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Hydroxylated polybrominated diphenyl ethers (OH-PBDEs) in paired maternal and neonatal samples from South China: Placental transfer and potential risks

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ABSTRACT

Hydroxylated polybrominated diphenyl ethers (OH-PBDEs) are attracting more and more attention for the neurodevelopment toxicity effects. We evaluated the concentrations of 15 individual OH-PBDEs and 3 bromophenol (BRP) congeners in 30 mother-newborn paired placenta, breast milk, fetal cord blood, and neonatal urine samples collected from South China. The geometric mean (GM) concentrations of ∑OH-PBDEs were 37.6, 61.3, and 76.8 pg g^{-1} ww in placenta, breast milk, and cord blood, respectively. The GM concentrations of ∑BRPs were 47.6, 119, and 30.2 pg g^{-1} ww in placenta, breast milk, and cord blood, respectively. The GM concentrations of ∑OH-PBDEs and ∑BRPs in neonatal urine were 72.0 and 79.8 pg ml^{-1}, respectively. Of the 15 OH-PBDE congeners analyzed, the three most frequently detected congeners were 2′-OH-BDE-68 (72.1%), 6-OH-BDE-47 (67.6%), and 2′-OH-BDE-28 (65.8%). The estimated daily intake (EDI) of OH-PBDEs for the breast-fed infants was 9.31 ± 4.00 ng kg^{-1} bw day. The accumulation of OH-PBDEs in newborns was much lower than the estimated lowest observed-effect concentration (LOEC) of neurotoxicity. The present study provided the first systematic fundamental data that exposure to OH-PBDEs for newborn and their mothers in South China.

1. Introduction

Polybrominated diphenyl ethers (PBDEs) have been detected ubiquitously in abiotic and biotic samples such as water, sediment, air, fish and human body due to the wide usage in recent years (Gaylor et al., 2014; Wang et al., 2011; Wang et al., 2013). Some studies revealed that concentrations of PBDEs in human samples such as blood and milk have been shown a increasing trend, particularly for the samples collected from the Asia for the past 20–30 years (Chen et al., 2014; Wang et al., 2007), although other reports suggested PBDEs in human tissues are remaining steady or decreasing in North America between 2008-2009 and 2011-2012 (Zota et al., 2013). Recently, hydroxylated- (OH-) PBDEs, the structural analogues of PBDEs, have been detected in environment and humans (Covaci et al., 2011; Zota et al., 2011). It suggested that OH-PBDEs are significantly accumulated in human tissues such as blood and fat. For example, the total concentration of OH-PBDEs ranged from 2.0×10^3 to 9.0×10^5 pg g^{-1} lipid (mean of 79×10^3 pg g^{-1} lipid) in blood serum of people enrolled during 2003–2004 from the United States (Qiu et al., 2009). Our previous

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studies also revealed that OH-PBDEs were widely detected in market fish and human blood collected from South China in 2010-2011 (Wang et al., 2012; Wang et al., 2011).

It was reported that prenatal and childhood PBDE exposures were associated with potential health and developmental risks such as poorer attention and cognition in school-age children (Eskenazi et al., 2013). OH-PBDEs are of particular interest since these compounds have been shown to have potent toxic properties including endocrine disruption, altered estradiol synthesis, and neurotoxic effects (Dingemans et al., 2008). They are structurally more similar to thyroid hormones than PBDEs, with stronger binding capability to human transthyretin (TTR) (Dingemans et al., 2011; Hamers et al., 2006). Therefore, OH-PBDEs can bind to major thyroxine transport protein- thyroxine binding globulin (TBG) in human plasma, then bind to thyroid hormone receptors α and β (TRα/β), and finally affect thyroid hormone signaling through nuclear receptor antagonism (Cao et al., 2010; Kojima et al., 2009). In addition, OH-PBDEs can bind to estrogen receptor α and β (ERα/β) (Meerts et al., 2001), modulate the gamma-aminobutyric acid (GABAA) and α4β2 nicotinic acetylcholine (nACh) receptor (Hendriks et al., 2010), and inhibit the activities of aromatase (Canton et al., 2008). Therefore, much more attention should be paid to health risks of OH-PBDEs on the development of fetuses.

Several studies showed that OH-PBDEs can cross placenta and accumulate in fetus (Chen et al., 2013; Wan et al., 2010). However, there were very limited data about distribution and placental transfer characteristics of OH-PBDEs in neonates. Kawashiro et al. (2008) found that the median concentration of 6-OH-BDE-47 in neonate serum samples (0.6 pg g^{-1} wet weight, ww) was lower than that of mothers (2.1 pg g^{-1} ww) in 6 pairs of mothers and neonates in Japan. While a study of 26 pairs in South Korea revealed that concentrations of 6-OH-BDE-47 in cord blood serum were significantly greater than that in placenta (Wan et al., 2010). In the United States, the results of only one mother-neonate pair suggested that concentrations of OH-PBDEs in cord serum were higher than mothers (Qiu et al., 2009). This was confirmed by a later study that equal or higher levels of total OH-PBDEs and total BDEs in cord serum were observed in 85% and 80% of the 20 mother-neonate pairs in Cincinnati, the United State (Chen et al., 2013). Due to the limited information, the placental transfer characteristics of OH-PBDEs in human samples of mother-newborn pairs need further study.

Considering placenta is the barrier which protects fetus against toxins such as OH-PBDEs circulating in maternal blood, therefore, there is an urgent need to evaluate the accumulation of OH-PBDEs and their placental transfer characteristics. The concentrations of OH-PBDE and bromophenols (BRPs) in 30 sets of human samples collected from five major cities of South China were measured in the present study, and then accumulation characteristics of OH-PBDEs were investigated.

2. Materials and methods

2.1. Sample collection and preparation

Studies were performed in accordance with the guidelines and approval of Human Investigation Ethics Committee of Department of Biology, Hong Kong Baptist University. Detailed information about sample collection and preparation was previously reported (Chen et al., 2014). Briefly, a total of 30 set of mother-newborn paired samples (each set contains human milk, placenta, fetal cord blood and neonatal urine) were recruited during February to December 2012 from five major cities (Guangzhou, Dongguan, Foshan, Zhongshan, and Zhuhai) in South China. Six set of samples were collected for each city. Samples of blood were collected in heparinized tubes, maintained at 4 °C , and centrifuged at 1000 × *g* for 15 min to allow collection of the plasma fraction. Neonatal urine was collected during the first 7 days after delivery. Urine was collected daily by use of urine collection bag placed at the perineum, which has an adhesive inlet which can be attached around external genitalia of the infants. Breast milk was collected at 3–10 days after the delivery. The whole placenta was collected immediately after delivery. About 50 g of placental tissue including maternal and fetal sides and central and peripheral parts was taken, frozen, and homogenized according to previous study (Vizcaino et al., 2014). Basic participant information on the mother and newborns was obtained from nurses and summarized in Table 1. All samples were collected with glass devices to avoid contamination by phthalates during handling and storage. All samples were kept at −20 °C until extraction.

Table 1
Physical characteristics of study subjects.

Subject characteristics (n=30)	Mean ± SD	Median	Min	Max
Maternal				
Age	27.6 ± 4.56	28	21	39
Pre-pregnancy body weight (kg)	49.5 ± 6.59	50.8	42.2	73.6
Post-pregnancy body weight(kg)	65.3 ± 10.8	67.9	51.3	86.1
Pre-pregnancy BMI (kg m^{-2})	20.1 ± 2.08	20.6	18.9	24.1
Gestation weeks	37.5 ± 1.9	38.4	34.8	41.0
Infants				
Body weight (kg)	3.10 ± 0.68	3.25	1.92	4.32
Length (cm)	47.3 ± 3.90	47.9	36.5	53.8
Head circumference (cm)	33.6 ± 4.02	34.1	30.1	38.2

2.2. Chemicals

Seventeen PBDE congeners (IUPAC congener numbers 17, 28, 47, 85, 99, 100, 138, 153, 154, 183, 184, 191, 196, 197, 206, 207, and 209) had been detected in our previous study for these samples (Chen et al., 2014). The surrogate ^{13}C-6′-OH-BDE-100 and internal standard ^{13}C-6′-OH-BDE-17 were purchased from Cambridge Isotope Laboratories (Andover, MA, USA). Fifteen target OH-PBDEs standards included 2′-OH-BDE-7 (HK), 3′-OH-BDE-7 (HK), 2′-OH-BDE-28, 4′-OH-BDE-17 (HK), 2′-OH-BDE-68 (HK), 6-OH-BDE-47, 2′-OH-BDE-66 (HK), 3-OH-BDE-47, 6′-OH-BDE-99, 4-OH-BDE-42 (HK), 6-OH-BDE-90 (HK), 5′-OH-BDE-99 (HK), 6-OH-BDE-85 (HK), 3-OH-BDE-100 (HK), and 4-OH-BDE-90 (HK) were purchased from Wellington Laboratories (Guelph, ON, Canada), except 11 OH-PBDE congeners (HK) which were synthesized in the Department of Biology and Chemistry of City University of Hong Kong with purities > 98% (Marsh et al., 2003). Three bromophenol (BRP) congeners: 2, 4-dibromophenol (2, 4-DBP), 2, 4, 5-tribromophenol (2, 4, 5-TBP) and 2, 4, 6-tribromophenol (2, 4, 6-TBP) were purchased from Accustandard (New Haven, CT, USA). All solvents used were GC grade obtained from Tedia Company, Inc. (Fairfield, Ohio, USA). All other reagents were of analytical grade or HPLC grade.

2.3. Extraction and instrumental analysis

The detailed procedures for extraction and instrumental analysis were described in the supplementary data (SD). Briefly, approximately 3 g breast milk, blood, urine, or freeze dried placenta were mixed with surrogate (100 pg ^{13}C-6′-MeO-BDE-100) overnight and then extracted and purified according to our previous method (Wang et al., 2012, 2011). Then, OH-PBDEs and BRPs were derivatized by adding 100 μL of N, *O*-bis-(Trimethylsilyl)