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Serum biomarkers of polyfluoroalkyl compound exposure in young girls in Greater Cincinnati and the San Francisco Bay Area, USA

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ABSTRACT

PFC serum concentrations were measured in 6–8 year-old girls in Greater Cincinnati (GC) ($N = 353$) and the San Francisco Bay Area (SFBA) ($N = 351$). PFOA median concentration was lower in the SFBA than GC (5.8 vs. 7.3 ng/mL). In GC, 48/51 girls living in one area had PFOA concentrations above the NHANES 95th percentile for children 12–19 years (8.4 ng/mL), median 22.0 ng/mL. The duration of being breast fed was associated with higher serum PFOA at both sites and with higher PFOS, PFHxS and Me-PFOSA-AcOH concentrations in GC. Correlations of the PFC analytes with each other suggest that a source upriver from GC may have contributed to exposures through drinking water, and water treatment with granular activated carbon filtration resulted in less exposure for SWO girls compared to those in NKY. PFOA has been characterized as a drinking water contaminant, and water treatment systems effective in removing PFCs will reduce body burdens.

1. Introduction

Some polyfluoroalkyl compounds (PFCs) and their derivatives, such as perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS), are surfactants that have wide consumer and industrial applications as well as known environmental persistence. PFOS-related substances, including PFOA, are used in metal plating, semi-conductors, film processing and fire-fighting foams. PFOA can be found as a residual impurity in some paper coatings used on containers for processed food. Some PFCs have been detected in wildlife as widespread as polar bears in Greenland and giant pandas in China (Giesy and Kannan, 2001; Dai et al., 2006). In the United States, in serum samples collected from 1562 participants of the 1999–2000 National Health and Nutrition Examination Survey (NHANES), males and females age 12 years and older, both PFOA and PFOS were detected in every sample analyzed (geometric mean values: PFOS, 30.4 ng/mL and PFOA, 5.2 ng/mL) and other PFCs were detected in over 90% of the study population (Calafat et al., 2007a). In 2120 samples collected from NHANES participants in 2005–2006, after changes in the manufacturing practices for some PFCs, serum concentrations of PFCs had decreased, but PFOA, PFOS, and other PFCs were still detected in over 98% of the samples (CDC, 2012). The New Jersey Department of Environmental Protection measured PFCs in untreated water samples in 2006 and detected PFOA in 78% and PFOS in 57% of the 23 water treatment plants sampled (New Jersey Department of Environmental Protection, 2007). In 2009, water concentrations of PFOA in the Ohio River ranged from 2.5 ng/L in Pittsburgh, Pennsylvania (upstream of a plant processing PFCs), to 35.2 ng/L in Ravenswood West Virginia,

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and 13.1 ng/L in Cincinnati, Ohio at two locations downriver (Emery et al., 2010).

Species variation in the biological half-life of PFCs is substantial, from hours in some rodent strains to several years in humans (Kudo and Kawashima, 2003; Olsen et al., 2007). The perfluorinated portions of these molecules have extreme resistance to environmental and metabolic degradation; the longer the carbon chain of the PFC, the greater the persistence. PFOA and PFOS, with 7 and 8 carbon chains, have greater environmental and biological persistence in humans (about 3–4 years) than those with shorter chains. The exception is perfluorohexane sulfonate (PFHxS), with 6 carbons, and a half-life of 7.3 year (Olsen et al., 2007). PFCs have been detected in cord blood, breast milk, infant formula and food (Llorca et al., 2010; Karrman et al., 2007; Antignac et al., 2013; Kubwabo et al., 2013) and cord blood and breast milk concentrations are correlated with maternal serum concentrations (Karrman et al., 2007; Von Ehrenstein et al., 2009; Mondal et al., 2012; Lee et al., 2013; Ode et al., 2013).

The PFC exposure assessment reported here was carried out as part of the puberty cohort studies of the National Institute of Environmental Health Sciences and National Cancer Institute Breast Cancer and the Environment Research Program (BCERP). The objective of these studies is to elucidate influences of environmental factors on early pubertal development in girls, and thereby possible future risk for breast cancer and other chronic diseases among women (Hiatt et al., 2009). For this purpose, the research design employs biomarkers to assess a variety of environmental exposures. We previously published the results of the urinary exposure biomarkers (Wolff et al., 2010) and some of the persistent organo-halogenated compounds in serum (Windham et al., 2010) showing broad exposure. In this report, we describe the serum concentrations of PFCs measured among the puberty study participants. We conducted analyses to determine if factors such as location and years of residence, drinking water source and being breast fed were predictors of the serum PFC concentration.

2. Methods

2.1. Data and biospecimen collection

Of the three BCERP puberty cohort studies, only two collected blood serum: Greater Cincinnati (GC) (Cincinnati Children's Hospital Medical Center (CCHMC) and University of Cincinnati (UC) College of Medicine) and the San Francisco Bay Area (SFBA) (Kaiser Permanente of Northern California and University of California, San Francisco). Study participants at the GC Center were recruited from public and parochial schools in GC, through letters to parents, and through the Breast Cancer Registry of Greater Cincinnati. Informed consent was obtained from parents and child assent was verified. The SFBA study group was recruited through the Kaiser Permanente Health Plan membership in the SFBA, and consent and assent also were obtained. Serum samples were collected at the time of the first or second year clinical study visit, using a collection and processing protocol and sampling materials provided by the Centers for Disease Control and Prevention (CDC) laboratory conducting the analyses (CDC IRB #4824 and #4769). Serum was aliquotted into 2 mL polypropylene cryovials and stored frozen until shipment. PFCs were measured in the serum of 704 6–8 year old girls. An additional 119 girls participated in the study, but refused blood collection. Most biospecimens of the GC girls were collected between February 2005 and December 2006 (81.2%), but a few as late as October 2007. Biospecimens of the SFBA girls were collected primarily from February 2005 until December 2007 (89.2%), but some as late April 2009.

At both sites, baseline and yearly questionnaires were administered to the girls' parents or guardians. These included items about potential sources of environmental exposures (e.g. drinking water source and residential history) and the health histories of the girl and her parents. At each study visit, research staff, trained and certified through a common protocol, measured height and weight using calibrated stadiometers and scales. Body mass index (BMI) was calculated as weight/(height)^2 in kilograms/meter^2, and then related to age- and sex-specific percentiles using the CDC growth charts (CDC, 2000). BMI was categorized as either $<$ or $\geq$ the 85th percentile. BMI percentile was included in the calculation of geometric mean, but not included in regression models because, in other studies, PFOA has been found to be related to lower birth weight in infants (Maisonet et al., 2012; Halldorsson, 2012; Lee et al., 2013) and higher BMI in adults (Maisonet et al., 2012; Ji et al., 2012). For the purpose of this analysis, race/ethnicity has been categorized as Hispanic, Black, non-Hispanic White, and Asian.

Table 1
Study population characteristics.

Characteristic	Greater Cincinnati		SF Bay Area		Both sites	
	N	%	*N*	%	*N*	%
Number of subjects	353	50.1%	351	49.9%	704	100.0%
Age at sample collection (years)						
6.0–6.9	59	16.7%	62	17.7%	121	17.2%
7.0–7.9	137	38.8%	176	50.1%	313	44.5%
≥8.0	157	44.5%	113	32.2%	270	38.4%
Race/ethnicity						
Asian	5	1.4%	41	11.7%	46	6.5%
Black	119	33.7%	77	21.9%	196	27.8%
Hispanic	14	4.0%	84	23.9%	98	13.9%
White	215	60.9%	149	42.5%	364	51.7%
BMI for age						
Below the 85th percentile	250	70.8%	247	70.4%	497	70.6%
At or above the 85th percentile	103	29.2%	104	29.6%	207	29.4%
Sample collection time						
June–August	22	6.2%	27	7.7%	49	7.0%
September–May	331	93.8%	324	92.3%	655	93.0%
Ever used bottled water[a]	234	66.3%	238	67.8%	472	67.0%
Parity of mother at child's birth[a]						
1	105	29.7%	142	40.5%	247	35.1%
More than 1	218	61.8%	209	59.5%	427	60.7%
Child breast fed[a]	229	64.9%	329	93.7%	558	79.3%
Parental education[a]						
Grade School (1–8), Some High School (9–11) or a High School Diploma/GED	33	9.3%	65	18.5%	98	13.9%
Some College/Technical/Trade/ Vocational School or an Associate's Degree	116	32.9%	110	31.3%	226	32.1%
Bachelor's Degree	103	29.2%	101	28.8%	204	29.0%
Master's Degree or Higher	83	23.5%	44	12.5%	127	18.0%

[a] Data is missing for some participants.

2.2Serum analysis

Concentrations of PFCs in all blood sera were measured at the CDC, using methods published previously (Kuklenyik et al., 2005; Kato et al., 2011). Briefly, after dilution with formic acid (and without protein precipitation), one aliquot of 100 μL serum was analyzed by online solid-phase extraction high performance liquid chromatography–tandem mass spectrometry to measure trace concentrations of eight PFCs including PFOS and PFOA. Perfluorodecanoic acid (PFDeA) was not measured for the early sample analyses. Most analyses incorporated isotopically-labeled internal standards for PFOS, PFOA and 2-(N-methyl-perfluorooctane sulfonamide) acetate (Me-PFOSA-AcOH), 2-(N-ethyl-perfluorooctane sulfonamide) acetate (Et-PFOSA-AcOH) and perfluorononanoate (PFNA). The CDC laboratory is certified according to the Clinical Laboratories Improvement Amendments, and procedures incorporate quality control (QC) measures to ensure accuracy and precision of results, including annual proficiency testing compliance. A laboratory batch must meet QC criteria, including acceptable blanks, or the batch is entirely reanalyzed (Caudill et al., 2008). Results are blank-corrected if applicable. For all our statistical analyses, we used PFC measurements from the first serum sample collected from all girls.

2.3Statistical methods

We examined possible environmental and lifestyle factors to determine if they could explain the variation in PFOA concentrations. Questionnaire data were used to determine the proportion of water consumed by the girl that came from bottled water, parity of the mother, history and duration of being breast fed, and education of the parents. After first conducting these analyses on all girls, we then performed the analyses separately on the site specific sub-cohorts. For the girls from the GC area, we incorporated information on residence location and number of years at each residence. Parts of the GC metropolitan area where the girls resided are served by two different water treatment systems. The GC municipal water departments provided information about their water distribution systems and the zones serviced by each of the water treatment plants. Residential history information from the questionnaires was used to assign each GC study participant to a water treatment plant for each address.

All statistical analyses were conducted using SAS (version 9.2, SAS Institute, Cary, NC). We calculated Pearson correlation coefficients for the relationships between each of the eight PFC serum concentrations with each other. For analytes