Bone 63 (2014) 76–80

Contents lists available at ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone

Original Full Length Article

Effects of lead and cadmium co-exposure on bone mineral density in a Chinese population

Xiao Chen [a,b,*,1], Keyue Wang [c,1], Zhongqiu Wang [a], Caohui Gan [d], Ping He [e], Yihuai Liang [e], Taiyi Jin [e], Guoying Zhu [d,**]

[a] Department of Radiology, The Affiliated Hospital of Nanjing University of Traditional Chinese Medicine, Nanjing, Jiangsu Province, China
[b] Department of Radiology, Shanghai East Hospital, Tongji University School of Medicine, Shanghai, China
[c] Department of Preventive Medicine, Zuiyi Medical College, Zunyi, Guizhou Province, China
[d] Institute of Radiation Medicine, Fudan University, Shanghai, China
[e] Department of Occupation Medicine, School of Public Health, Fudan University, Shanghai, China

ARTICLE INFO

Article history:
Received 4 September 2013
Revised 24 February 2014
Accepted 25 February 2014
Available online 4 March 2014

Edited by: Doug P. Kiel

Keywords:
Cadmium
Lead
Co-exposure
Bone mineral density

ABSTRACT

It has been indicated that both cadmium (Cd) and lead (Pb) may have adverse effects on the bone. However, most studies have only focused on a single factor. The primary and main and interactive effects of Cd and Pb on bone mineral density (BMD) in a Chinese population were observed in this study. A total of 321 individuals (202 women and 119 men), aged 27 years and older, living in control and polluted areas, were recruited to participate in this study. The BMD was measured through dual energy X-ray absorptiometry (DXA) at the proximal radius and ulna. The samples of urine and blood were collected to determine the levels of Cd and Pb in the urine (UCd and UPb) and blood (BCd and BPb). The Cd and Pb levels of people living in the polluted area were significantly higher than those living in the control area ($p < 0.05$). The BMD of women living in polluted area was significantly lower than that of women living in the control area ($p < 0.05$). Furthermore, the BMD decreased with increasing of BCd ($p < 0.05$), BPb and UPb in women. The likelihood of low BMD was associated with higher BCd in women (OR = 2.5, 95% CI: 1.11–5.43) and BPb in men (OR = 4.49, 95% CI: 1.37–14.6). The relative extra risk index of low BMD for female and male subjects with both high levels of BCd and BPb was 0.45 and 1.16, respectively. This study strengthens previous evidence that cadmium and lead may influence the bone and also demonstrates that cadmium and lead may have interactive effects on BMD.

Introduction

Cadmium (Cd) is one of the important heavy metals that are widely distributed in the environment, including water, air and soil, and can eventually enter the human body through the food chains. Once absorbed, it accumulates and retains in the body throughout life [1,2]. It has been suggested that the bone is one of the important target organs of Cd toxicity. Exposure to Cd at the environmental level can result in low bone mineral density (BMD), cause osteoporosis, and increase the risk of bone fracture [2–7]. A number of studies have indicated that Cd may have direct effects on osteoblasts and osteoclasts [8–10].

Lead (Pb) is another important heavy metal that is broadly used in the industrial field. It has been shown that Pb can disturb hemoglobin synthesis and influence behavior and the neurological system in children [11–14]. Some studies have also indicated that Pb can influence kidney function [15,16]. The bone is the main organ in which Pb is accumulated, and more than 90% of Pb is found in the bone [4,17]. In the 1990s, Goyer [12] suspected that exposure to Pb may be related to bone damage. A few studies have demonstrated that Pb may interfere with bone formation and bone strength and increase the risk of osteoporosis and bone fracture [18–26]. Some experimental studies have also suggested that Pb may affect osteoblast and osteoclast function [27–30].

In many circumstances, Cd and Pb pollution may co-exist and people may be co-exposed to Cd and Pb. It has been shown that Cd in the blood may be positively correlated with the blood Pb level [31]. In addition, the biological half-lives of Cd and Pb are both very long: 10–30 years for Cd [2] and 5–20 years for Pb [32,33]. It has been shown that Cd and Pb co-exposure may increase the risk of hearing loss and increase renal damage [34,35]. A recent study suggested that Pb and Cd may have additive-toxic effects on the testicle, liver and kidneys [36]. However, only a few studies have investigated the bone damage caused by co-exposure to Cd and Pb. Alfvén et al. showed a decrease in bone mineral density related to Cd but not to Pb in a Swedish population with environmental Cd and Pb co-exposure [4]. However, the Cd and

* Correspondence to: Department of Radiology, The Affiliated Hospital of Nanjing University of Traditional Chinese Medicine, Nanjing 210019, Jiangsu Province, China.
** Correspondence to: G. Zhu, Institute of Radiation Medicine, Fudan University, Shanghai 200032, China. Fax: +86 21 64049847.
E-mail addresses: chenxiao19@gmail.com (X. Chen), chx_win@hotmail.com (G. Zhu).
[1] The authors contributed equally to this work.

http://dx.doi.org/10.1016/j.bone.2014.02.017
8756-3282/

Pb levels in the blood were relatively low in their study. In the present study, we observed the effects of Cd and Pb on bone mineral density in a Chinese population that were exposed to both Cd and Pb at relatively high levels through food.

Materials and methods

Study area and population

The study area was Magu in Hezhang County, which is located southwest of Guizhou Province, approximately 340 km west of Guiyang City. Zinc smelting using indigenous methods had been broadly used in this area since the 17th century. The zinc smelting activities were ceased in 2004 due to environmental protection concerns. Huge quantities of waste gases and water containing many types of heavy metals were previously released into the environment. A previous investigation showed that the local air, water and soil compartments are seriously contaminated with heavy metals [37]. The Cd and Pb levels in the soil are significantly higher than the national standard [37]. The Cd and Pb levels in Chinese cabbages are 0.57 mg/kg and 1.46 mg/kg which are significantly higher than the national standard (0.2 mg/kg for Cd and 0.4 mg/kg for Pb). In addition, the Cd and Pb levels in meat were 1.09 mg/kg and 1.47 mg/kg, which are also significantly higher than the national standard (0.1 mg/kg for Cd and 0.5 mg/kg for Pb). A non-Cd-polluted town (Yaozhan, 40 km from Hezhang) was selected as the control area, which represents a lower exposure (the Cd and Pb levels in Chinese cabbages were 0.03 mg/kg and 0.097 mg/kg, respectively, and the Cd and Pb levels in meat were 0.49 mg/kg and 0.48 mg/kg, respectively). This area, however, has many conditions in common with the polluted area, including the social, economic and living habits.

Only individuals who were born in the respective areas and consumed local food were recruited to this study. Each participant provided informed consent and completed a questionnaire, which included questions regarding their medical and drug history, cigarette smoking, food habits, and menopause status (females) with the help of local people. Subjects with impairment of the kidney and liver or hyperparathyroidism and subjects who had received drugs that are known to alter the bone metabolism were excluded. A total of 321 persons (202 women and 119 men), aged 27 years and older, were included in this study. Samples of urine and blood were collected to determine the levels of Cd and Pb in the urine and blood.

Exposure assessment

Food samples (e.g., corn grain, read bean, and Chinese cabbage) from each area were collected from 3 to 10 families. The food samples were then ashed and digested in HNO_3 (for trace element) for further analysis. The Cd and Pb levels in the blood (BCd and BPb) and urine (UCd and UPb) were assessed as previously described [38,39]. Briefly, the samples were collected in acid-washed containers and stored frozen at −20 °C until analysis. The Cd and Pb contents in the urine and blood were measured by graphite-furnace atomic absorption spectrometry (GF-AAS). The analytical quality was ensured using freeze-dried standard reference materials and calibration standards. The concentrations of the two standard references were 6.5 ± 0.5 μg/kg and 1.58 ± 0.1 μg/kg for Cd and 111 ± 15 μg/kg and 357 ± 12 μg/kg for Pb. The obtained Cd concentrations were 6.0 ± 0.7 μg/kg and 1.49 ± 0.3 μg/kg. The obtained Pb concentrations were 115 ± 16 μg/kg and 348 ± 15 μg/kg. The between- and within-bottle homogeneity testing results were lower than 8% and 10%, respectively. The UCd and UPb concentrations were adjusted for creatinine and are expressed as μg/g creatinine.

Bone densitometry

Dual energy X-ray absorptiometry (DXA, Norland) was used to measure the bone mineral density at the proximal radius and ulna of the non-dominant arm. The measurement precision, expressed as the coefficient of variation (CV) was within 2%. The repetition of the measurements in the same person ten times showed that the repeatability of the results was 99.4%. The apparatus was checked every day, including quality assurance and phantom scanning, and one experienced machine operator made all of the measurements.

The degree of low BMD was assessed by computing the Z-score, i.e., the number of SDs from the mean of sex- and age-matched controls, and calculated according to Z-score = (Xμ − Xm) / SD, where Xμ is the measured bone density, Xm is the group mean for the same age and sex in the control area, and SD is the standard deviation in the same control group. A common definition of low BMD was considered as Z-score < −1.

Ethical consideration

The guidelines set forth in the declaration of Helsinki were followed in this study. The present study was conducted with the permission of the Ethics Committees of Fudan University and Zunyi Medical College. Informed consent was obtained from each participating individual. The participant of all of the subjects was on a completely voluntary basis.

Statistical analysis

The database management and analysis were performed using SPSS 11.5 (SPSS Inc., Chicago, IL, USA) and EPI INF (Version 3.5.1, Centers for Disease Control and Prevention, Atlanta, GA, USA). A logistic regression analysis was applied to analyze the association between BMD and BCd, UCd, UPb and BPb after adjusting for age, height, weight, alcohol habits and menopause status (females). The arithmetic means were compared by using one way-ANOVA. Analysis of covariance (ANCOVA) was employed to adjust for other potentially influential variables (age, body mass index, menopause status, smoking, and alcohol habits). BCd, UCd, BPb, and UPb were set to two levels. The joint effects of blood Cd and Pb on low bone mass were examined in fully adjusted models using combined categorical variables classified as low Cd and low Pb, low Cd and high Pb, high Cd and low Pb, and high Cd and high Pb. Departures from additive joint effects (RERI: relative excess risk due to interaction) were computed as recommended by Knol and VanderWeele [40]. When appropriate, variables with a skewed distribution (BCd, UCd, BPb, and UPb) were log-transformed to achieve a normal distribution. The data are expressed in terms of the means ± SD/SE or the geometric means. The criterion significance level was set to $p < 0.05$.

Results

Characteristics of study population

The main characteristics of the populations, including age, height, weight, BCd, BPb, UCd, UPb, and BMD in each area are listed in Table 1. For both genders, the participants from the polluted area were significantly older compared with those living in the control area. There were no obvious differences in the smoking and alcohol habits between the people living in the two areas. The BCd, UCd, BPb, and UPb levels of the people living in the polluted area were significantly higher than those of people living in the control area.

BMD of the populations living in different areas

The women but not the men presented a significantly lower BMD in the polluted area compared with that in the control area after adjusting for variables (Table 1). Table 2 displays the average BMD in the different age-based sub-groups in the different areas. The BMD of the female subjects older than 60 years living in the polluted area was significantly lower than that of the matched individuals living in the control area