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Transplacental transfer characteristics of organochlorine pesticides in paired maternal and cord sera, and placentas and possible influencing factors☆

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ABSTRACT

Organochlorine pesticides (OCPs), including dichlorodiphenyltrichloroethane (DDT) and its metabolites [dichlorodiphenyldichloroethylene (DDE) and dichlorodiphenyldichloroethane], hexachlorocyclohexanes (HCHs), and hexachlorobenzene (HCB), are widely detected in humans despite the considerable decline in environmental concentrations. To understand the placental transfer of OCPs and the possible maternal influence on them, we measured the concentrations of DDTs, HCHs, and HCB in 102 paired samples of maternal and cord sera, and placentas collected in Shanghai, China. The median concentrations of DDTs and HCHs were the highest in maternal sera (601, 188 ng g^{-1} lipid), followed by umbilical cord sera (389, 131 ng g^{-1} lipid), and placentas (65, 37 ng g^{-1} lipid). 4,4′-DDE, β-HCH, and HCB were the predominant contaminants in the three matrices. The ubiquitous existence of OCPs, and the significant concentration relationships of DDTs, HCHs, and OCPs in the three matrices suggested placental transfer from mother to fetus. The lipid-based concentration ratios of 4,4′-DDE, β-HCH, and HCB in umbilical cord serum to those in maternal serum (F/M), and ratios of placenta to maternal serum (P/M) ranged from 0.66 to 1.01, and 0.12 to 0.25, respectively. Maternal variables affected the levels of fetal contamination. For primiparous women, significant correlations between maternal age and maternal HCHs, and between pre-pregnancy body mass index (BMI) and maternal HCHs were found. The negative effect of parity, and the positive effect of food consumption on maternal OCP concentrations were also observed, although there were no significant differences. The possible influence of parity on F/M and P/M of 4,4′-DDE suggested borderline significant differences between primiparous and multiparous women. Also, slight group differences were observed between elder and younger women, and between overweight and normal/underweight women. Parity seems to have a potential influence on transfer ratios of some OCP pollutants.

1. Introduction

Organochlorine pesticides (OCPs) are persistent toxic substances of anthropogenic origin, which had been intensively used in agriculture and vector control. They include dichlorodiphenyltrichloroethane (DDT) and its metabolites, such as dichlorodiphenyldichloroethylene (DDE) and dichlorodiphenyldichloroethane (DDD), as well as hexachlorocyclohexanes (HCHs) and hexachlorobenzene (HCB) (Bigot et al., 2017; Pintado-Herrera et al., 2017). The typical pesticides were banned in the early 1970s because of their high toxicity in some developed countries, and the ban was subsequently extended to most countries in the world (Stockholm Convention on Persistent Organic Pollutants, 2001).

Despite the considerable decline in OCP concentrations in most regions, detection of DDTs (DDT and its metabolites including DDE and DDD), HCB, and HCHs (HCH isomers including α-, β-, γ-, and δ-HCH) in humans indicates that the toxicants still pose a potential threat, especially for vulnerable populations such as neonates (Kyriklaki et al., 2016; Limon-Miro et al., 2017; Monteagudo et al., 2016; Woodruff et al., 2011). Adverse birth outcomes are associated with the maternal burden of persistent organic pollutants including

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OCPs (Dewan et al., 2013; Lopez-Espinosa et al., 2016). There is also an increased risk of cancer development in adulthood that is associated with early-life toxicant exposure. Thus, exposure of pregnant women to OCPs should be of public concern (Lopez-Espinosa et al., 2016; Vizcaino et al., 2014; Yu et al., 2013).

By the detection of contaminants in maternal sera, umbilical cord sera, and placentas, scientists can determine the prenatal exposure and transplacental transfer of the contaminants (Chen et al., 2017; Kyriklaki et al., 2016; Mori et al., 2014; Sakamoto et al., 2016). Parity, maternal age, body mass index (BMI), food consumption, and dietary intake, as well as lifestyle can influence on prenatal contaminant exposure (Bergonzi et al., 2009; Jakobsson et al., 2012; Luo et al., 2016). The extent of transplacental transfer from the mother to the fetus mainly depends on the physical characteristics of the maternal–placental–embryonic–fetal group, and the physiochemical and structural characteristics of the xenobiotics, such as octanol–water partition coefficient, molecular weight, polarity, and degree of chlorination (Lancz et al., 2015; Mori et al., 2014; Vizcaino et al., 2014; Zhang et al., 2017). Passive diffusion has been suggested to control the transport of most xenobiotics across the placenta (Myllynen et al., 2005). In addition, the transporter proteins and metabolic enzymes, expressed in the placenta may affect the transfer characteristics and distribution patterns (Evseenko et al., 2006; Myllynen and Vähäkangas, 2013).

Similarly, OCPs can cross the placenta and may interfere with fetal development and growth (Lopez-Espinosa et al., 2016; Needham et al., 2011; Vizcaino et al., 2014; Yu et al., 2013). For example, Needham et al. (2011) measured the overall mean partition ratios of placenta (P) to maternal serum (M) of HCB and β-HCH. The concentration ratios of OCPs in umbilical cord serum (F) compared to maternal serum were generally lower than or close to one (Lopez-Espinosa et al., 2016; Vizcaino et al., 2014). Different F/M and P/M ratios of OCPs have also been observed (Bergonzi et al., 2009; Lopez-Espinosa et al., 2016), which might be attributed to geographic location, sample size, and genetic differences (Dewan et al., 2013; Eguchi et al., 2015; Tsang et al., 2011). However, knowledge of maternal anthropometric factors that influence the transplacental transfer of OCPs is still limited (Patayová et al., 2013). China has ~20% of the world population, therefore, placental transfer of OCPs in the Chinese population warrants attention by researchers, taking into consideration the aforementioned influences. However, such investigations in China have been very scarce (Li et al., 2014; Tsang et al., 2011).

To understand the characteristics of transplacental transfer of OCPs and the possible maternal influence on them, 102 paired samples of maternal serum, umbilical cord serum, and placenta (a total of 306 individual samples) from a maternal–fetal cohort were collected from Shanghai, a metropolis with a population of more than 24 million. We analyzed the possible influence of maternal variables on transfer ratios, as well as contamination levels. To the best of our knowledge, this is the first report investigating the possible influence of maternal variables on transplacental transfer characteristics of contaminants in China.

2. Materials and methods

2.1. Chemicals

A mixed standard solution of OCPs, including HCHs (α-, β-, γ-, and δ-HCH), DDTs (4,4′-DDT, 2,4′-DDT, 4,4′-DDE, 2,4′-DDE, 4,4′-DDD, and 2,4′-DDD), and HCB were obtained from Dr. Ehrenstorfer GmBH (Augsburg, Germany). Mixed surrogate standards including 2,4,5,6-tetrachloro-m-xylene and decachlorobiphenyl were obtained from AccuStandard Inc. (New Haven, CT, USA). Pentachloronitrobenze (AccuStandard) was used as an injection internal standard. Hexane and dichloromethane were of analytical grade and redistilled in a glass system before use.

2.2. Sample collection

Volunteers were randomly enrolled by their midwives and gynecologists at a hospital located in Shanghai during 2013 and 2014. Inclusion criteria were delivery at term in the hospital, and no occupational exposure of OCPs. Data including age, height and weight, weight gained during pregnancy, parity, occupation, education, dietary habits, and neonatal parameters were all collected through questionnaires. A total of 110 pregnant women were asked to participate this project, and eight primiparas of them declined. One hundred and two maternal serum, umbilical cord serum, and placenta paired samples were collected at the time of delivery from the 102 volunteers. Although samples were obtained blindly, selection bias may not have been completely excluded. The hospital Ethics Committee approved the study protocol. Informed consent was obtained from all the volunteers. Serum and placenta samples were obtained as described previously (Zhang et al., 2017).

2.3. Sample treatment and instrument analysis

The serum and placenta samples were treated as previously described (Zhang et al., 2017) (Supporting Information): 4–5 mL maternal serum, 8–12 mL umbilical cord serum, or 3–4 g of lyophilized placenta were used in the detection. Five nanograms of surrogate standards were added before extraction.

OCPs were detected using an Agilent 6890N gas chromatograph (GC) coupled with a microelectron capture detector. A DB-5MS (30 m × 0.25 mm × 0.25 μm; J & W Scientific, Folsom, CA, USA) fused-silica capillary column was used. The oven temperature was programmed as follows: 110–170 °C at a rate of 1.5 °C min^{-1} (held for 5 min), then to 230 °C at 2 °C min^{-1}, and to 280 °C at 40 °C min^{-1}, finally, held for 10 min. A splitless injection mode at 230 °C was used, and the detector temperature was set at 310 °C. Quality control criteria were used to ensure the identification of OCPs. GC retention time had to be within ±0.05 min compared to the standard; then, standard solutions were co-injected with some of the samples.

2.4. Quality assurance and quality control

A procedural blank was included in each batch of samples, and the procedural blanks were not found. Surrogate standards were used during the sample treatment with average recoveries generally >75% in the three matrices. The limits of detection (LODs) were derived from six blanks spiked with 1 ng of mixed standards, and defined as the products of 3.36 and the standard deviations of the results. The LODs were between 0.5 and 8 ng g^{-1} lipid for the chemicals. The limits of quantification (LOQs) were 1–16 ng g^{-1} lipid, which were twofold higher than the LODs. Standard calibration curves used for the quantification of all target substances had $R^2 > 0.998$.

2.5. Calculations and statistical analysis

Placental transfer was calculated using the concentration ratios between paired samples as follows:

$$F/M = C_U / C_M \quad (1)$$

$$P/M = C_P / C_M \quad (2)$$

where C_U, C_M, and C_P are the concentrations of contaminants in