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Perfluoroalkyl and polyfluoroalkyl substances in matched parental and cord serum in Shandong, China

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ABSTRACT

Background: Perfluoroalkyl and polyfluoroalkyl substances (PFASs) have been widely detected in different populations. However, limited data is available about exposure among family members.
Objectives: To investigate the PFASs levels in parents and their newborns and to understand their correlation and health implications of in utero exposure to PFASs.
Methods: Ten PFASs were measured in matched parental and cord serum (N = 369 families) from a birth cohort in Shandong, one of the regions seriously polluted by PFASs in China. The correlation of PFASs levels within families was examined. A questionnaire survey on maternal factors and risk assessment using the hazard quotients (HQs) approach based on maternal PFASs levels was conducted.
Results: Within a family, the father had the highest levels of all PFASs. Among the 10 PFASs, perfluorooctanoic acid (PFOA) was the highest, with 103.38, 42.83, and 34.67 ng/ml in paternal, maternal and cord serum, respectively. PFASs levels were positively correlated among family members ($r = 0.14$–0.91, $p < 0.01$). Maternal age, body mass index (BMI); smoking history; and intake of fish, milk, poultry, vegetables and tap water were significantly related to PFASs concentrations in cord serum. Twenty-seven (7.3%) HQ values exceeded 1 for both PFOA and the sum of PFOA and perfluorooctane sulfonate (PFOS), indicating potential concern for developmental toxicity in the local newborns.
Conclusions: PFASs, and especially PFOA levels were extremely high and positively correlated between parents, indicating heavy pollution in this region and common sources of exposure. In utero exposure to PFASs might pose potential concern for developmental toxicity in the local newborns.

1. Introduction

Perfluoroalkyl and polyfluoroalkyl substances (PFASs) are synthetic fluorinated chemicals widely used in consumer and industrial products, including fire-fighting foams, non-stick cookware, insecticides etc. (Paul et al., 2009). PFASs are resistant to environmental degradation and can accumulate in mammals. Epidemiological studies have indicated their toxic effects on human reproduction and endocrine functions (Darrow et al., 2014; Fei et al., 2009; La Rocca et al., 2014). In particular, some PFASs can cross the placenta and influence the developing fetus, such as increasing the risk of low birth weight (Robledo et al., 2015; Wang et al., 2016b), thyroid disruption (Kato et al., 2016; Shah-Kulkarni et al., 2016) and neurodevelopmental disorders (Goudarzi et al., 2016).

The production and use of some PFASs have been prohibited in Western Europe, America and Japan (Land et al., 2015; Paul et al., 2009) in the past decade, and the levels of PFASs have sustained a continued decline in humans, including in susceptible populations, such as pregnant women (Bjerregaard-Olesen et al., 2016; Glynn et al., 2012). However, in China, the production and use of PFASs are still allowed, and an increase over the past 15 years has been seen (Xie et al., 2013). From 1999 to 2002, the levels of PFASs increased 7.5-fold for PFOS and 5.0-fold for perfluorooctanoic acid (PFOA) in adult serum (Jin et al., 2007). Recently, a study from Shanghai showed that

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concentrations of PFOA in cord blood samples were much higher than those in previous reports from other countries (Wang et al., 2016a). However, in China, limited data is available on paired pregnant women and newborns, a vulnerable population. There is even less information on the similarities of PFASs exposure among family members, which would help us explore the possible pathways and sources of exposure.

Food consumption, drinking water, consumer products, house dust and air have been suggested to be the potential routes in adults (Zhang et al., 2010). However, the contributions of demographic characteristics, lifestyle, food consumption and sources of drinking water to PFASs concentrations in serum may vary depending on the geographic location, population characteristics, and specific PFASs compounds. Yet information on potential determinants in China is still limited.

In addition, whereas the widespread use of PFASs in China has resulted in higher exposure levels in pregnant women, little is known about the potential risk of maternal PFASs exposure to their newborns. Only one study assessed the risk in Shanghai newborns based on the PFASs levels in cord plasma, in which no potential developmental toxicity was found (Wang et al., 2016a). Because of limited literature and the uncertainties in the existing data, there is a compelling need to evaluate the potential risk of prenatal exposure of PFASs to newborns in China, especially in high-exposure areas such as industrial zones.

To address these problems, we quantified 10 PFASs in 369 matched parental and cord serum samples from a birth cohort at an industrial area, one of the major chemical product manufacturing bases in China. Our aims were to describe PFASs levels in members from the same family in China, to examine the correlation between them and explore potential maternal factors related to PFASs levels in cord serum, and to assess newborns' health risk resulting from prenatal exposures to PFOS and PFOA, using an HQ approach.

2. Materials and methods

2.1. Study population

The Laizhou Wan Birth Cohort (LWBC) was a prospective birth cohort study conducted between September 2010 and December 2013 to assess the effects of environmental exposures on the health of parents and their children living in the south coast of Laizhou Wan (Bay), Shandong Province, in East China. We recruited and briefly interviewed the couples when they were preparing for delivery in the only county hospital located in this area. Eligibility criteria included: pregnant women older than 18 years, a singleton pregnancy, having lived in this area for at least 3 years and agreement to participate in our program (signing an informed consent). The exclusion criteria included: pregnant women with history of using assisted reproductive technology, preexisting or gestational diabetes, chronic or pregnancy-associated hypertension, AIDS or HIV infection, and illicit drug use. Their newborns were enrolled at birth and have been followed throughout childhood.

In total, 773 families participated in this study, of which 404 families without matched parental or cord serum samples were excluded (the excluded group). Finally, 369 families with matched parental and cord serum samples were enrolled in this analysis (called the PFASs group). The demographic and exposure characteristics were comparable between the PFASs group and the excluded group, and there was no difference between the two groups in demographic characteristics (see Table S1). Therefore, the present study families (PFASs group) can reflect the original one with 773 families. Every participant signed a written informed consent, and the study protocol was approved by the Medical Ethics Committee of Xinhua Hospital affiliated to Shanghai Jiao Tong University School of Medicine.

2.2. Questionnaires and medical records

After delivery, the parents were interviewed face to face by trained nurses using a 20-minute questionnaire. The questionnaire included the following parental socio-demographic factors: age, height and pre-pregnancy weight, educational level, smoking and passive smoking before and during pregnancy, and alcohol intake before and during pregnancy. We used a semi-quantitative food frequency questionnaire to estimate the maternal dietary factors during pregnancy. The mothers were asked to report how often they consumed 12 kinds of foodstuffs per week during the previous 10 months. The frequency categories included: none (0 time/month), rarely (< 1 time/week), not regularly (1–3 times/week), regularly (4–7 times/week), and everyday (≥ 8 times/week). Information related to maternal reproductive history and current pregnancy complications was obtained through interview and confirmed with medical records. Other relevant information, such as type of delivery, gestational age, and the baby's sex was acquired from the medical records.

2.3. Serum collection and analysis of PFASs

The parental random blood samples were collected upon admission for labour. The cord blood samples were obtained immediately following delivery of the placenta. The parental and cord blood samples were centrifuged at 3000 rpm for 15 min and 1500 rpm for 20 min, respectively, and the serum was poured into pre-cleaned glass vials. The serum was then immediately stored at −80 °C, followed by shipment on dry ice to the laboratory at Xinhua Hospital affiliated to Shanghai Jiao Tong University School of Medicine for analysis.

Concentrations of PFOS, PFOA, perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUA), perfluorohexane sulfonic acid (PFHxS), perfluorobutane sulfonic acid (PFBS), perfluorododecanoic acid (PFDoA), perfluorooctane sulfonamide (PFOSA) and perfluoroheptanoic acid (PFHpA) were detected in 100 μl serum using high-performance liquid chromatography coupled with tandem mass spectrometry (HPLC–MS/MS, Agilent 1290–6490, Agilent Technologies Inc., USA). Details of the analytical methods used have been described previously (Wang et al., 2016a). Briefly, extraction of the serum samples was conducted by methanol and acetonitrile of 1% formic acid. Quantification of PFASs was determined using the internal-standard method (internal standards: $13C_4$-PFOS and $13C_4$-PFOA). Both quality control and calibration standard materials were prepared by spiking the standard mixture of the 10 analytes into blank fetal bovine serum. For each analysis, according to the six standard concentrations, a calibration curve was obtained and was used for quantification. The coefficient of determination of the calibration curve was high, with $R \geq 0.99$ for all compounds. We also used replicated analysis of two samples to estimate the accuracy and precision. The percentage recovery (± SD) ranged from 91.4 (± 7.6) to 103.5 (± 1.8). The intra-day and inter-day precision (% RSD) ranged from 0.8 to 8.5 and 1.7 to 8.4%, respectively. The limits of detection (LOD) were defined as 3-fold higher than the signal-to-noise ratio, which ranged from 0.009 to 0.12 ng/ml for 10 PFASs.

2.4. Assessment of infant health risk

We assessed the potential health using the hazard quotient (HQ) approach, which is defined as the ratio between actual serum levels and reference serum levels observed at points of departures (PoDs) (Borg et al., 2013; Ludwicki et al., 2015). Established dose-response relationship, i.e. no observed adverse effect level (NOAEL) or benchmark dose (BMD) is identified as PoDs for relevant toxicological outcomes (Kirman et al., 2011). Because of lack of epidemiological data clearly indicating a PoD, animal studies are often used to indicate a PoD for a specific toxicological outcome with appropriate uncertainty factors (UFs) being taken into calculation for variations. In our study, the PoDs and UFs were applied according to the relevant studies of the United States Environmental Protection Agency (EPA) (US EPA, 2016a,b). Their risk assessment was based on two animal toxicity experiments,