the blood mercury levels in a cohort of 711 South Korean children aged between 8-9 years. Oral examinations were conducted to detect the number of amalgam filling surfaces on the teeth of these individuals. Blood samples were also taken from these children to assess the levels of mercury accumulation in the body. The amalgam filling surfaces were classified into four groups based on their number: 0 (n = 368), 1-5 (n = 219), 6-10 (n = 89), and 11+ (n = 35). The blood mercury levels in the children with more than 10 amalgam surfaces was 0.47 μg/L higher on average than those with no amalgam surfaces after adjusting for the frequency of fish or seafood consumption, age, and gender ($P < 0.05$). We found from our data that a higher number of dental amalgam fillings correlated with a higher blood mercury level in Korean children. Further studies are needed to investigate whether these elevated mercury levels exert neurotoxic or nephrotoxic effects.

Key words: amalgam, blood, child, mercury, South Korea

*Corresponding author: Youn-Hee Choi, Department of Preventive Dentistry, School of Dentistry, Kyungpook National University, Daegu 700-412, Korea. Tel: +82-53-660-6871, Fax: +82-53-423-2947, E-mail: cyh1001@knu.ac.kr

Introduction

Today the most common sources of exposure to mercury are to vaccines (MacIntyre, 2001; MacIntyre and Leask, 2003), dental amalgam fillings and fish consumption (Clarkson *et al.*, 2003). Especially, dental amalgam is known to be a potential source of exposure to inorganic mercury (Melchart *et al.*, 2008; Shenker *et al.*, 2008; Tsuji *et al.*, 2003), mostly in the form of mercury vapor, for the general population (Clarkson *et al.*, 2007; Dodes, 2001). Mercury in dental amalgam is released by chewing or toothbrushing as well as from restorative procedures (Bates, 2006). Absorbed vapor mercury in the body through the bloodstream gets transported to various tissues and organs, and inhaled mercury vapor is oxidized by catalase to Hg^{2+} as an ultimate mediator of mercury toxicity, which reacts with the tissue and may cause neurotoxic (Murata *et al.*, 2004) and nephrotoxic effects depending on the dose (Clarkson *et al.*, 2003); the remaining Hg^0 circulates and then crosses the placental and blood-brain barriers (Clarkson *et al.*, 2007).

Mercury concentration in blood is one of the measurements reflecting internal mercury amount in the body (Halbach *et al.*, 2008). There have been several studies that reported the association between amalgam exposure and total mercury concentrations in blood (Abraham *et al.*, 1984; Bergdahl *et al.*, 1998; Bjorkman *et al.*, 2007; Ganss *et al.*, 2000; Kingman *et al.*, 1998). Mercury concentration in blood can be affected by high levels of methylmercury derived from fish or seafood consumption and other intake sources though (Innis *et al.*, 2006; Kingman *et al.*, 1998).

There has been a controversy in a toxic effect of amalgam to the human body as a restorative material (Clarkson *et al.*, 2007; Scott *et al.*, 2004). However, it is important to note that results of studies of dental amalgam conducted among adults might not be generalizable to children who are more sensitive to it and also there are not many epidemiological evidences that dental amalgam is the cause of the systemic absorption of mercury in children.

The aim of this study was to investigate the relationship between the number of amalgam filling surfaces on teeth and the level of mercury in blood among children in South Korea after adjusting confounding factors related to increasing blood mercury concentration such as fish or seafood intake, gender, age and region where they had lived.

Materials and Methods

Study population

Children who were selected from seven elementary schools located in three metropolitan areas (Seoul, Daegu, and Busan) and one urban area (Cheonan) of South Korea participated in the Children's Health and Environmental Research (CHEER) study during 2007-2008. All of 8-9 year-old children in CHEER study (n = 711) included in this study. The study population and method of the CHEER study are described in detail elsewhere (Ha *et al.*, 2009). These areas were primarily chosen to represent major industrialized cities and urban regions. All their parents or guardians provided written consents, and the study protocols were reviewed and approved by the Institutional Review Board of the Dankook University College of Medicine and Ulsan University College of Medicine.

Oral examination

Oral examination was conducted to detect decayed, missing, and filled surfaces, to discern filling materials and to examine how many amalgam filling surfaces existed for deciduous and permanent teeth by two dentists trained for the examination protocol according to World Health Organization (WHO) guidelines ("World Health Organization. Oral Health Surveys; Basic Methods," 1997) using dental mirror and WHO probe under proper artificial lights. The number of amalgam filling surfaces on deciduous and permanent teeth were counted and they were classified into four groups: 'none', '1-5', '6-10', and '11 or more'.

Data collection

Blood samples were analyzed to measure the level of mercury accumulated in the body using cold vapor atomic absorption spectrophotometry (M-6000A, CETAC, USA) with a detection limit of 0.003 μg mercury per liter. To measure the total mercury levels in whole blood, 3-5 ml of the blood was drawn from each child using a syringe and then sealed in a heparin containing tube. For the determination of the total mercury, the blood sample was digested in nitric acids and then the red blood cell (RBC) component was used for the analysis. The reference sample was incorporated at the determinations of the total mercury concentration. The mean and standard deviation was 5.76 ± 0.31 μg/L and the coefficients of the variation (CV) for the blood mercury measurements were 5.32%, which satisfied as the CV standard.

Confounders

Main sources of methylmercury in the body were intake of fish and/or marine mammals. Methylmercury is demethylated to mercuric mercury (Hg^{2+}), which can influence the mercury concentration in the whole blood (Counter and Buchanan, 2004; Halbach *et al.*, 2008; Vahter *et al.*, 2000). Gender is also one of the controversial factors affecting the internal mercury burden related to amalgam restorations (Maserejian *et al.*, 2008; Woods *et al.*, 2007). For that reason, the adjustment of confounding factors such as fish intake, gender and age were conducted in statistical models.

Statistical analysis

Blood mercury levels depending on area were tested by one-way ANOVA and Tukey *post hoc* analysis. Multiple regression models were built to analyze the association between the number of surfaces with amalgam fillings and the concentration of mercury in blood with frequency of fish or seafood intake, gender and age as important confounders. An effect modification between amalgam surfaces and the frequency of fish consumption was also considered in multivariate analysis. Data analysis was performed using SAS 9.1.3 (SAS Institute, Inc., Cary, NC, USA).

Results

The percentage of boys and girls of all children (n = 711) were 51.5% and 48.5%, respectively (Data not shown). The average of the number of amalgam surfaces on deciduous teeth was 2.17 ± 3.39 (mean ± SD, the range; 0 to 17). Daegu showed the highest number in amalgam surfaces (2.91 ± 3.72, the range; 0 to 16). The average of the number of amalgam surfaces on permanent teeth was 0.27 ± 1.06 (the range; 0 to 8). As the same results of deciduous teeth, Daegu showed the highest number (0.38 ± 1.25, the range; 0 to 8). However, in Cheonan, there is no child having an amalgam filling on permanent teeth (Table 1).

The concentration of mercury in blood by area

The average of blood mercury concentration of total subjects was 2.15 ± 1.14 μg/L and blood mercury levels significantly differed by area ($P < 0.05$). Children in Busan had the highest mercury concentration in blood (2.39 ± 0.96 μg/L) whereas children in Cheonan exhibited the lower concentration (1.85 ± 0.80 μg/L) than the average level of blood mercury concentration (Fig. 1).

Table 1. Distribution of surfaces with amalgam fillings by area (Mean ± SD)

Area	Seoul (n = 172)	Cheonan (n = 111)	Daegu (n = 296)	Busan (n = 132)	Total (n = 711)
Deciduous teeth	1.83 ± 1.13	1.24 ± 2.64	2.91 ± 3.72	1.76 ± 3.19	2.17 ± 3.39
Permanent teeth	0.20 ± 0.96	0.00 ± 0.00	0.38 ± 125	0.33 ± 1.12	0.27 ± 1.06

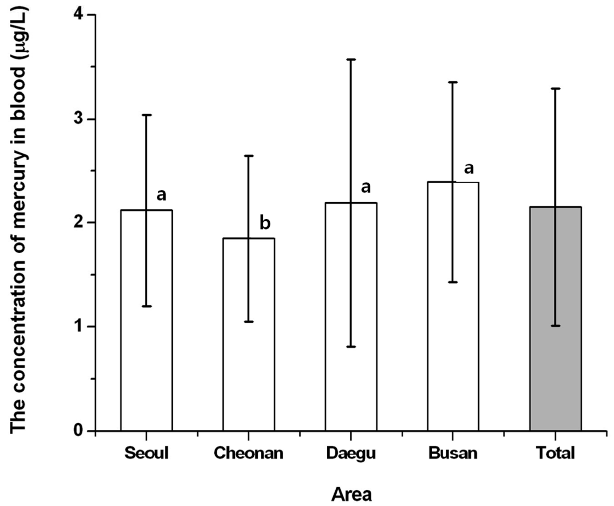

Fig. 1. The concentration of blood mercury by area in 8-9 year-old Korean children (Mean ± SD). Blood mercury levels significantly differed by area ($P < 0.05$). Distinct lower case letters denote statistical difference in blood mercury concentration (Tukey *Post-hoc* test).

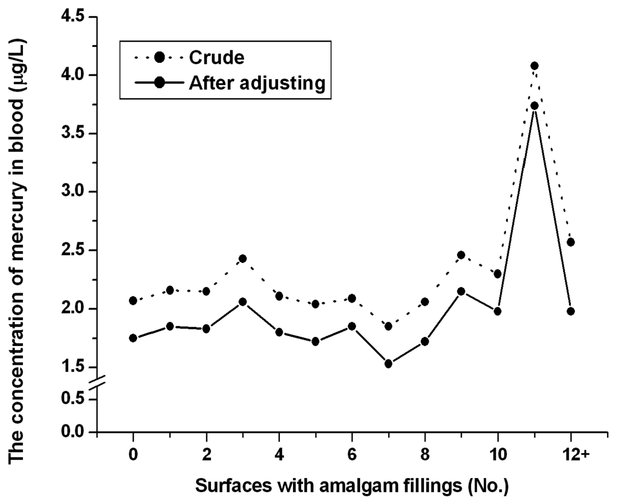

Fig. 2. The association between tooth surfaces with amalgam filling and the concentration of blood mercury in 8-9 year-old Korean children: Crude and after adjusting for age, gender, and seafood and fish-intake (Mean).

The association between surfaces with amalgam filling and the concentration of mercury in blood

In Fig. 2, the straight line representing crude blood mercury concentrations appeared to be extremely similar just below the dotted line representing blood mercury concentrations after adjusting confounding factors such as fish or seafood-intake, gender and age. The changes of the mercury concentration in blood depending on surfaces with amalgam fillings were not distinct until it came to get 8-9 amalgamated filling materials. Both of dotted and straight lines displayed the peak at the

Table 2. Associations between the numbers of amalgam filling surfaces and the concentration of mercury in blood (μg/L)

		Model I		Model II		Model III	
		Beta coefficients	*P-value*	Beta coefficients	*P-value*	Beta coefficients	*P-value*
Surfaces with amalgam filling (No.)							
	0	reference		reference		reference	
	1-5	0.11	0.27	0.10	0.30	0.11	0.26
	6-10	0.06	0.64	0.09	0.52	0.07	0.58
	11+	**0.71**	**0.00**	**0.48**	**0.02**	**0.47**	**0.02**
Frequency of fish or seafood intake (No./Week)							
	None			reference		reference	
	Less than 2			0.35	0.28	0.33	0.30
	2-3			0.52	0.11	0.50	0.12
	4-5			**0.79**	**0.04**	**0.77**	**0.04**
	everyday			**1.43**	**0.02**	**1.39**	**0.03**
Gender							
	Boy					reference	
	Girl					-0.07	0.45
Age						0.09	0.29

*Statistically significant values shown in bold ($P < 0.05$)

surfaces with 11 amalgam fillings. There seems to be no linear trend.

In Table 2, regression model I represented the crude association between the numbers of amalgam filling surfaces and the blood mercury concentrations. Blood mercury levels without adjusting confounding factors were 0.71 μg/L higher in the group with 11 or more surfaces with amalgam filling than that with no amalgam filling surfaces as a reference ($P < 0.01$, model I).

The frequency of fish or seafood intake was included in regression model II to adjust confounding factors, and gender and age as well as fish intake were included in regression model III. Fish or seafood intake was measured by counting the intake-frequency per week: none, less than 2 times a week, 2-3 times a week, 4-5 times a week, and every day. Daegu showed a higher frequency than other areas in all categories except every day (Data not shown).

Children eating fish or seafood everyday had 1.43 μg/L higher level of mercury than the reference group ($P < 0.05$, model II). At the end of modifying a crude regression model with fish-intake, gender and age together, blood mercury levels in group with 11 or more surfaces with amalgam filling were 0.47 μg/L higher than the reference group ($P < 0.05$, model III) (Table 2). An interaction between the number of amalgam and fish consumption is not significant in the multiple regression model (Data not shown).

Discussion

There have been controversies regarding the harmful effects of dental amalgam as a restorative material to human body. ATSDR (1999) ("Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological profile for mercury" 1999) concluded that estimations of the amount of mercury released from dental amalgams range from 3 to 17 μg/day, and exposure to these very small amounts of mercury does not pose a health risk. In this study, seven hundred and eleven Korean children aged 8-9 years were examined to investigate the number of dental amalgam surfaces in their oral cavity and mercury concentration in blood. The average of total mercury levels in blood was 2.15 μg/L. The average mercury concentration of children having 11 or more surfaces restored with amalgam was 0.47 μg/L higher compared to those with no amalgam surfaces after adjusting the confounding factors such as the frequency of fish or seafood intake, gender, and age ($P < 0.05$).

These results are consistent with previous studies (Bjorkman *et al.*, 2007; Ganss *et al.*, 2000; Kingman *et al.*, 1998) of mercury levels in blood according to surfaces with amalgam filling. A cross-sectional study (Kingman *et al.*, 1998) of 1127 US military population who were 41 to 78 years old and almost non-African-American found that the average concentration of total blood mercury was 2.6 μg/L. The mercury level and amalgam exposure were weakly related. Another study (Bjorkman *et al.*, 2007), which involved 30 autopsies of individuals having on average 13.2 dental amalgam surfaces (range 0 to 50 surfaces), 41 to 91 years of age showed that the median concentration of the total mercury and inorganic mercury in blood were 3.3 μg/L and 1.0 μg/L, respectively. There was a significant correlation between inorganic mercury in blood and the number of surfaces filled with dental amalgam at the time of death. The other study (Ganss *et al.*, 2000) has also reported the similar findings to our result that more dental amalgam exposure higher mercury level in human body.

In this study, the highest point of the mercury concentration was shown in children with 11 amalgam surfaces and after that, the line fairly dropped as surfaces with amalgam fillings increased. That's because the numbers of each group of children who had 12 or more amalgam surfaces were too small to provide good precision. However, children with 11 or more surfaces with amalgam filling had a 0.47 μg/L higher blood mercury concentration, which accounted for about 20% of average mercury concentration in blood (2.15 μg/L). It is chance that inclusion of data on fish consumption seems to have appreciably altered the co-efficient for children in the 11+ amalgam category, but not in other categories. In other words, high levels of fish eating are a proxy for better nutrition and therefore less dental caries. However, no interaction was found between the number of amalgam and fish consumption.

Strengths of this study are the large sample size of participating Korean children and the clinical assessment of amalgam filling tooth surfaces by trained dentists using the current examination guideline. There are few epidemiologic studies on concentration levels of mercury in blood targeting children. However, this cross-sectional study has some limitations. Regarding amalgam exposure and blood mercury measurement, several studies consistently used inorganic mercury concentration detected in excreted urine (DeRouen *et al.*, 2006; Maserejian *et al.*, 2008; Olstad *et al.*, 1987), which reflected the mercury burden level from the kidney (Clarkson *et al.*, 2007; Counter and Buchanan, 2004), as biomarker of mercury (Dye *et al.*, 2005; Factor-Litvak *et al.*, 2003; Maserejian *et al.*, 2008; Woods *et al.*, 2007). But in this study, total mercury concentrations in blood which mainly reflected the accumulated organic mercury level were measured rather than urinary mercury. The second limitation of this study as a cross-sectional one is that we do not have the information about how long dental amalgam masses have stayed in children's mouth. This can affect the exact exposure dose of released mercury from mouth. Finally, other factors which could affect the blood mercury concentration such as gum-chewing habits being related to elevated mercury levels (Minoia *et al.*, 2008) and the body weight or size being associated with mercury elimination in children (Maserejian *et al.*, 2008) were not considered in this study.

In conclusion, the exposure from many dental amalgam surfaces such as more than ten may lead to higher blood mercury level in children after accounting for the frequency of fish or seafood intake, gender, and age. This finding might be a guideline to choose a restorative material for dental decay in children. A further study is needed to investigate whether the increased mercury concentration in children's body leads to toxicity such as neurotoxic and nephrotoxic effects and the related mechanism.

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Conflict of interest

None of the authors have reported any conflict of interest.

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