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Environmental exposure to DDT and its metabolites in cord serum: Distribution, enantiomeric patterns, and effects on infant birth outcomes

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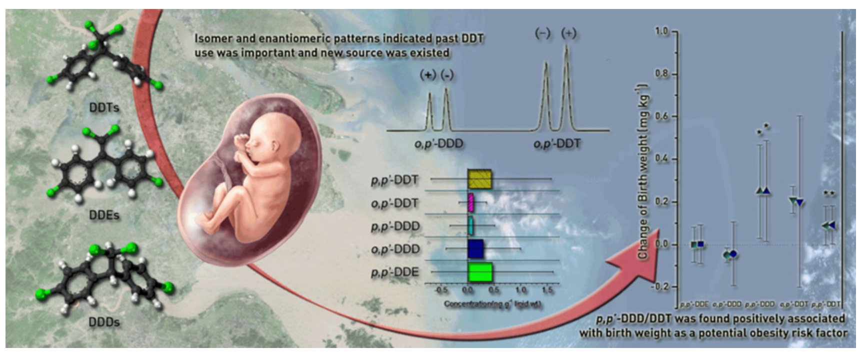
HIGHLIGHTS

- DDT and its isomers were tested to look for the exposure pattern and its effect on birth outcomes.
- Several maternal characteristics were identified as influence factors on exposure pattern.
- Isomer and enantiomeric patterns indicated past DDT use were important and new source existed.
- *p,p*'-DDD/DDT was found positively associated with birth weight as a potential obesity risk factor.

GRAPHICAL ABSTRACT



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ABSTRACT

Previous *in vivo* studies have suggested that prenatal exposure to dichlorodiphenyltrichloroethane (DDT) is endocrine disrupting, and may cause adverse health risks to newborns. In this cross-sectional study, non-invasive cord serum samples were collected from maternal-neonate pairs of an island population. Concentrations of DDT and its metabolites were analyzed to provide insights into the environmental exposure patterns and to elucidate their effects on birth outcomes. The average concentrations of *p,p*'-DDE, *o,p*'-DDD, *p,p*'-DDD, *o,p*'-DDT, *p,p*'-DDT and total DDTs were 0.463, 0.293, 0.089, 0.098, 0.441 and 1.384 μg g^{-1} lipid weight, respectively. Several maternal characteristics were identified as influencing factors on the environmental exposure distribution. The isomer ratios of individual components and the enantiomeric patterns of *o,p*'-DDD and *o,p*'-DDT indicated that historical technical DDT remains the predominant exposure source, though new sources of dicofol-type of DDT pollution must not be ignored. Using multivariable linear regression, increasing *p,p*'-DDD and *p,p*'-DDT levels were found to be significantly associated with an increase in neonatal birth weight, which deserves additional attention to obesity risks. No other birth outcome was found to be significant regarding DDT exposure. These findings raise the awareness of the prenatal risk of DDT and its metabolites among infants in contaminated areas.

1. Introduction

As one of the most important organochlorine pesticides (OCPs), 1,1,1-trichloro-2,2′-bis (4-chlorophenyl)ethane (DDT) was widely employed in agricultural production and the vector-borne diseases

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control. Although it has been banned for >30 years, it is still categorized as a ubiquitous environmental pollutant by the United Nations Environment Programme (UNEP) (Stockholm Convention, 2001) because of its prolonged environmental persistence and toxicity on human beings. DDTs in the environment can undergo slow transformation into 1,1-dichloro-2,2-bis (p-chlorophenyl)ethylene (DDE) and 1,1-dichloro-2,2-bis (p-chlorophenyl)ethane (DDD), which are more stable and persistent than the parent compound (Wang et al., 2008). Usually, technical grade DDT contains 75% *p,p*'-DDT, 15% *o,p*'-DDT, and 5% *p,p*'-DDE, with the other compounds accounting for the remaining 5% (WHO, 1989).*o,p*'-DDT, along with its derivative *o,p*'-DDD, have chiral carbons with the enantiomeric couples of (−)-*o,p*'-DDT, (+)-*o,p*'-DDT and (−)-*o,p*'-DDD, and (+)-*o,p*'-DDD (Lewis et al., 1999; Naudé and Rohwer, 2012). Although produced as a racemic mixture, the enantioselective degradation of chiral DDTs is preferentially used as an effective indicator for tracking the fate and source of OCPs in the environment (Bosch et al., 2015; Yuan et al., 2014).

Developing neonates are at higher risks than adults to these contaminants since they are known to be more susceptible to the toxicological consequences of pollution. Adverse birth outcomes were previously observed in infants whose mothers were exposed to organic pollutants such as DDT during and before the pregnancy (Choi et al., 2004; Farhang et al., 2005). The ability of DDT to pass through the placental barrier has been demonstrated, and the high correlation coefficient between maternal and cord serum concentrations indicated that the cord serum levels of DDT compounds could be used to estimate the maternal burden (Vizcaino et al., 2010). Moreover, as a non-invasive human sample, cord serum is more convenient and safer to collect during the delivery process compared with neonatal blood or urine (Jaraczewska et al., 2006; Yin et al., 2016). The concentration of pollutants in the cord serum reflects the portion passed through the placental barrier, which is likely to be close to the actual concentration in newborns. Therefore, this type of low-fat matrix is believed to be an adequate bio-indicator to assess DDT levels in newborns and infants (Maervoet et al., 2007). Previous research based on cord serum samples indicated that exposure to DDT could affect the foetus and have continuing adverse effects on birth development (Falcon et al., 2004). A cross-sectional study suggested that low *in utero* DDT exposure led to a reduction in birth weight, birth height, crown-heel length and head circumference (Al-Saleh et al., 2012). Two birth cohort studies in Spain showed that cord serum DDT concentrations at birth were inversely associated with cognitive functioning at 4 years of age (Ribas-Fitó et al., 2006). However, other population-based studies did not provide reliable conclusions. For example, in a Spanish birth cohort and a Michigan fish consumer cohort, no statistically significant correlation was found between offspring birth weight and cord serum DDE concentrations (Valvi et al., 2012).

Very few studies have been performed on exposure patterns, especially the enantiomeric composition of chiral components (*e.g.*, *o,p*'-DDD and *o,p*'-DDT), on the health of Chinese pregnant women and their newborns. The widespread contamination of DDTs has been previously documented (Müeller et al., 2008) throughout the Yangtze River Delta, which is the most important agricultural and industrial region in China (Yang et al., 2005). In 2012, the Chinese Marine Environment Bulletin reported that the East China Sea had poor water quality in the offshore waters (Cigui, 2013). Samples in this study originated from the Shengsi Islands, which sit 140 km from the Shanghai Coast and located in the centre of the East Sea fishing grounds. Fishes and other types of seafood play a prominent role in the islanders' daily dietary, and such food is a significant contributor to the accumulation of DDTs in human tissue (Karmaus and Zhu, 2004; Rylander et al., 1996).

In the present work, a Chinese population-based cross-sectional study was conducted on the Shengsi Island using cord serum samples to quantify concentrations of DDT and its metabolites. The correlations of maternal characteristics on the exposure patterns and the sources of contamination were examined in this research, with a particular emphasis on the enantiomeric enrichment of *o,p*'-DDD and *o,p*'-DDT. The effects on birth outcomes from exposure to these pollutants were also explored. It is expected that these results would provide valuable information on raising risk awareness to infants and their families in contaminated areas.

2. Materials and methods

2.1. Study population

This study was performed in the only hospital with a department of gynecology and obstetrics on Shengsi Islands. These marginal islands have a unique geographic location on the East China Sea, near the Yangtze River Estuary and the Hangzhou Bay in China (Fig. 1). As a major pollution destination, these islands have been threatened by large-scale agricultural pollution from non-point source discharges through the Yangtze River estuary and the sea. A total of 120 Chinese pregnant women living on the Shengsi Islands for >10 years agreed to participate in this study from July 2011 to May 2012. Participants provided samples of umbilical cord serum with completed structured questionnaires about the general characteristics including the maternal age, education level, drinking water sources, pre-pregnancy BMI, pregnancy weight gains and the reproductive history (abortion times and parity). Neonatal anthropometric measurements (birth height, weight, and head circumference) were received after the new birth. Informed consent was signed and obtained by all subjects. Specific exclusion criteria were applied in the baseline cohorts. The women who suffered from the following conditions were excluded: (1) chronic diseases like hypertension, diabetes, cardiac, renal pathologies, and any other maternal history of illness; and (2) bad habits such as drug use ($n = 5$). Eligible infants were selected as only singleton births and no congenital diseases ($n = 2$). After excluding the undersized samples (10 mL) ($n = 4$) or faulted samples ($n = 3$), a total of 106 mother-infant couples were used in this research.

2.2. Sample collection and extraction

Experienced and certified midwives or obstetricians collected the cord blood aseptically at delivery. The cord blood was stored in sterile tubes and centrifuged immediately at 3000 rpm for 10 min to separate the serum. The serum was then collected and stored at −20 °C until further analysis.

Detailed methods of the extraction and clean-up process of the DDT residues in the cord serum are described in the Supporting Information (SI). We note that the methods were performed according to the US Environmental Protection Agency (U.S. EPA) method 608 with minor adjustments (Farhang et al., 2005; Jaraczewska et al., 2006). Thawed and homogenized samples were spiked with surrogate standards in 30 mL glass centrifuge tubes. Formic acid, ethanol, and hexane were added to each sample for ultrasonic extraction. The upper layer of the organic phase was collected after the centrifugation separation, and then the extraction was repeated with fresh solvents. The combined extracts were then filtered through anhydrous sodium sulfate and a 30% deactivated sulfuric acid silica clean-up column to remove the lipids. Finally, the extracts were carefully concentrated to approximately 1 mL by rotary evaporator and then to 50 μL in a GC vial insert using a gentle stream of nitrogen.

2.3. Quantification and enantioselective analysis of DDT and its metabolites

DDT and its metabolites were quantified by gas chromatography (GC, Agilent 7890)-mass spectrometry (MS, Agilent 5975C) equipped with an HP-5 MS column (30 m × 0.25 mm × 0.25 μm). The helium flow rate was set at 1.5 mL min^{-1}. The monitored ions in single ion monitoring (SIM) mode for DDE were 176, 246, and 318. Additionally, the monitored ions were 163,176 and 235 for DDD and DDT, respectively. For the enantioselective analysis of the *o,p*'-DDD and *o,p*'-DDT