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Prenatal exposure to polybrominated diphenyl ethers and birth outcomes

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ABSTRACT

This study aimed to examine the potential association between maternal PBDEs and birth outcomes, including birth weight (g), length (cm), head circumference (cm) and gestational age (week). 215 mothers were recruited from a prospective birth cohort in rural northern China between September 2010 and February 2012. Serum PBDE congeners were detected and their association with birth outcomes were examined. The median maternal serum concentrations of BDE-28, -47, -99, -100, -153 were 2.27, 2.26, 3.58, 2.13, 4.87 ng/g lipid, respectively. Maternal LgBDE-28 and LgBDE-100 were negatively associated with birth length ($\beta = -0.92$, 95% confidence interval (CI): −1.82, −0.02; $\beta = -0.97$, 95% CI: −1.83, −0.08). A negative association was found between LgBDE-28 and birth weight among male infants ($\beta = -253.76$, 95% CI: −438.16, −69.36). PBDE congeners were not associated with head circumference, or gestational age. Our results contribute to growing evidence suggesting that PBDEs have adverse effects on birth outcomes.

1. Introduction

Polybrominated diphenyl ethers (PBDEs) are brominated flame retardants (BFRs) that are widely used in polymer-based commercial applications, furniture and infant products. PBDEs have been produced commercially in different formulations, the most commonly used being penta-, octa- and deca-BDEs are the most commonly-used types (Ni et al., 2013). Because PBDEs are not chemically bound to products, they have the potential to leak into the surrounding air, dust, soil, and water (Hu et al., 2015; Wang et al., 2015). Studies have indicated that PBDEs have been detected in various types of human biological samples, including blood, breast milk, hair, the liver, adipose tissue, meconium, placental tissue and amniotic fluid (Harley et al., 2011; Cui et al., 2012; Zhao et al., 2009; Ma et al., 2011; Ni et al., 2013; Tang et al., 2014).

Prenatal exposure to PBDEs is a major pathway of PBDEs exposure in infants (Ni et al., 2013). Exposure to PBDEs has been associated with adverse health outcomes in epidemiologic studies: most studies on human exposure to PBDEs were performed in America, Europe and Japan (Wang et al., 2012). Previous studies have suggested a potential impact of PBDEs on infant development (Chao et al., 2007; Harley et al., 2011) and neurodevelopment (Shy et al., 2012; Hoffman et al., 2012), as well as thyroid homeostasis in newborns (Mazdai et al., 2003; Kim et al., 2009, 2011; Lin et al., 2011; Gascon et al., 2011). However, few studies have focused on the relationship between prenatal PBDEs exposure and infant birth outcomes and the results are inconsistent (Mazdai et al., 2003; Wu et al., 2010; Harley et al., 2011; Robledo et al., 2015). A study performed by Chao et al. (2007) found that an increase PBDEs in breast milk was significantly associated with adverse birth outcomes, including low birth weight, short birth length and chest

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circumference (n = 20). Other research found that prenatal exposure to PBDEs may predispose infants to a higher risk of low birth weight (n = 286) (Harley et al., 2011). However, a conflicting study found no association between concentrations of PBDEs and birth weight (n = 41) (Tan et al., 2009).

Until 2011, decreasing temporal trends on concentrations of PBDEs were identified in general populations of the USA, Australia and European countries. While in Asia, especially in China, temporal trends on the concentrations of PBDEs in the general population remain unclear due to limited reports (Law et al., 2014). China has become one of the countries with the highest production capacity and application of PBDEs. Researchers have raised concern regarding the adverse impacts of exposure to PBDEs on some susceptible populations, including pregnant females and children (Chao et al., 2007; Wu et al., 2010). However, few data are available on prenatal exposure to PBDEs and infant birth outcomes in China.

The aim of our current study was to determine the maternal serum concentrations of PBDEs in a birth cohort in the south coast area of Laizhou Wan (Bay), one of the major BFRs production areas in China, and to analyze the potential association between maternal exposure to PBDEs and infant birth outcomes.

2. Methods

2.1. Participants and recruitment

Our study was a prospective birth cohort study (Laizhou Wan birth cohort, LWBC) performed in the south coast area of Laizhou Wan (Bay) of the Bohai Sea, Shandong province, China. Detailed methods for the study are published elsewhere (Ding et al., 2013, 2014). Eligible females were those with a singleton pregnancy, ≥18 old, planning to deliver at the local hospital (the only county hospital located in the south coast area of Laizhou Wan), and living in the area for at least 3 years. All of the participants lived within 10 km away from the main chemical production sites and reported no preexisting or gestational diabetes, no chronic or pregnancy associated hypertension, and no HIV infection or AIDS. From September 2010 to February 2012, a total of 388 females met the eligibility criteria, and 347 (89.4%) females agreed to participate in our study. Of these females, the following subjects were excluded: 111(32.0%) females failed to provide a sufficient volume of serum for detection of PBDEs, and 21 (6.1%) females had missing values for major confounders. A total of 215 (62.0%) females were included in the analysis. As shown in Supplemental Table 1, the demographic characteristics were comparable between the study population and women without measurements of PBDEs, indicating that the study cohort generally reflects the original population (Online Supplemental Table 1).

Specifically trained nurses administered a 20-min questionnaire to the mothers shortly after fetal delivery. The questionnaire included the following parameters: demographic and socioeconomic information (maternal age, height, pre-pregnancy weight, BMI, education level, household income, and home address) and maternal characteristics (cigarette smoking and alcohol use during pregnancy, employment). Information about exposure to PBDEs during pregnancy included the woman's occupation, whether there were any BFRs production factories near their home, and, if so, the types of BFRs produced. Information on paternal exposure to PBDEs and occupation were also collected by interview. Maternal previous and current pregnancy complications, was obtained through interview and confirmed with medical records.

Information on the current delivery and birth outcomes was retrieved from medical records, including method of delivery, gestational age at birth, infant sex, birth weight, birth length, Apgar scores at birth, and total maternal weight gain during pregnancy. Low birth weight was defined as infant weight <2500 g and preterm delivery was defined a birth prior to 37 completed weeks of gestation. Written informed consent was obtained from each participating female, and the study protocol was approved by the Medical Ethics Committee of Shanghai Xinhua Hospital, Shanghai Jiao Tong University School of Medicine.

2.2. Analysis of PBDEs and QA/QC

Maternal blood samples were collected on the day of hospital admission for delivery. All blood samples were aliquoted into five 4-mL EDTA blood collection tubes. The serum was separated by centrifugation at 3000 rpm for 15 min and then transferred into new tubes and immediately stored at −80 °C until further analysis. Two milliliters of maternal serum was used to analyze PBDEs by GC/MS.

Extraction of PBDEs and gravimetric lipid determination procedures were previously published (Hovander et al., 2000). PBDEs were detected by GC/ECNI/MS using an Agilent 5975N mass spectrometer equipped with a 6890Gas Chromatograph. The identification of specific PBDEs was performed by comparing peak retention times with a standard solution containing eight identified tri-BDEs through octa-BDE congeners (BDE-28, -47, -99, -100, -153, -154, -85, and -183) (Jin et al., 2009; Cui et al., 2012).

The PBDEs in the samples were quantified using the internal standard method. Two masses (*m*/*z*: 79.0, 81.0) from the molecular ion cluster were selected for monitoring each target analyte, and *m*/*z* 574.6 and 576.6 were used to monitor $^{13}C_{12}$-BDE-139 as a surrogate standard. The average recovery of $^{13}C_{12}$-BDE-139 in the serum was 102.7 ± 10.8%. This method was sufficiently robust to accommodate a satisfactory quantitative analysis. To ensure the reproducibility of the measurements of PBDEs concentrations, one sample out of 20 was randomly selected for repeated experiments, and the reproducibility of the serum analyses were good. Blank controls were analyzed simultaneously with every batch of 12 samples to check for interference or contamination from solvents and glassware (Jin et al., 2009; Cui et al., 2012). The limit of detection (LOD) of the method was defined as the mean blank mass plus three standard deviations. The LOD ranged from 0.24 to 0.48 ng/g lipid in serum samples. The blanks were less than LOD for all PBDE congeners in the samples.

2.3. Statistical analysis

Due to the skewed distributions, the concentrations of maternal serum PBDEs were transformed into their decimal logarithms and the geometric means were calculated. Five PBDE congeners (BDE-28, -47, -99, -100, and −153) were detected in more than 90% of the population and therefore were analyzed as continuous variables to assess the relationship between maternal PBDEs and birth outcomes. An aggregate variable ($\sum_5$PBDE) was generated using the molar sum of these five congeners. Half of the LOD was used if the concentration of PBDEs in the serum was below the LOD.

Multiple linear regression models were performed to determine the relationships between infant birth outcomes and PBDEs concentrations. Several variables were initially considered as confounders based on the literature (Harley et al., 2011; Eskenazi et al., 2013; Robledo et al., 2015), including maternal age, education, parity, pre-pregnancy BMI, gestational age, marital status, household monthly income, smoking during pregnancy, and the sex of the infant. The confounders were further tested if they were associated with the outcomes at $p < 0.2$ in separate bivariate models. Finally, we included the following confounders in the model, including infant sex, maternal age, education, parity, household monthly income, pre-pregnancy BMI, gestational age.