Environmental Pollution 212 (2016) 1–6

Contents lists available at ScienceDirect

Environmental Pollution

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

Positive associations of serum perfluoroalkyl substances with uric acid and hyperuricemia in children from Taiwan☆

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ARTICLE INFO

Article history:
Received 15 January 2016
Received in revised form
24 February 2016
Accepted 24 February 2016
Available online xxx

Keywords:
Perfluoroalkyl substances
Uric acid
Hyperuricemia
Children

ABSTRACT

To investigate the risk of hyperuricemia in relation to Perfluoroalkyl substances (PFASs) in children from Taiwan, 225 Taiwanese children aged 12–15 years were recruited from 2009 to 2010. Linear and logistic regression models were employed to examine the influence of PFASs on serum uric acid levels. Findings revealed that eight of ten PFASs analyses were detected in >94% of the participants' serum samples. Multivariate linear regression models revealed that perfluorooctanic acid (PFOA) was positively associated with serum uric acid levels ($\beta = 0.1463$, $p < 0.05$). Of all the PFASs analyses, only PFOA showed a significant effect on elevated levels of hyperuricemia (aOR = 2.16, 95%CI: 1.29–3.61). When stratified by gender, the association between serum PFOA and uric acid levels was only evident among boys (aOR = 2.76, 95%CI: 1.37–5.56). In conclusion, PFOA was found to be associated with elevated serum levels of uric acid in Taiwanese children, especially boys. Further research is needed to elucidate these links.

1. Introduction

Perfluoroalkyl and polyfluoroalkyl substances (PFASs) are a diverse class of chemicals that possess unique properties such as extremely high thermal and chemical stability and are widely used in various manufacturing and industrial processes, such as fire-fighting foams, paints, semiconductors, photographic films, and pesticide formulations (Rahman et al., 2014). Because of their chemical stability and widespread use, a growing number of studies have found that PFASs are ubiquitous and persistent in both

Abbreviations: PFASs, polyfluoroalkyl substances; PFBS, perfluorobutane sulfonate; PFHxS, perfluorohexane sulfonate; PFOS, perfluorooctane sulfonate; PFHxA, perfluorohexane acid; PFHpA, perfluoroheptanoic acid; PFNA, perfluorononanoic acid; PFOA, perfluorooctanic acid; PFDA, perfluorodecanoic acid; PFDoA, perfluorododecanoic acid; PFTA, perfluorotetradecanoic acid; GBCA, Genetic and Biomarkers study for Childhood Asthma; IQR, interquartile range; ORs, odds ratio; 95%CI, 95% confidence intervals.

☆ This paper has been recommended for acceptance by Eddy Y. Zeng.

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http://dx.doi.org/10.1016/j.envpol.2016.02.050
0269-7491/

biotic samples and the abiotic environment worldwide, for example, lakes (Cao et al., 2015), sea sediments (Zhu et al., 2014) and even in the world's southernmost marine mammal, the Weddell seal (Routti et al., 2015). In addition, human exposure to PFASs is well demonstrated, as these compounds have been found in blood samples from both children and adults (Fromme et al., 2007; Schecter et al., 2012; Zhou et al., 2014). In recent years, semiconductor, electrochemical, and optoelectronic industries have quickly grown in northern Taiwanese cities. This has resulted in high levels of PFOS and PFOA contamination in several river systems in Taiwan (PFOS up to 5440 ng/L; PFOA up to 310 ng/L) (Chimeddulam and Wu, 2013). As such, this situation may pose a potential health risk to children living near these rivers.

Some recent studies have already found adverse associations for PFASs on children (Frisbee et al., 2010; Vuong et al., 2016; Wang et al., 2015). For example, Frisbee et al. (2010) found a significant positive association between PFOA and PFOS exposure and dyslipidemia in children. Wang et al. (2015) reported that prenatal PFASs concentrations were inversely associated with children's intelligence quotient (IQ); also, another recent study from the United States found that PFASs exposure may be associated with executive function deficits in school-age children (Vuong et al., 2016). One adverse health outcome of PFASs that has recently attracted attention is serum uric acid. Uric acid, which has both oxidant and antioxidant properties, is the final metabolic product of purine metabolism in humans (So and Thorens, 2010). Elevated serum uric acid levels and hyperuricemia have been documented to be an independent precursor of kidney disease, including chronic kidney disease (Johnson et al., 2013; Miyaoka et al., 2014; Prasad and Qing, 2015). In addition, it is also associated with cardiovascular disease and hypertension in both children and adults (Feig et al., 2008; Heinig and Johnson, 2006; Mellen et al., 2006). Because of these considerations, it may be critically important to identify novel risk factors. Some of these novel risk factors could include environmental factors like PFASs that may be associated with elevated serum uric acid levels in children.

Studies sampled from adult populations demonstrating high PFASs levels have revealed a positive relationship between exposure to this class of chemicals and elevated serum uric acid levels. Two of these studies was comprised of occupational cohorts of workers from PFASs -handling chemical plants (Costa et al., 2009; Sakr et al., 2007), while another was derived from a community-based study of citizens residing near the Ohio River valley that was heavily exposed to PFOA in drinking water from a nearby chemical plant (Steenland et al., 2010). Recently, two other studies that analyzed data from the National Health and Nutrition Examination Survey (Gleason et al., 2015; Shankar et al., 2011) also found evidence of a link between PFASs and uric acid. However, it should be mentioned that Lin et al. (2013) did not find an association between PFOS and serum uric acid.

To the best of our knowledge, there has only been one study that has focused on examining associations between serum concentrations of PFASs and serum uric acid levels in children, which studied participants from the NHANES (Geiger et al., 2013). The objective of this study is to build on previous work among adults and assess the link between serum levels of PFASs and uric acid by using data from a well-executed community-based biomarker study of 225 healthy children (12–15 years of age) in Taiwan (Tsai et al., 2010).

2. Material and methods

2.1. Study participants

Study participants consisted of the entire control sample of the Genetics and Biomarkers study for Childhood Asthma (GBCA) in Taiwan. This sample was composed of a total of 225 healthy children (the response rate was 72% among those contacted by phone) selected from seven public schools in the Taipei area from 2009 to 2010 (Bao et al., 2014). The sample consisted of 102 boys and 124 girls who ranged in age from 12 to 15 years. A survey was used to acquire information regarding demographic variables and environmental exposures. The questionnaires were responded to by parents or guardians of participants. All children and their parents provided written informed consent. The study protocol was approved by the Institutional Review Board of the Institutional Review Board (National Taiwan University Hospital Research Ethics Committee).

2.2. Serum uric acid determination

The primary outcome of interest for this study was serum uric acid levels. Serum was divided from red blood cells, transported in tubes, and chilled prior to being shipped to an analytical laboratory. We measured uric acid in serum via the enzymatic uricase method (Geiger et al., 2013). Uricase oxidizes uric acid to allantoin and hydrogen peroxide. When in the presence of peroxidase, 3, 5-Dichloro-2-hydroxybenzene sulfonate coupled with 4-aminoantipyrine and hydrogen peroxide forms a compound that can be measured at 520 nm by its color (Geiger et al., 2013). The intensity of color is proportional to the uric acid concentration.

2.3. Serum PFASs measurement

Serum PFASs measurement has been described in recent publications (Zeng et al., 2015). Details regarding the analytical procedures capable of measuring ten PFASs analyses, consisting of perfluorobutane sulfonate (PFBS), perflurohexane sulfonate (PFHxS), PFOS, perfluorohexane acid (PFHxA), perfluoroheptanoic acid (PFHpA), perfluorononanoic acid (PFNA), PFOA, perfluorodecanoic acid (PFDA), perfluorododecanoic acid (PFDoA), and perfluorotetradecanoic acid (PFTA) in serum samples has been previously published (Bao et al., 2011).

2.4. Statistical analysis

Statistical analyses were performed using SPSS 18.0 J software (SPSS Inc. Chicago, IL, USA). Data were tested for normality (Shapiro–Wilks *W* test) and homogeneity (Bartlett's test for unequal variances) and all PFAS levels were natural log transformed to correct skewed distributions. Continuous variables with normality and homogeneity were given as the mean ± SD, otherwise, as median [Quartile 1(Q1)-Quartile 3(Q3)]. We performed linear regression analyses with uric acid as the outcome variable. Uric acid was treated as a continuous variable in a separate linear regression model with each single PFASs exposure variable. Except for the coefficients of total population, we analyzed the coefficients stratified by gender. Covariates including age, gender, body mass index (BMI), regular exercise (yes/no, defined as yes if the participant has exercised at least 1 h per day in the past year excluding physical education in the school, and no if vice versa), parental education (less than high school, more than high school), and environmental tobacco smoke exposure (ETS, the information was collected from the current and past household smoking status of each participant's adult household members and regular household visitors) were chosen by a priori whether their established relation to uric acid (independent of whether they are associated with PFASs), and all covariates were statistically significant predictors of uric acid, in the predicted direction.

In addition to linear regression, a logistic regression model was