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The effects of prenatal exposure to low-level cadmium, lead and selenium on birth outcomes

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HIGHLIGHTS

- Maternal Cd, Pb, Se exposure correlated with their umbilical cord concentration.
- Cord blood Se was a new factor associated with newborn birth weight.
- Increasing the Se intake might reduce the cord blood cadmium concentration.

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ABSTRACT

To evaluate the current maternal and fetal exposure to cadmium (Cd), lead (Pb) and selenium (Se), and their potential effect on newborn birth outcomes, a cross-sectional study involving an assessment of the levels of these three metals in maternal blood, urine and umbilical cord blood was conducted in 209 pregnant women living in Eastern China. The maternal blood, urine and cord blood samples were collected and measured with inductively coupled plasma mass spectrometry (ICP-MS). The maternal blood concentrations of Cd, Pb and Se (the geometric means (GMs) were 0.48, 39.50 and 143.53 $\mu g\ L^{-1}$) were significantly higher than and correlated with those in the cord blood (GM: 0.09, 31.62 and 124.61 $\mu g\ L^{-1}$). In the urine samples, the GMs for Cd, Pb and Se were 0.13, 0.48, and 4.78 $\mu g\ L^{-1}$, respectively. Passive smoking was found to positively correlate with urine Cd ($r = 0.16$) and negatively correlate with urine Se ($r = -0.29$). The maternal blood Se level was negatively associated with the cord Cd levels ($r = -0.41$). The blood Cd concentration in the mother could significantly affect the newborn birth weight ($r = -0.22$), but it was not correlated with birth height. We identified cord Se as a new factor which significantly correlated with birth weight. In conclusion, maternal Cd, Pb, Se exposure correlated with their umbilical cord concentration, and maternal Cd exposure might affect the newborn birth weight. Increasing the Se intake might reduce the cord blood Cd concentration and promote the fetal growth.

1. Introduction

Cadmium (Cd) and lead (Pb) are metals well known for their potential toxicity in pregnant women (Osman et al., 2000; Guan et al., 2010). Environmental exposure to Cd in humans comes from two main sources: food and smoking (Jarup et al., 1998). Cd is easily transferred from polluted soils to rice (Uraguchi and Fujiwara, 2012), and the Cd-polluted rice has received much attention in Chinese populations (Fu et al., 2008; Williams et al., 2009). Large amounts of Cd are also present in cigarettes. A standard cigarette contains 1–2 μg of Cd, and smokers absorb approximately 10–30% of this amount through inhalation (Andujar et al., 2010). During pregnancy, Cd absorption increase in the gastrointestinal tract, and urinary Cd levels do not significantly change, subsequently more Cd is retained in the body (Zhang et al., 2004). The effects of Cd toxicity on fetal development have received much attention, as the negative effects of tobacco on Cd accumulation have been observed in the placenta during gestation (Ronco et al., 2005). Cd exposure has been associated with hazardous birth outcomes, such as lower birth weight or birth height (Salpietro et al., 2002; Zhang et al., 2004). However, these studies have reported conflicting results. Salpietro et al. (2002) reports that birth weight is inversely correlated with maternal and cord blood

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cadmium concentrations, while these correlations are not observed in other studies (Zhang et al., 2004; Al-Saleh et al., 2013). So further study are still needed on this field.

Exposure to the Pb impacts neurodevelopment, particularly when prenatal exposure occurs (Rice and Barone, 2000). Similar to Cd, the relationship between Pb exposure and newborn anthropometry has also received much attention but remains unclear. No association between high-level maternal blood Pb (mean: 57.7 $\mu g\ L^{-1}$) or cord blood Pb (mean: 105.2 $\mu g\ L^{-1}$) and birth weight or height is observed in 194 Kuwaiti women (Rahman et al., 2012), but low-level maternal blood Pb exposure (32.0 $\mu g\ L^{-1}$) is associated with decreasing birth weight in 252 Chinese women (Xie et al., 2013).

Se is an essential nutrient that causes toxic effects if exposure is too high (Foster et al., 2012), and some studies have reported the mutual interaction between toxicity and Se in animals exposed to areas contaminated with metals (Brzoska et al., 2000), and Se was correlated with toxic metals in a study involving Chinese males (Wang et al., 2012). But relatively few studies concerned the mutual action of Cd, Pb and Se in mothers and newborns.

China is a developing country, and many environmental pollution issues have emerged during the economic development. The combustion of leaded petrol is once the most important source of Pb, but has been forbidden in the year 2000. After that, the industrial pollution becomes the primary source of metals exposures. We know few about the population's exposure to metals, especially in vulnerable pregnancy and infants. So the first aim of the present study is to characterize the metals burden in pregnant women and newborns in eastern China and determine the association between Cd, Pb and Se levels in these individuals. And because relatively few studies have estimated the relationship between the prenatal Pb, Cd or Se exposure and birth outcomes (Xie et al., 2013), we further examine the association of current prenatal metals exposure with birth outcomes. We aim to examine whether the current prenatal exposure is associated with reduced birth weight or length, after adjusting for potential confounders.

2. Materials and methods

2.1. Study participants

This study was conducted as a part of the Chinese National Health Research Program, and the protocol was approved through the Ethnic Commission of the Chinese Center for Disease Control and Prevention. The research area was located in the middle of Jiangsu province, eastern China. The participants were recruited from three hospitals located in three different towns. All subjects were residents of this location for at least 2 years, with no known occupational exposure to metals or other occupational hazards. The participants were requested to finish a questionnaire and donate the maternal blood, urine and cord blood samples, and 209 pregnant women provided complete information and blood samples. The women provided written consent forms which stated that participation was voluntary. Participants' confidentiality was assured, and the individual results for contaminants were available to each participant before reporting for treatment elsewhere. The participants could withdraw from the program at any time, and the overall results would contribute toward the city and national efforts to reduce heavy metal contamination.

2.2. Questionnaire

Trained hospital staff conducted standardized face-to-face interviews with the women before delivery. The interview was used to obtain a variety of information, including demographic and socioeconomic data, living habits, living environment, occupation, diet and nutrition (including the nutrition addition containing Se, Zn, Fe), delivery and birth outcomes. The gestational age was estimated based on the onset of the last menstrual period (LMP); if the LMP was uncertain or if there was a significant discordance between the clinical estimate and the LMP (>2 weeks), a B-type supersonic fetus measurement was obtained.

2.3. Sample collection and analysis

We collected maternal blood and urine samples in the third trimester. The blood samples were obtained from the antecubital vein and collected into vacutainer tubes (2 mL purple top EDTA tubes) for trace metal measurement. Midwives collected the cord blood samples from the placenta using a common aseptic procedure. The cord blood was collected into 2 mL purple top EDTA tubes. The whole blood samples were stored at 4 °C until further analysis. Cd is primarily localized in red blood cells and is a useful marker for recent, ongoing exposure. Because the blood Cd half-life is approximately one month, but could range from 10 to 30 years in other organs (Jarup and Akesson, 2009), and the urine Cd could be used as a marker for the accumulation of the total heavy metal burden. Thus, maternal urine samples were also collected in this study.

The concentrations of Cd, Pb and Se in the collected samples were measured with an inductively coupled plasma mass spectrometer (ICP-MS; Thermo fisher X-series 2, Houston, TX, USA), using a previously described operating method (Wang et al., 2012), with some modified parameters for ICP-MS instrument showed in Table 1. All reagents were of analytical grade, and deionized water was used throughout. The certified reference material, Seronorm™ trace elements whole blood level-1 (SERO, Norway), was used. The observed values for each element were within the certified range. The abnormal results were re-measured to exclude possible contamination during the operations. The limit of detection (LOD) in the acid digest was set at three times the standard deviation of the reagent blanks. The undetected samples were assigned a value of one-half the detection limit. The urine creatinine concentration was spectrophotometrically determined using commercial kits (Beijing Jiuqiang Co., Beijing, China) on a Hitachi 7180 chemistry analyzer.

2.4. Measures of birth outcomes

Information concerning the newborns (including gestational age at birth, sex, birth weight and length) was retrieved from the medical records. Trained nurses measured the birth weight and body length just after delivery.

2.5. Statistical analyses

SPSS 18.0 for Windows (SPSS Inc., Chicago, IL) was used for the statistical analyses. All descriptive statistics were calculated prior to the correlation analysis. The Anderson–Darling test showed that

Table 1
ICP-MS measurement conditions for Thermo fisher X_2.

Parameters	Values
Nebulizer gas low	0.96 $L\ min^{-1}$
Sampling depth	150 mm
Forward power	1350 W
Cool gas flow	13 $L\ min^{-1}$
Auxiliary gas flow	0.8 $L\ min^{-1}$
Sampling uptake rate	1.0 $mL\ min^{-1}$
Plasma gas flow	15 $L\ min^{-1}$