Environment International 102 (2017) 1–8

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Isomers of perfluorooctanesulfonate (PFOS) in cord serum and birth outcomes in China: Guangzhou Birth Cohort Study

Meng Li [a,1], Xiao-Wen Zeng [a,1], Zhengmin (Min) Qian [b,1], Michael G. Vaughn [c], Sébastien Sauvé [d], Gunther Paul [e], Shao Lin [f], Long Lu [g], Li-Wen Hu [a], Bo-Yi Yang [a], Yang Zhou [a], Xiao-Di Qin [a], Shu-Li Xu [a], Wen-Wen Bao [a], Ya-Zhi Zhang [a], Ping Yuan [a], Jia Wang [a], Chuan Zhang [a], Yan-Peng Tian [a], Min Nian [a], Xiang Xiao [a], Chuanxi Fu [h,i,*], Guang-Hui Dong [a,**]

[a] Guangzhou Key Laboratory of Environmental Pollution and Health Risk Assessment, Department of Preventive Medicine, School of Public Health, Sun Yat-sen University, Guangzhou 510080, China
[b] Department of Epidemiology, College for Public Health and Social Justice, Saint Louis University, Saint Louis 63104, USA
[c] School of Social Work, College for Public Health and Social Justice, Saint Louis University, Saint Louis 63104, USA
[d] Department of Chemistry, Université de Montréal, Montreal, QC H3C 3J7, Canada
[e] Faculty of Health, School of Public Health and Social Work, Queensland University of Technology, Kelvin Grove, QLD 4059, Australia
[f] Department of Epidemiology and Biostatistics, School of Public Health, State University of New York, Albany, NY 12144-3445, USA
[g] Liwan District Maternal and Child Health Hospital, Guangzhou 510375, China
[h] Zhejiang Chinese Medical University, Hangzhou 310053, China
[i] Guangzhou Center for Disease Control and Prevention, Guangzhou 510440, China

ARTICLE INFO

Article history:
Received 12 October 2016
Received in revised form 6 March 2017
Accepted 6 March 2017
Available online xxxx

Keywords:
Polyfluoroalkyl substances (PFASs)
Isomers
Birth weight
Gestational age

ABSTRACT

Prior investigations on the associations of polyfluoroalkyl substances (PFASs) with fetal growth are mixed. Moreover, little research has accrued pertaining to the association between isomers of PFASs with gestational age and birth weight. To address this gap and present novel information, we conducted a study including 321 pairs of mothers and their infants recruited from Guangzhou, China. High performance liquid chromatography-mass spectrometry was utilized to analyze isomers of perfluorooctanesulfonate (PFOS), perfluorooctanoate (PFOA) along with other PFAS levels in cord serum samples. Mothers' and infants' characteristics were gathered from medical records. The resulting data revealed that higher PFOS, PFOA and isomers of PFOS were associated with lower birth weight. Per ln-unit (ng/mL) increase in cord serum total branched PFOS isomers was associated with a 126.3 g (95% CI: −195.9, −56.8) reduction in the weight of infants at birth, while an ln-unit (ng/mL) increase of serum linear PFOS isomers (*n*-PFOS) was associated with a 57.2 g (95% CI: −103.1, −11.3) reduction in the weight of infants at birth upon the subsequent adjustment for potential confounding variables. Notably, the association between cord PFAS level and birth weight was more pronounced in male infants. Furthermore, a positive association among branched PFOS isomers (1m-PFOS and 3 + 4 + 5m-PFOS) and gestational age was found. No associations could be found among other PFASs in conjunction with gestational age or birth weight. In conclusion, this investigation suggests that higher PFAS concentrations are associated with lower birth weight, and branched PFOS isomers show greater impact on infant birth weight than linear PFOS.

1. Introduction

An emergent body of research has revealed evidence concerning the absorption in some populations of a class of persistent organic pollutants, perfluoroalkyl as well as polyfluoroalkyl substances (PFASs). The absorption of PFASs has been observed in both humans and animal studies (Buck et al., 2011; Lau et al., 2007; Olsen et al., 2012; Zeng et al., 2015). While a range of pollutants fall within the category of PFASs, perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) have gained the most attention. The focus on these particular pollutants is due to their tendency to bioaccumulate. Once absorbed

* Correspondence to: C. Fu, Zhejiang Chinese Medical University, Huangzhou 310053 and Guangzhou Center for Disease Control and Prevention, Guangzhou 510440, China.
** Correspondence to: G.-H. Dong, Guangzhou Key Laboratory of Environmental Pollution and Health Risk Assessment, Department of Preventive Medicine, School of Public Health, Sun Yat-sen University, 74 Zhongshan 2nd Road, Yuexiu District, Guangzhou 510080, China.
E-mail addresses: fucx@gzcdc.org.cn (C. Fu), donggh5@mail.sysu.edu.cn (G.-H. Dong).
[1] These authors contributed equally to this work and should both be list as the first author.

http://dx.doi.org/10.1016/j.envint.2017.03.006
0160-4120/

into the system, the half-lives of these chemicals ranges somewhere between 3 and 5 years within human serum (Olsen et al., 2007).

Because PFASs are commercially appealing (owing to their increased surface area, chemical and thermal stability, and tensioactive properties), they have been used as surfactants in detergents, fire-fighting foams, preparation of leather, food packaging, along with a number of other common items (Cariou et al., 2015; Kantiani et al., 2010; Trier et al., 2011). The production of these pollutants involves electrochemical fluorination (ECF) as well as telomerization. The ECF method—which has been utilized in the manufacturing of the majority of PFOS (and precursor materials that have a larger molecular weight), perfluorohexane sulfonate (PFHxS), along with PFOA by the 3M Company since 1949, and was phased-out in 2001—results in 20–30% branched isomers (Beesoon et al., 2011; Paul et al., 2009). In contrast, the telomerization method, which DuPont originally developed in the 1970s and continues to be used for PFOA manufacturing, produces isomers that are almost completely linear (Benskin et al., 2010; Kissa, 2005). Although data from the National Health and Nutrition Examination Survey has indicated a decrease in cord serum PFAS levels in the general U.S. population following the discontinuation of some PFASs (Kato et al., 2011), other countries in Europe and Asia (Benskin et al., 2010; Jiang et al., 2014), especially China, continue to produce PFASs using the ECF method. The manufacturing of PFOS in China has rapidly increased in 2003–2006, having reached approximately 250 tons in 2006 and continuing (Xie et al., 2013).

Perhaps what is most concerning is that epidemiologic evidence shows that PFASs can cross through the placenta into the fetus, thereby influencing fetal growth processes (Beesoon et al., 2011; Fei et al., 2007; Inoue et al., 2004; Kim et al., 2011; Koustas et al., 2014; Midasch et al., 2007). This evidence, however, is equivocal. For example, some studies found that exposure to PFOS and PFOA during pregnancy may lead to detrimental effects on fetal growth (Apelberg et al., 2007; Chen et al., 2012; Fei et al., 2007; Kishi et al., 2015; Maisonet et al., 2012; Washino et al., 2009; Wu et al., 2012), but other investigations have not observed such associations (Arbuckle et al., 2013; Bach et al., 2016; Darrow et al., 2013; Hamm et al., 2010; Kim et al., 2011; Lee et al., 2016; Lee et al., 2013; Monroy et al., 2008; Savitz et al., 2012a, 2012b; Whitworth et al., 2012). Johnson et al. (2014) executed a systematic review and meta-analysis of the links between PFOA and fetal growth that demonstrated consistent incremental impact on fetal growth when pooling the data together.

Some studies have reported the differences of isomer-specific and branched-specific PFASs in their pharmacokinetic properties (De Silva et al., 2009a, 2009b; Loveless et al., 2006; O'Brien et al., 2011). Prior research has indicated that branched PFOS isomers possess a higher transcriptional response than linear PFOS isomers alone, when cultured in embryonic chicken hepatocytes (O'Brien et al., 2011). In contrast, some pharmacokinetic studies indicated that linear PFOS isomers along with the linear PFOA isomers are preferentially accumulated (Benskin et al., 2009; De Silva et al., 2009a, 2009b; O'Brien et al., 2011; Sharpe et al., 2010), and demonstrated that linear PFOA isomers harbor greater toxicity than branched PFOA isomers (Loveless et al., 2006). In a recent human study, Beesoon et al. (2011) reported that total branched isomers moved though the placenta more efficiently compared to linear isomers. For both PFOS and PFOA, it was also shown that the placental transfer of branched isomers of PFOS increased in number as the branching point shifted closer to the sulfonate (SO_3^-) end of the molecule. This finding suggests that the branched and linear PFASs show differential toxicity and accumulation.

Given the aforementioned research context, we hypothesized that isomer-specific associations between exposure to PFASs and fetal growth may differ, and that branched isomers of PFASs would be more strongly associated with adverse pregnancy outcomes than linear isomers of PFASs. Moreover, when considering observed gender-specific differences of the toxic impact induced by PFASs in previous research (Bach et al., 2016; Keil et al., 2008; Peden-Adams et al., 2008; Wang et al., 2011; Washino et al., 2009; Zhu et al., 2016), we also hypothesized differential gender-specific associations. Few studies have adequately examined isomer profiles of PFASs in human cord serum (Zhang et al., 2013a, 2013b; Zhang et al., 2014; Beesoon et al., 2011), and in particular, in umbilical cord serum (Beesoon et al., 2011). And to the best of our knowledge, no study has reported the connection between an exposure to isomer profiling of PFASs and the growth of a fetus.

2. Methods

2.1. Study population and sample collection

The overall objective of the Guangzhou Birth Cohort Study (GBCS) was to assess the potential effect of environmental pollution exposure in utero on the development of the nervous system in childhood. From July through October 2013, pregnant women were recruited from one hospital in Guangzhou City in Southern China. Cord blood samples were collected immediately after delivery and centrifuged within 3 h. Next, cord serum was kept at −80 °C in 2-mL methanol-rinsed polypropylene cryovials (Apelberg et al., 2007). The final study sample included 321 women, and further, four women had to be excluded due to insufficient volume of the biospecimen. Written informed consent was collected from each participant. The study protocol was approved by the Institutional Review Board (Sun Yat-sen University Research Ethics Committee), and all study procedures were in compliance with the principles detailed within the Helsinki Declaration.

2.2. Outcomes

Outcomes examined in the present study (obtained from medical records) included gestational age (weeks), birth weight (grams), preterm birth, low birth weight (LBW). Gestational age was calculated based on last menstrual period (LMP). Preterm birth was defined as a gestational age < 37 weeks. LBW was characterized as a birth weight < 2500 g.

2.3. Covariates

Information regarding demographic characteristics such as maternal age and educational level were obtained from prenatal questionnaires. In addition to these characteristics, other information such as pregnancy-induced hypertension (PIH), gestational diabetes mellitus (GDM), parity, and anemia during pregnancy were obtained from medical records. PIH was assessed in concordance with the criteria of the International Society for the Study of Hypertension in Pregnancy as diastolic blood pressure > 90 mm Hg and/or systolic blood pressure > 140 mm Hg, measured on ≥2 separate occasions ≥4 h apart (Brown et al., 2001). GDM was diagnosed according to the IADPSG criteria at 24–28 weeks of gestation but with fasting plasma glucose (FPG) <4.4 mmol/L (International Association of Diabetes and Pregnancy Study Groups Consensus Panel et al., 2010). Anemia occurring during pregnancy was defined as hemoglobin (Hb) < 11 g/dL. Parity was defined as any previous live birth.

2.4. Serum total PFASs and isomeric PFASs analysis

PFASs were measured from 0.5 mL of serum utilizing Agilent high-performance liquid chromatography (HPLC) in tandem with an Agilent 6410 Triple Quadrupole (QQQ) mass spectrometer (MS/MS) (Agilent, Palo Alto and Santa Clara, CA). Information regarding the standards and reagents, sample preparation and extraction, instrumental analysis, quality assurance and quality control, along with recovery experiments in the present study is provided in the Supplementary material and is also described elsewhere (Benskin et al., 2007; Kuklenyik et al., 2004). PFASs and isomers were analyzed in serum samples, and the detail of abbreviation of PFASs and nomenclature of PFOS/PFOA isomers are provided in the Supplemental material, Table S1. Online Resource Table S2