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Lead, mercury, and cadmium in blood and their relation to diet among Swedish adults

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ABSTRACT

The aim of the present study was to examine the body burden of lead (Pb), mercury (Hg), and cadmium (Cd) in blood among Swedish adults and the association between blood levels, diet and other lifestyle factors.

The study was based on a subgroup (n = 273) of the national survey Riksmaten 2010–2011 (4-day food records and questionnaire). Lead, Hg, and Cd were measured in whole blood, and Cd additionally in urine, by mass or fluorescence spectrometry methods.

The median values (5–95th percentiles) of the metals in blood were as follows; Pb: 13.4 (5.8–28.6) μg/L, Hg: 1.13 (0.31–3.45) μg/L, and Cd: 0.19 (0.09–1.08) μg/L. All three metals increased with increasing age. Lead levels in blood were positively associated with intakes of game and alcohol, Hg was related to fish intake, and blood Cd related to smoking and low iron stores and to a low meat intake.

Body burdens of the studied metals were generally below health based reference values, but several individuals had blood Pb levels above the reference point for possible nephrotoxic and developmental neurotoxic effects. As health effects cannot be excluded, individuals with high Pb exposure should aim at decreasing their body burden, both from food and from other exposure routes.

1. Introduction

Toxic metals such as lead (Pb), mercury (Hg) and cadmium (Cd) are natural components of our earth crust. However, the environment has been enriched by industrial processes, and man-made sources such as mining, industries, motor vehicle exhaust, and batteries contribute to the environmental levels and to human exposure. Even though the contribution from the man-made sources has decreased substantially, the environmental contamination will remain for many decades. Pb and Hg, and probably also Cd have detrimental effects on the central nervous system in the developing infant (Bellinger, 2008; Mendola et al., 2002; Kippler et al., 2012). Even if neurotoxicity is the most sensitive endpoint, Pb may also affect blood pressure, kidney function, cause mutagenesis and have reproductive effects (Nordberg et al., 2007). Humans are exposed to Pb by a number of contributing food sources, but also by drinking water and air, whereas in case of Hg there is one major source, namely fish (Florea and Busselberg, 2006; Martorell et al., 2011). The toxic effects of Cd are mainly affecting the kidneys and skeleton. Long-term exposure can cause renal tubular dysfunction. In addition, Cd exposure may lead to osteoporosis, and the metal has been classified as a human carcinogen (Nordberg et al., 2007; Satarug and Moore, 2004). Diet is considered the main source of Cd intake among non-smokers (Skerfving et al., 1999), and especially food cultured in Cd-rich soil constitutes a major source for Cd (Satarug and Moore, 2004).

In Sweden, the body burdens of Pb and Hg are decreasing with time whereas this is not evident for Cd levels (Barregard et al., 2010; Wennberg et al., 2006), for Cd levels perhaps with the exception for smoking men. Thus, the dietary Cd exposure in Sweden seems to be unchanged (Wennberg et al., 2006) and in a market basket study from 2010, similar Cd exposures from food were reported in studies from 1987, 1999 and 2010 (NFA, 2012a). This fact needs further investigation, especially since the toxic effects on kidney and bone may be observed at lower Cd concentrations than previously believed (Akesson et al., 2005; Ferraro et al., 2010; Engstrom et al., 2011). At low urinary (U-) Cd levels, associations

Abbreviations: Pb, lead; Hg, mercury; Cd, cadmium; OEMC, Occupational and Environmental Medicine Center; BMI, body mass index; B, blood; U, urine; CTQ, Centre de Toxicologie du Quebec; SD, standard deviation; SE, standard error.

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between U-Cd and proteinuria may reflect renal physiology rather than toxicity of Cd (Chaumont et al., 2012; Akerstrom et al., 2013), but this problem does not occur for effects found on bone.

Due to the irreversible health effects of Pb, Hg, and Cd, primary prevention is essential. It is therefore necessary to examine the exposure and body burden of these metals in the general population using biomarkers, and to obtain knowledge about the major sources of the metals. The aim of the present study was to examine the biomarkers of Pb, Hg, and Cd among Swedish adults. The dietary associations, based on a 4-day food record and a food frequency questionnaire, as well as associations with other lifestyle factors for the metal concentrations in blood were also investigated. Measured levels of these metals were subsequently compared to internationally agreed reference health values.

2. Material and methods

2.1. Study design and population

The study was based on a subgroup of Riksmaten 2010–2011, a Swedish national survey investigating dietary habits among adults (18–80 years) conducted between May 2010 and July 2011 (Amcoff et al., 2012). The subgroup consisted of participants who in addition to dietary registration and questionnaire also donated blood and urine samples. The sampling was performed at Occupational and Environmental Medicine Centers (OEMCs). Therefore Sweden was divided into seven regions according to affiliation to Swedens seven OEMCs (Fig. 1). Each region included the region capital (Linköping, Lund, Stockholm, Umeå, Uppsala, Gothenburg, Örebro) and two additional counties that were randomly selected. Data were collected at four occasions; May/June 2010, August/September 2010, January/February 2011, and April/May 2011. Within each region, an equal number of individuals were asked to participate independently of population size (12 individuals per county and occasion). Of the 1008 randomly selected individuals, 300 (30%) chose to participate in the blood and urine sampling. Blood metal concentrations were measured in 297 participants. Of these, 22 individuals lacked food records and/or questionnaire data and were excluded. Moreover, since the investigated metals are excreted via urine and feces, two individuals with known kidney disease were omitted. Thus, 273 participants with blood analyses were included in the present study. Urine levels of Cd were measured in 289 individuals. Since urinary flow can affect Cd concentrations, we corrected assessed urinary cadmium concentrations for creatinine levels. Also, we excluded individuals with creatinine concentrations $\leqslant 1$ mmol/L ($n = 3$) since very dilute urine samples are considered not to provide good estimates of the urinary excretion of biomarkers, even after adjustment (Aitio et al., 2007; Soharan et al., 2008). After further exclusion of those lacking food records or questionnaire and the two individuals with kidney disease, 262 individuals were included in the statistical analyses with U-Cd levels. The sample selection was performed by Statistics Sweden (SCB). The study was approved by the regional ethical committee in Uppsala. All participants gave oral informed consent before entering the study.

2.2. Assessment of diet and lifestyle

In the national dietary survey Riksmaten 2010–2011, a representative sample of 5000 individuals between 18–80 years and living in Sweden were invited to participate (Amcoff et al., 2012). The data collection took place between May 2010 and July 2011. The participants, all together 1797 women and men, reported everything they ate and drank during four consecutive days. The reporting was done in a web-based food diary. To cover all days of the week, starting day was randomly selected (Tuesday, Wednesday, Saturday or Sunday). A questionnaire with about 50 questions was additionally used to collect data about less frequently consumed food items (e.g. consumption frequency of different classes of fishes and meat), education, smoking, and breast-feeding. Education was divided into elementary school, high-school, and higher education. Smoking status was classified according to never smoker, former smoker, occasional smoker, and daily smoker. Self-reported weight and height were assessed and body mass index (BMI) was calculated (weight [kg] divided by height [m] squared). Associations between metal concentrations and the following food groups were tested: dairy products, eggs, poultry, vegetables, fruits, potatoes, cereals, fish, meat, sausage, offal, alcohol, and discretionary food (defined as sweets, snacks, ice-cream, pastries, jam, and soft drinks).

2.3. Sampling of blood and urine

Non-fasting blood and single spot urine were sampled at the OEMC in each region or by district health care centers. Blood was drawn from an antecubital vein. Plasma for the ferritin analyses was separated by centrifugation before storage. The samples were stored at −20 °C until analysis.

2.4. Chemical analyses

The concentrations of Cd in urine (U-Cd) corrected for molybdenum oxide interference and Cd and Pb in whole blood (B-Pb) were determined by inductively coupled plasma mass spectrometry (ICP-MS; Thermo X7, Thermo Elemental, Winsford, UK) (Barany et al., 1997). The limits of detection (LOD) for U-Cd, B-Cd and B-Pb were 0.02, 0.04 and 0.11 μg/L, respectively. Mercury in whole blood (B-Hg) was determined in acid-digested samples by cold vapor atomic fluorescence spectrophotometry (Sandborgh-Englund et al., 1998). The detection limit was 0.09 μg/L. To ensure the accuracy of the analytical methods and results, quality control (QC) samples were analysed along with the collected samples (Table 1). All analysed samples were prepared in duplicate and the method imprecisions (calculated as the coefficients of variation in measurements of duplicate preparations) were 6.3%, 4.0%, 1.6%, and 8.2%, for U-Cd, B-Cd, B-Pb and B-Hg, respectively. Plasma ferritin concentration was assessed by chemiluminescent microparticle immunoassay (ARCHITECT®, Abbott, US). Creatinine was measured in urine by an enzymatic method as previously described (Mazzachi et al., 2000).

2.5. Statistical analyses

The statistical analyses were carried out by STATA version 12 (StataCorp LP, US). Variables are presented as mean ± SD or median (percentiles 5–95th). Non-normal variables were logarithmically transformed and if not attaining normality, non-parametric tests were used. The relationships between metal concentrations and explanatory variables were examined by stepwise forward regression (significance level: $p < 0.05$). Comparisons between groups were performed by ANOVA or Kruskal–Wallis test and adjusted for potential confounders by ANCOVA or residual method. Adjusted means were calculated by linear model. Correlations were investigated by Pearson correlation and, for non-normal variables, Spearmans rank correlation. To avoid bias caused by outliers, the analyses were also performed after excluding outliers (3rd quartile + 1.5 * interquartile range). Limits and number of outliers were as follows; B-Pb: 32.33 μg/L ($n = 6$), B-Hg: 3.98 μg/L ($n = 11$), B-Cd: 0.58 μg/L ($n = 23$), U-Cd: 0.57 μg/g creatinine ($n = 17$). $P < 0.05$ was considered statistically significant.

3. Results

3.1. Population characteristics

Population characteristics and metal concentrations in whole blood and urine by gender are presented in Table 2. None of the participants had B-Pb and B-Cd levels below the detection limit (<0.11 and <0.04 μg/L, respectively), four individuals had B-Hg $\leqslant$ 0.09 μg/L, and eight individuals had U-Cd $\leqslant$ 0.02 μg/L. These results were included even if measured concentrations were below the detection limit. The median values (5–95th percentiles) of the metals in blood among all participants were as follows; B-Pb: 13 (5.8–29) μg/L, B-Hg: 1.1 (0.31–3.5) μg/L, and B-Cd: 0.19 (0.09–1.1) μg/L. The median (5th–95th percentiles) of U-Cd was 0.16 (0.04–0.63) μg/g creatinine. The distributions of the metal concentrations are shown in Fig. 2. Among fertile women (18–45 years, $n = 64$), blood concentrations were as follows; B-Pb: 9.8 (4.7–18) μg/L, B-Hg: 0.70 (0.12–2.5) μg/L, and B-Cd: 0.19 (0.08–0.94) μg/L. Urinary Cd concentrations among fertile women ($n = 60$) were 0.11 (0.04–0.34) μg/g creatinine.

3.2. Blood concentrations of lead

B-Pb levels were positively associated with age (mean% increase per year [standard error, SE]: 1.0 [0.2]), male gender (mean% difference [SE]: 22.5 [6.4]), and smoking (mean% change from non-smoker to daily smoker [SE]: 22.3 [10.7]), but not with education, BMI, reported energy intake or plasma ferritin in multivariable analysis. There were no statistically significant differences in B-Pb concentrations between Swedish regions (i.e. areas of Linköping, Lund, Stockholm, Umeå, Uppsala, Gothenburg, Örebro; see map, Fig 1).

In stepwise regression analysis, B-Pb was associated with intakes of alcohol and potatoes (mean% changes per g/d [SE]: 0.04 [0.01] and 0.08 [0.03], respectively), but not vegetables, fruits, cereals, fish, meat, sausage, offal, or discretionary food. Alcohol but not potatoes remained related after adjustments for age,