Environmental Pollution 243 (2018) 1–8

Contents lists available at ScienceDirect

Environmental Pollution

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

Associations between lipid/lipoprotein levels and perfluoroalkyl substances among US children aged 6–11 years☆,☆☆

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ARTICLE INFO

Article history:
Received 9 March 2018
Received in revised form
18 August 2018
Accepted 19 August 2018
Available online 21 August 2018

Keywords:
Isomers of PFOA and PFOS and PFNA
Fluorocarbons
Cholesterol
Perfluoroalkyl substances
Children

ABSTRACT

Observed levels of lipid/lipoproteins are known to be associated with exposure to perfluoroalkyl substances (PFAS). In order to evaluate and update these associations among US children aged 6–11 years, data (N = 458) from National Health and Nutrition Examination Survey for 2013–2014 were used. The associations between the observed levels of total cholesterol, high density lipoprotein (HDL) cholesterol, and non-HDL cholesterol and selected PFAS were studied. PFAS data were available for perfluorononanoic acid (PFNA), perfluorohexane sulfonate (PFHxS), linear isomer of perfluorooctanoic acid (PFOA), linear isomer of perfluorooctane sulfonate (PFOS), monomethyl branch isomer of PFOS, and sum of PFAS. Regression models were fitted to evaluate these associations. A statistically significant ($p = 0.03$) positive association between the levels of linear isomer of PFOS and total cholesterol was observed. A 10% increase in the levels of linear isomer of PFOS measured in ng/L was found to be accompanied by a 0.03 −0.42% increase in the levels of total cholesterol measured in mg/dL. For PFNA, girls in the first quartile of PFNA were found to have lower adjusted levels for total cholesterol than the girls in the fourth quartile of PFNA (152.6 vs. 164.7 mg/dL, $p < 0.01$). Also, non-Hispanic blacks in the first quartile of PFNA were found to have lower adjusted levels for total cholesterol than the non-Hispanic blacks in the fourth quartile of PFNA (143.4 vs. 160.5 mg/dL, $p = 0.04$). A negative association between branch isomer of PFOS and non-HDL cholesterol was also observed ($\beta = -0.0066$, $p = 0.04$). The adjusted levels of non-HDL cholesterol were higher in the second quartile of ∑PFAS than in the fourth quartile of ∑PFAS (103.0 vs. 97.5 mg/dL, $p < 0.01$). Linear PFOS and possibly PFNA are associated with total cholesterol in the most recent NHANES childhood sample. Concentrations of PFAS and associations with cholesterol have both decreased compared to previous literature.

1. Introduction

The perfluorolalkyl substances (PFAS) are man-made, environmentally persistent chemicals with a wide variety of historic industrial and commercial applications including non-stick and stain and water resistant coatings, fire suppression foams, and cleaning products. Due to their environmental persistence and long half-lives, they have been detected in wildlife (Rotander et al., 2012; Yeung et al., 2009) and humans worldwide (Kannan et al., 2004).

The PFAS such as perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) can be linear or branched. The branched isomers are reported to come primarily from electrochemical fluorination production techniques, which produce mostly linear (PFOÃ78%, PFOS~70%) and a mixture of branched (~22%, ~30%) isomers. A competing and more recent technology for creating the same products, telomerization, produces a less complex, linear product (Benskin et al., 2010; Jiang et al., 2015). In addition, the isomeric profile of environmental contaminants can vary for different media of exposure (Houde et al., 2008; Filipovic and Berger, 2015) leading to variations of accumulated branched and linear chains in humans, a difference that can be especially

☆ Primary Author declares that he received no funding from any private or public sources to conduct this research. He also declares that he has no competing financial or other interests that could have affected the conclusions arrived at in this communication. Alan Ducatman has received funding for health communications related to the enrollment of the C8 Health Population, and he has provided scientific support to communities seeking similar class action support to institute medical monitoring.

☆☆ This paper has been recommended for acceptance by David Carpenter.

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https://doi.org/10.1016/j.envpol.2018.08.060
0269-7491/

marked for PFOS (Gebbink et al., 2015; Miralles-Marco and Harrad, 2015).

Human serum contamination with common PFAS, such as PFOA and PFOS, has been associated with higher serum cholesterol in studies (He et al., 2017; Liu et al., 2018; Skuladottir et al., 2015; Frisbee et al., 2010) and also higher LDL-cholesterol (LDL) in many of these (Khalil et al., 2018; Zeng et al., 2015; Fu et al., 2014). This association includes higher total and LDL cholesterol in children and adolescents (Mora et al., 2017; Khalil et al., 2018; Zeng et al., 2015; Geiger et al., 2014; Frisbee et al., 2010). Most of this work has been done without distinction between branched and unbranched PFAS isomers, but there may be differences in the biological activities, and Liu et al. (2018) found that linear isomer of PFOA was responsible for the association with total cholesterol in adults, whereas both isomers were associated with HDL. The 2013–2014 update for the National Health and Nutrition Examination Survey (NHANES) examines both linear and branched chains of the PFAS for both PFOA and PFOS. NHANES data provide an opportunity to examine the contribution of both isomers to lipids in children.

The goal of this paper is to evaluate this relationship in children for the four most commonly encountered PFAS. A subsidiary goal is to evaluate the sum of all PFAS isomers including those less commonly detected.

2. Materials and methods

Data for the children aged 6–11 years on demographics, body measures, exposure to environmental tobacco smoke (ETS), selected PFAS, HDL, and total cholesterol were downloaded and match merged by the ID of the NHANES participants. Data on a total of 458 participants were available (Table 1). Race/ethnic categories for which adequate sample sizes were available were non-Hispanic whites and non-Hispanic blacks. Sample sizes details by gender are given in Table 1. Because of the inadequate sample sizes, data for Hispanics, non-Hispanics, and of unclassified race/ethnicities were merged in to a single race/ethnicity category. Among boys (N = 247), there were 72 non-Hispanic white, 65 non-Hispanic black, and 110 participants of other race/ethnicities. Among girls (N = 211), there were 53 non-Hispanic white, 54 non-Hispanic black, and 104 participants of other race/ethnicities. Data on measured heights and weights were used to compute body mass index percentiles (BMIPCT) based on the growth charts developed by US Centers for Disease Control and Prevention (Kuczmarski et al., 2002).

2.1. Availability of data for PFASs and lipid levels

Data for observed levels of 14 PFAS in serum (CDC, 2017a), namely, perfluorooctane sulfonamide (PFSA), 2(N-methyl-perfluorooctane sulfonamide) acetic acid (Me-PFOSAA), 2(N-ethyl-perfluorooctane sulfonamide) acetic acid (Et-PFOSAA), perfluorodecanoic acid (PFDA), perfluorobutane sulfonic acid (PFBS), perfluoroheptanoic acid (PFHpA), PFNA, perfluoroundecanoic acid (PFUnDA), perfluorododecanoic acid (PFDoA), PFHxS, linear and branch isomers of PFOA, linear and monomethyl branch isomers of PFOS. However, percent observations at or above the limit of detection for Et-PFOSAA, Me-PFOSAA, PFBS, PFDA, PFDoA, PFHpA, PFSA, PFUnDA, and branch isomer of PFOA were too low (substantially below 60%) to do a meaningful data analysis for these PFAS species individually. Consequently, data were analyzed for only five PFAS as specific species, namely, linear isomer of PFOA, linear isomer of PFOS, branch isomer of PFOS, PFHxS, and PFNA. Percent observations ≥ LOD for branch isomer of PFOS, linear isomer of PFOA, linear isomer of PFOS, PFHxS, and PFNA were ≥ 99.9%. In addition, sum of PFAS, ∑PFAS was computed as the sum of all 14 PFAS listed above.

For children aged 6–11 years, data on lipids were available for HDL (CDC, 2016a) and total cholesterol (CDC, 2016b) only. Data on non-HDL cholesterol were generated by taking the difference between the values for total cholesterol and HDL. It should be noted that there were only 23 children who were found to have hypercholesterolemia defined as cholesterol ≥ 200 mg/dL as per guidelines of Cincinnati's children's hospital (https://www.cincinnatichildrens.org/patients/child/encyclopedia/diseases/hyperlipidemia) and only 3 children had cholesterol > 240 mg/dL. The number of children with hypercholesterolemia (N = 23) was inadequate for sufficient statistical power to do comparisons between those who had hypercholesterolemia and those who had normal levels of cholesterol.

2.2. Data on exposure to environmental tobacco smoke

Data on self-reported exposure to environmental tobacco smoke

Table 1
Study characteristics of the population investigated including sample sizes, unadjusted geomteric means with 95% confidence intervals, and percent observations at or above the limit of detection (LOD). Data from National Health and Nutrition Examination Survey 2013–2014.

	Total	Male	Female	Percent observations ≥ LOD**
N	458	247	211	
Age, mean (SD) in years	8.5 (1.8)	8.3 (1.8)	8.5 (1.8)	
Unadjusted geometric means with 95% confidence intervals				
HDL in mg/dL	53.5 (51.1–56.1)	55.2 (51.9–58.6)*	51.9 (49.4–54.5)*	
Total Cholesterol in mg/dL	156.5 (152.5–160.7)	154.4 (149.1–159.9)	158.7 (155.2–162.2)	
PFNA[a] in ng/mL	0.81 (0.68–0.96)	0.85 (0.7–1.03)	0.77 (0.65–0.92)	99.8
PFHxS[b] in ng/mL	0.91 (0.8–1.04)	1.05 (0.89–1.25)*	0.79 (0.7–0.89)*	99.8
PFOA[c] in ng/mL	1.78 (1.61–1.97)	1.84 (1.63–2.08)	1.72 (1.54–1.92)	100.0
PFOS[d] in ng/mL	2.67 (2.43–2.92)	2.95 (2.57–3.4)*	2.4 (2.22–2.59)*	100.0
PFOS[e] in ng/mL	1.35 (1.19–1.52)	1.44 (1.23–1.67)	1.26 (1.06–1.5)	100.0
∑PFAS[f] in ng/mL	9.15 (8.36–10.02)	9.89 (8.89–11)*	8.45 (7.63–9.37)*	

*Statistically significantly different at $\alpha = 0.05$
**for all participants (LOD = limit of detection).
[a] Perfluorononanoic acid.
[b] Perfluorohexane sulfonic acid.
[c] Linear isomer of perfluorooctanoate.
[d] Linear isomer of perfluorooctane sulfonate.
[e] Monomethyl branch isomers of PFOS.
[f] Sum of 14 PFAS.