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Perfluoroalkyl substances in umbilical cord serum and gestational and postnatal growth in a Chinese birth cohort

Wencheng Cao[a,1], Xiao Liu[a,1], Xiaofang Liu[b,a], Yan Zhou[a], Xiaotian Zhang[a], Haoyuan Tian[c], Jin Wang[c], Shixian Feng[d], Yongning Wu[e], Parveen Bhatti[f], Sheng Wen[a,*,2], Xin Sun[c,**,2]

[a] Hubei Provincial Key Laboratory for Applied Toxicology, Hubei Provincial Center for Disease Control and Prevention, #6 Zhuo Daoquan North Road, Wuhan 430079, PR China
[b] Analytical Chemistry, School of Chemical and Environmental Engineering, Wuhan Institute of Technology, LiuFang Campus, No.206, Guanggu 1st road, Wuhan 430205, PR China
[c] Key Laboratory of Chemical Safety and Health, National Institute of Occupational Health and Poison Control, Chinese Center for Disease Control and Prevention, #27 Nan Wei Road, Beijing 100050, PR China
[d] Institute of Chronic and Non-Communicable Disease Control and Prevention, Henan Provincial Center for Disease Control and Prevention, Nongye Donglu South, Zhengzhou 450016, PR China
[e] The Key Laboratory of Food Safety Risk Assessment, Ministry of Health (CFSA) and China National Center for Food Safety Risk Assessment, #7 Panjiayuan Nanli, Beijing 100021, PR China
[f] Public Health Sciences Division, Fred Hutchinson Cancer Research Center, 1100 Fairview Ave. N., Seattle, WA 98109, USA

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ABSTRACT

Although animal studies have found that perfluoroalkyl substances (PFASs) affect gestational and postnatal growth, the epidemiological findings are limited and not in agreement. We explored the associations of PFAS concentrations in umbilical cord blood with gestational and postnatal growth in China. Three hundred thirty-seven singleton newborns and their mothers were recruited from November 2013 to December 2015 in Zhoukou City, China. Umbilical cord blood was collected to measure eleven PFASs by liquid chromatography-mass spectrometry. The index of gestational and postnatal growth contained fetal weight, length, and head circumference. These were obtained at birth and at the follow-up investigation (mean 19 months). Exposed to higher perfluorooctanoic acid (PFOA) were connected with reduced length at birth (p for trend = 0.01) and decreased postnatal weight (β = −429.2 g; 95% CI: −858.4, −0.121 for 2nd VS. 1st). Exposed to perfluoroundecanoic acid (PFUdA) were positively associated with indications of gestational growth and postnatal growth (p for trend = 0.02 for birth length; p for trend = 0.04 for postnatal length). Exposed to higher perfluorododecanoic acid (PFDoA) were associated with lower birth weight (β = −122.9 g, 95% CI: −244.7 to −1.2 for 2nd VS. 1st), but higher postnatal length (p for trend = 0.03). Neonates in the highest exposure group of per-fluorohexanesulfonate (PFHxS) showed decreased birth length (β = −0.33 cm, 95% CI: −0.68 to −0.01, for 2nd VS. 1st), but increased postnatal head circumference (p for trend = 0.04). Increased PFOA concentrations was associated with shorter birth length only in girls (p for trend = 0.04), suggesting that the effect of PFASs on gestational growth were different between boys and girls. In utero exposure to PFASs may affect gestational and postnatal growth.

1. Introduction

Because of their water and oil repelling properties, perfluoroalkyl substances (PFASs) are utilized in fluoropolymer manufacturing, for example, food packaging, clothes, shoes, furniture, and non-stick cookware (Giesy and Kannan, 2002). PFASs persist globally, and easily accumulate in wildlife and humans (Lau et al., 2006; Morikawa et al., 2006; Olsen et al., 2004). Exposure to PFASs is caused by ingestion, inhalation, and dermal contact (Fromme et al., 2009). Uniting with proteins, PFASs accumulate mainly in organ tissue, such as liver, blood,

* Correspondence to: S. Wen, Institute of Health Inspection and Detection, Hubei Provincial Academy of Preventive Medicine, Hubei Provincial Center for Disease Control and Prevention, Wuhan, Hubei, PR China.
** Corresponding author.
E-mail addresses: wenshenggy@aliyun.com (S. Wen), sunxin@chinacdc.cn (X. Sun).
[1] The two authors contributed equally to this work and should be considered to be the co-first author.
[2] The two authors contributed equally to this work.

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kidney, and their biological half-life was fairly long (3–9 years) (Jones et al., 2003; Olsen et al., 2007).

In rats and mice, PFASs have been associated with developmental toxicities, including neonatal and postnatal developmental abnormality of offspring, congenital malformation, pregnancy loss, and low survival rate (Butenhoff et al., 2004; Lau et al., 2004). Nevertheless, the results on the impact of exposure to PFASs on neonatal and postnatal development are inconsistent in humans. Maternal blood perfluorooctanoic acid (PFOA) and perfluorooctanesulfonate (PFOS) concentrations during gestation have been inversely connected with birth weight (Fei et al., 2007; Wu et al., 2012). Apelberg et al. (2007) also reported that higher cord serum PFAS concentrations were related to decreased ponderal index (PI). Others did not report any effect of exposure to PFASs during pregnancy on neonatal growth (Hamm et al., 2009; Nolan et al., 2009).

Previous studies have mainly focused on maternal blood PFAS levels, with fewer studies evaluating levels in umbilical cord serum. PFAS concentrations in cord blood have been correlated with those in maternal blood (Kim et al., 2011), suggesting that maternal serum is a proxy for cord serum. However, PFAS composition between the two matrices may be different due to chemical-specific differences in transfer efficiency, indicating that the relative exposure of PFASs to the fetus during in utero growth can be different among mothers (Kim et al., 2011).

The present study measured PFAS concentrations in umbilical cord blood as in utero exposure and explored to the relationships between exposure to PFASs and gestational and postnatal growth in a longitudinal birth cohort based in Zhoukou City, China.

2. Method

2.1. Study design and population

We recruited the study population in a longitudinal birth cohort established from November 2013 to December 2015 in Zhoukou City, China. At first, we recruited a total of 375 mother-infant pairs in this cohort at birth. Among them, 365 (97.3%) provided cord blood samples. We set the following inclusion criteria for our subjects: native Chinese mothers with a single live infant who had lived in the local residence for > 1 year. Thus, 28 participants were excluded. Finally, 337 mother-infant pairs were included for analysis. Excluding 55 infants lost to follow-up, 282 (83.6%) infants underwent the follow-up investigation on postnatal growth from December 2014 to December 2015. The present study was examined and ratified by the Ethics Committee of the National Institute for Occupational Health and Poison Control of the Chinese Center for Disease Control and Prevention.

2.2. Questionnaires

All mothers were interviewed by the practical investigators to complete a questionnaire survey when they stayed in the hospital for delivery and at the postpartum follow-up survey. The questionnaire assessed various demographic factors (parents' age, maternal education, and monthly household income), fathers' job, smoking and drinking habits, and parity.

2.3. Measurements on gestational and postnatal growth

Measurements on gestational growth, including infants' gender, birth weight (g), birth length (cm), and ponderal index (PI), were extracted from the birth records in the hospital. Measurements on postnatal infant's data, included age (months), postnatal weight (g), postnatal length (cm), and postnatal head circumference (cm). Postnatal length and weight were measured by a nurse at the follow-up interview. PI was calculated by the following formula: PI = [weight (g) / length^3 (cm^3)] × 100.

2.4. Blood sample collection and analyses

The nurse collected ten milliliters of cord blood in ethylenediaminetetraacetic acid (EDTA) vials at birth, and then centrifuged serum samples were sent with dry ice to the Dioxin Reference Laboratory (Chinese Ministry of Health) for analysis. The serum samples were frozen and preserved at −40 °C before analysis.

We used the highest purity reagents and solvents (such as methanol, ammonium acetate, TBA, and MTBE). A list of all native and labelled standards of PFASs used in this study is provided in the Supplementary material, Page S3.

Detailed information about sample preparation and analysis has been recorded elsewhere (Yang et al., 2016). In short, the ion-pair extraction method was conducted to extract the serum sample. One milliliter of serum and 1 ng of internal standard solution were added into a 15-mL polypropylene tube and then mixed with 1 mL × 0.5 M tetra-*n*-butylammonium hydrogen sulfate (TBA, Mreda, Beijing, China) solution and 2 mL × 0.25 M sodium carbonate (analytical grade, Beijing Chemical Works, Beijing, China) buffer. After centrifugation, 5 mL of methyl tert-butyl ether (MTBE, HPLC, Tedia, Fairfield, USA) rinsed the aqueous mixture twice. All supernatants were transferred to another polypropylene tube, and evaporated to dryness under nitrogen flow at 45 °C. Then, 1 mL of methanol/water (1:1) (Methanol, HPLC, Fisher, Hampton, USA) was added in the tube. Finally, a 0.2-μm nylon filter (Sartorius, Gottingen, Germany) was used to filter the supernatant.

PFASs were separated and quantified by liquid chromatography combined with a triple quadrupole mass spectrometry (Agilent, Santa Clara, USA). BEH C18 2.1 mm × 100 mm × 1.8 μm column (Agilent, USA) was used for separation of compounds. Multiple reaction monitoring (MRM) mode was chosen to conduct quantitative detection. The mass transition for each compound has been described in Supplementary material Table S1. Negative electrospray ionization (ESI^-) was adopted for the mass spectra. We used methanol and 2 mmol of aqueous ammonium acetate (HPLC, Sinopharm, Shanghai, China) solutions as mobile phases at a flow rate of 0.3 mL/min.

We compared the area of target compound with the isotopic labelled PFAS compound to perform quantification of 11 PFASs [PFOA, perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUdA), perfluorododecanoic acid (PFDoA), perfluorotridecanoic acid (PFTrDA), perfluorotetradecanoic acid (PFTeDA), perfluorohexadecanoic acid (PFHxDA), per-fluorohexanesulfonate (PFHxS), PFOS, and perfluorodecanesulfonate (PFDS)]. Analytes without an isotope labelled standard were quantified using the internal standard with the closest retention time (see Supplementary material, Table S1). For each analyte a six point calibration curve was made, ranging from 0.05 to 10 ng/mL. Calibration curves were linear over the concentration range with r values > 0.99 for all compounds. The details on quality control have been described in the Supplementary material p S2. The limits of detection (LODs) for PFASs ranged from 0.01 to 0.02 ng/mL, and the extraction recovery rate was between 76% and 103%, respectively.

2.5. Statistical methods

Total PFASs was defined as the sum of 11 PFASs in the present study. PFASs with the high detection rate (> 70%, including PFOA, PFOS, PFHxS, PFNA, PFDA, PFUdA, and PFDoA) and total PFASs, were divided into tertiles; PFASs with the low detection rate (< 40%, including PFTrDA, PFTeDA, PFHxDA, and PFDS) were divided in to two groups by the LODs. We made the lowest group as the reference category, and then treated the PFAS concentration groups as ordinal variables in regression models to conduct tests for trend.

Data analysis was conducted using PASW version 21.0 (IBM corporation, Armonk, New York, USA), and statistical significance was defined as a p value ≤0.05. We made use of general linear models to estimate the relationship between PFASs concentrations and continuous