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Body burden of cadmium and its related factors: A large-scale survey in China

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HIGHLIGHTS

- We performed a Cd exposure survey that involved more than 6000 Chinese subjects.
- The body burden of Cd in most of subjects of non-polluted Shanghai is relatively safe.
- The UCd levels were much higher in the subjects from polluted areas than from Shanghai.
- The UCd levels in the population from Guizhou substantially exceeded the safety limit.
- Age and region were significant determinants of UCd.

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ABSTRACT

A survey of more than 6000 participants from four distinct non-polluted and polluted regions in China was conducted to evaluate the body burden of cadmium (Cd) on the Chinese populations using urinary Cd (UCd) as a biomarker. The findings revealed that the UCd level was 1.24 μg/g creatinine (μg/g cr) for the sample population from non-polluted Shanghai, and the UCd levels exceeded 5 μg/g cr, which is the health-based exposure limit set by the World Health Organization (WHO), in 1.1% of people. The mean UCd levels in moderately polluted (Hubei and Liaoning) and highly polluted areas (Guizhou) were 4.69 μg/g cr, 3.62 μg/g cr and 6.08 μg/g cr, respectively, and these levels were 2.9 to 4.9 times the levels observed in Shanghai. Notably, the UCd levels exceeded the recently updated human biomonitoring II values (i.e., intervention or "action level") in 44.8%–87.9% of people from these areas compared to only 5.1%–21.4% of people in Shanghai. The corresponding prevalence of elevated UCd levels (>WHO threshold, 5 μg/g cr) was also significantly higher (30.7% to 63.8% vs. 1.1%), which indicates that elevated Cd-induced health risks to residents in these areas. Age and region were significant determinants for UCd levels in a population, whereas gender did not significantly influence UCd.

1. Introduction

Cadmium (Cd) is a non-essential element in the human body and is one of the most toxic heavy metals along with lead (Pb), mercury (Hg), and chromium (Cr). An early clinical indicator of Cd-induced toxic effects is renal tubular damage, which is characterized by the increased excretion of low molecular weight proteins in the urine (Järup and Åkesson, 2009; Volpe et al., 2009). Cd and its compounds are considered human carcinogens (i.e., lung cancer) (IARC, 1993), and Cd exposure is associated with breast cancer development in female subjects (Järup and Åkesson, 2009). The mortality risk significantly increases at a urinary Cd (UCd) level exceeding 3 μg/g cr after adjustment for age (Nakagawa et al., 2006). Moreover, exposure to high levels of Cd causes bone damage, which was first recognized in a severe bone disorder known as Itai-itai disease. Itai-itai disease was mainly observed in elderly Japanese women, who were heavily exposed to Cd via the consumption of contaminated rice (Järup and Åkesson, 2009; Suwazono et al., 2010; WHO, 1992).

Environmental Cd, which is released from various industrial processes and human activities (e.g., smelting, mining, waste disposal, fertilizer and pesticide application, and vehicle exhaust), is extensively distributed in China (Bi et al., 2006; Ke and Qiao, 2013; Li et al., 2009). Approximately 133 million square meters of soil in China were contaminated with Cd several decades ago (Chen, 1976). The soil, water, air, and various foods in China are reportedly currently polluted with Cd (Ke and Qiao, 2013). The Xiangjiang river, which has been one of the most polluted rivers in China since 1978, has been increasingly polluted with heavy metals (e.g., Pb, Cd, and Cr) since the 1990s (Ke and Qiao, 2013). The Beijiang (Shaoguan, Guangdong Province), Liuyang (Hunan Province), and Longjiang rivers (Guangxi Province) are also reportedly

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polluted with Cd (Ke and Qiao, 2013). Moreover, several studies have revealed that rice, vegetables, fish, and pig kidneys are contaminated with Cd, which increases health risks to local residents (Ding, 2008; Cao et al., 2010; Yang et al., 2011). The Cd exposure in the general population should be evaluated, and the modifying factors (e.g., age, sex, and lifestyle) should be identified to provide scientific evidence for risk assessment, evaluate the reference levels for health effects, set exposure limits, and protect people from the adverse effects of Cd exposure.

Previous studies have reported that the UCd levels in occupationally exposed subjects are significantly higher than those in the control population (Chen et al., 2005; Lei, 2005). Given the increase of environmental Cd pollution in China, Cd exposure in the non-occupationally exposed population has attracted the interest of researchers. According to a study of a Chinese population (N = 207) from Shanghai, 93.4% of the population did not exhibit adverse health effects due to dietary Cd exposure; vegetables, rice, and tobacco were the main sources of Cd exposure in non-occupational populations (He et al., 2013). The mean value of UCd was 1.88 μg/L, and the UCd level positively correlated with age. In another Chinese population (N = 693) from a non-polluted area in Guangdong Province, the UCd levels were 0.84 μg/g cr in males and 1.23 μg/g cr in females (Ding, 2008). UCd levels of 2.2 μg/g cr in males and 1.9 μg/g cr in females were observed in a population from another non-polluted area, whereas the UCd levels reached 10 μg/g cr in males and 13 μg/g cr in females in a polluted area (Hong, 2003). The UCd levels of populations from different non-polluted areas ranged from 0.02 μg/g cr to 2.6 μg/g cr, whereas the UCd levels ranged from 1.4 μg/g cr to 13.5 μg/g cr in populations from polluted areas (Hong et al., 2004; Sun et al., 2013; Zhao et al., 2009). Itai-itai disease, which mainly results from Cd exposure, is known as one of the Four Big Pollution Diseases of Japan. Because Cd pollution is more severe in several areas in China than in Japan, environmental epidemiological studies of Cd pollution in China deserve immediate attention. However, information on Cd exposure in the general Chinese population in relation to area, age and gender is lacking. Moreover, existing studies have only examined small samples of populations from a single area (94 to 783 participants) (Sun et al., 2013; Li et al., 2001; Zhao et al., 2009; Zhu et al., 2002).

Thus, this study consisted of a large sample survey that involved 6232 participants from one non-polluted and three polluted areas in China to investigate Cd exposure in the general Chinese population. Our study objectives are as follows: (1) evaluate the body burden of Cd in the Chinese population in non-polluted areas, (2) assess the increase in chronic Cd exposure in the population in polluted areas based on the UCd levels, and (3) preliminarily investigate region, gender, and age differences in the body burden of Cd based on a large sample survey of the Chinese population.

2. Materials and methods

2.1. Area and study population

We included population groups from four municipalities and provinces in China: Shanghai (Eastern China), Hubei (Central China), Liaoning (northeast China), and Guizhou (Southwest China). These areas included one control area without known industrial Cd pollution (Shanghai), two slightly/moderately exposed areas (Hubei and Liaoning), and one relatively highly exposed area (Guizhou). Hubei had less industrial Cd contamination than Guizhou, with soil Cd concentrations ranging from 0.8 mg/kg to 1.47 mg/kg (Gao et al., 2001; Wen et al., 2007). The Cd pollution in Liaoning was mainly due to industrial wastewater irrigation that has been in place since the 1950s, with soil Cd concentrations ranging from 0.24 mg/kg to 2.6 mg/kg (Liu and Guo, 2003; Wang et al., 2006a; Zhang, 2001). Extensive smelting and mining contributed to serious Cd pollution in Guizhou. Although a low level of soil Cd contamination was also observed in some unpolluted regions in these provinces, the average values of soil Cd concentrations in some polluted areas were as high as 5.7 mg/kg (Ke and Qiao, 2013; Shang et al., 2010).

Our study population included inhabitants of different Cd non-polluted and polluted areas. Approximately 12,000 subjects were randomly selected from the cities, towns, and/or villages in these municipalities and provinces. The subjects were asked to fill out a brief questionnaire. A total of 8400 subjects (70% of 12,000 subjects) completed the questionnaire, and approximately 900 subjects (11% of 8400 subjects) were diagnosed with kidney and/or liver disease and excluded from the study. Participants who were occupationally exposed to heavy metals were also excluded. The eligible subjects were asked to provide urine samples for biological measurements. A total of 6232 participants (52% of 12,000 subjects), 1346 from Shanghai, 1828 from Hubei, 1635 from Liaoning, and 1423 from Guizhou, completed the questionnaires and provided urine samples. Of the participants who provided urine samples, 45% (2795) were males and 55% (3437) were females aged 3 and older. Women were slightly more likely than men to participate in this study and return a sample. Tables 1 and 2 present data on the number and ages of all participants from each province. Ethical permission was obtained from the Ethics Committee at Beijing Jiaotong University. Informed consent was obtained from all participants, and in the case of children, from their parents.

2.2. Sampling and chemical analysis

UCd is an accepted indicator of Cd body burden and kidney accumulation (Järup and Åkesson, 2009; Jin et al., 2002a). Morning urine samples were collected from eligible participants. Each sample was divided into several aliquots immediately after collection to measure the urinary Cd and creatinine (cr) levels. The UCd was measured using the national standard methods (WS/T32-1996) described in previous studies (Jin et al., 1999, 2002a; Shao et al., 2007). Urine samples were collected in acid-washed plastic containers and frozen at −20 °C until further analysis. The urine samples were acidified with concentrated nitric acid to determine the Cd levels. The Cd concentrations in the urine samples were then measured by graphite-furnace atomic absorption spectrometry with peak area evaluation. The calibration curve (R^2 = 0.996 to 0.999) was linear from 0 to 20 μg/L. The method was validated by evaluating the quality control sample and recovery. Quality control samples of two concentrations (5.1 μg/L and 15.0 μg/L) were analyzed and yielded Cd concentrations of 4.9 ± 0.2 μg/L and 14.6 ± 0.4 μg/L. The relative standard deviations for Cd were 4.5% and 2.7% in the two quality control samples, respectively. The average recovery when analyzing the UCd ranged from 97.8% to 103.0% for different amounts Cd. The UCd limit of detection was 0.07 μg/L. For analytical quality assurance, both the calibration standards and one run of quality control samples for every analytical run were used. The urinary creatinine (cr) levels were measured as previously described (Hare, 1950; Shao et al., 2007). All urinary parameters were normalized to the creatinine concentration and expressed as μg/g creatinine (μg/g cr) (Jin et al., 2002a).

2.3. Statistical analysis

SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA) and Origin 8.0 were used to conduct statistical analyses. The variables were log-transformed to meet the normal distribution requirements. The geometric mean (GM), median, range, 5th and 95th percentiles of UCd were calculated. A generalized linear model was used to compare the GM of UCd after adjusting for age and gender. A ONEWAY-ANOVA was used to test for univariate differences among groups. Multiple linear regression analysis was used to test the relationships between covariates (region, age, gender) and UCd concentrations. The results were considered statistically significant at $p < 0.05$ or 0.01 based on a two-tailed test. The data are expressed in terms of tmean or geometric mean.

The prevalence of elevated UCd levels was calculated, and the cut-off values were selected according to available risk assessment-based