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Urinary level of triclosan in a population of Chinese pregnant women and its association with birth outcomes☆

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ABSTRACT

Triclosan (TCS) is a suspected endocrine disrupting chemical which is widely used in consumer products as an antibacterial agent. But findings in human studies focusing on the fetal developmental effects of prenatal TCS exposure were rare and inconsistent. This study aimed to determine maternal urinary TCS and investigate its association with birth outcomes. Pregnant women (n = 1006) were randomly selected from the prospective Healthy Baby Cohort (HBC) enrolled in 2014. TCS levels were determined in maternal urine samples collected at delivery and recorded birth outcomes were obtained from the medical records. Multiple linear regressions were applied to evaluate associations of maternal urinary TCS levels with birth outcomes including birth weight, birth length, and gestational age. Logistic regressions were used to evaluate associations with preterm birth, late term birth, and low birth weight. The geometric mean concentrations for TCS and specific gravity (SG) adjusted TCS in maternal urines were 0.73, 0.78 ng/mL, respectively. In the crude model, one ln-unit increase of urinary SG-adjusted TCS concentration was associated with a 0.30-day [95% confidence interval (CI): 0.00, 0.60] increase in gestational age; however, the associations were not statistically significant after adjustment for covariates. No significant associations of SG-adjusted TCS concentrations with birth weight and birth length were observed. Maternal SG-adjusted TCS concentrations were not related to preterm birth, late term birth, and low birth weight (all $p > 0.10$). Our findings reported a relatively low level of TCS among Chinese pregnant women. With such exposure level, we did not find strong evidence for associations between maternal TCS exposure and birth outcomes. Longitudinal studies concerning about different potential effects of TCS on perinatal health are necessary.

1. Introduction

Triclosan (TCS), as a synthetic, broad-spectrum antimicrobial chemical, is extensively used in diverse personal care products, including toothpaste, soap, cosmetics, mouthwash, deodorants, as well as in toys, and kitchenware (Bhargava and Leonard, 1996; Calafat et al., 2008; Perencevich et al., 2001). Due to its widespread use, human beings are widely exposed to TCS mainly through ingestion and dermal route (Moss et al., 2000; Sandborgh-Englund et al., 2006). After oral exposure, TCS is primarily excreted in urine with a half-life of about 11 h (Sandborgh-Englund et al., 2006). Therefore, urinary TCS can be used as a valid biomarker for human exposure assessment (Calafat et al., 2008).

As a ubiquitous environmental contaminant (Petrie et al., 2015), TCS exposure has posed a threat to public health. Extensive use of TCS may lead to microbial resistance (Russell, 2003; Schweizer,

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2001), dermal irritations (Bhargava and Leonard, 1996), and increased incidence of allergies in children (Bertelsen et al., 2013; Savage et al., 2012). In addition, being a potential endocrine disruptor listed by USEPA (Westerhoff et al., 2005), evidence has shown TCS can affect estrogen (Stoker et al., 2010), testosterone (Kumar et al., 2009), and thyroid levels (Crofton et al., 2007; Zorrilla et al., 2009) in experimental animals. Associations between TCS exposure and hormone levels have also been observed in several epidemiological studies (Den Hond et al., 2015; Koeppe et al., 2013).

TCS is able to cross the placental barrier with detectable concentrations in umbilical cord blood (Pycke et al., 2014) and amniotic fluid (Philippat et al., 2013), leading the fetus to be exposed to its potential harmful health effects. In experimental animal studies, TCS is demonstrated to have toxic effects on fetal development (Axelstad et al., 2013; Paul et al., 2010, 2012; Rodriguez and Sanchez, 2010) and reproductive system (Rodriguez and Sanchez, 2010). Exposure to TCS in rats over the duration of gestation can induce decreases of body weight, reduction of gravid uterine weight, the occurrence of abortion, and impairment of thyroid homeostasis in offspring (Axelstad et al., 2013; Feng et al., 2016; Rodriguez and Sanchez, 2010). In humans, few epidemiological studies have examined the relationship between prenatal exposure to TCS and fetal growth, and their results have also been equivocal. Lassen et al. observed a significant positive relationship between maternal urinary TCS levels and birth length in male infants from Denmark (Lassen et al., 2016), and Wolff et al. found a possible sex-specific effect of TCS on birth length in a multiethnic cohort conducted in America (Wolff et al., 2008). However, other studies conducted in France and America reported no significant associations of maternal urinary TCS levels with birth outcomes (Geer et al., 2017; Philippat et al., 2012, 2014).

In short, the associations between prenatal TCS exposure and infant birth size remain unclear, and previous studies implicated there may exist sex-specific differences which have not been well examined (Wolff et al., 2008). The discrepant results may be caused by different exposure levels and different study populations. In consideration of absent data on the levels of TCS exposure in Chinese pregnant women and relatively lower exposure levels among Chinese general population than people from America and Europe (Calafat et al., 2008; Engel et al., 2014; Lankester et al., 2013; Li et al., 2013; Philippat et al., 2014; Yin et al., 2016), to better understand the potential developmental risk of TCS, it is critical to measure the levels of TCS exposure among Chinese pregnant women and assess its association with offspring size at birth among both male and female infants. In this study, we took advantage of our large prospective birth cohort to analyze TCS levels in maternal urines and explore the associations between maternal TCS exposure and infant birth outcomes in 1006 pregnant women in Wuhan, China.

2. Material and methods

2.1. Study population and data collection

This study was conducted among pregnant women participating in the “Healthy Baby Cohort (HBC)” project in China, which has been described in detail in a previous study (Yang et al., 2016). The longitudinal prospective study was conducted to explore the environmental exposures and genetic factors, and investigate their associations with the health of mothers and infants. The research protocol was approved by the ethics committees of the Tongji Medical College, Huazhong University of Science and Technology. All pregnant women received a detailed explanation and offered informed consent prior to participation.

Briefly, the prospective birth cohort has recruited 11,311 mother-infant pairs at Wuhan maternity hospital between September 2012 and October 2014. This study was designed to investigate pregnant women who provided urine samples and participated in this cohort during January to October 2014 ($n = 2245$). Considering the time and cost of analytes detection, we further randomly selected 1016 participants from those women to determine their urinary TCS levels. After exclusion of women who had an infant with a birth defect ($n = 7$), and who had missing pre-pregnancy BMI data ($n = 3$), a total of 1006 eligible pregnant women was included in this study. Pregnant women in this analytic population were generally similar to women in the full Healthy Baby Cohort with regard to demographics and other key covariates (Table S1).

2.2. Outcomes and covariates

Basic information on infants including birth weight, birth length, and gestational age were all retrieved from medical records. Nude birth weight [in grams (g)] and birth length [in centimeters (cm)] were measured for each infant within one hour after birth by experienced obstetric nurses using standardized procedures. Birth weight was measured by an electronic scale with the precision of 10 g which was used typically and routinely to weigh newborns at hospitals, and birth length was measured by a stadiometer (accurate to 1 mm). Gestational age (in days as a birth outcome, or in weeks as a covariate through dividing the days by 7) was estimated based on the date of the last menstrual period (LMP), or the first ultrasonographic estimation of the gestational age when women could not report accurate date of the LMP or there was a significant difference between the reported LMP and the ultrasonographic estimation (>7 days in this study). Preterm birth was defined as a birth with a gestation age less than 37 weeks. Late term birth was defined as a delivery at 41 weeks 0–6 days according to the recommendations from the Defining “Term” Pregnancy Workgroup (Spong, 2013). Low birth weight (LBW) was defined as an infant with birth weight less than 2500 g.

Covariate information was collected using questionnaires and medical records. The participants were interviewed face-to-face by trained nurses to collect information on their socio-demographic data (e.g., annual household income, occupation, and self-reported weight before pregnancy), medical history as well as lifestyle factors during pregnancy (such as smoking, passive smoking, and alcohol consumption). The interviews were conducted in the hospital within three days before or after delivery. The other information on maternal age and weight at delivery, maternal education, infant sex, birth date, delivery mode, and history of pregnancy outcomes and disease was retrieved from medical records. The mothers' pre-pregnancy body mass index (BMI) was calculated using self-reported pre-pregnancy weight and height measured by a stadiometer.

2.3. Urine sample collection and TCS measurement

Maternal urine samples were collected from pregnant women immediately after they were admitted to the hospital before they took any medical examination or medical therapy as awaiting delivery, and divided into aliquots storing in the polypropylene tubes at −20 °C (°C) until further analysis.

The urinary TCS was measured by liquid-liquid extraction-ultra performance liquid chromatography tandem mass spectrometry (UPLC-MS/MS), as previously detailed by Asimakopoulos et al. (Asimakopoulos et al., 2014) with some modifications. In brief, one milliliter aliquots of urine samples were spiked with 25 μL isotope-labeled internal standard working solution containing 10 ng of $^{13}C_{12}$-TCS [purchased from Cambridge Isotope Laboratories (Andover, MA, USA)], and then 200 μL of 1 M ammonium acetate buffer

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