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Per- and polyfluoroalkyl substances in sera from children 3 to 11 years of age participating in the National Health and Nutrition Examination Survey 2013–2014

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ABSTRACT

Several per- and polyfluoroalkyl substances (PFAS) have been measured in U.S. National Health and Nutrition Examination Survey (NHANES) participants 12 years of age and older since 1999–2000, but PFAS data using NHANES individual samples among children younger than 12 years do not exist. To obtain the first nationally representative PFAS exposure data in U.S. children, we quantified serum concentrations of 14 PFAS including perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorohexane sulfonic acid (PFHxS), and perfluorononanoic acid (PFNA), in a nationally representative subsample of 639 3–11 year old participants in NHANES 2013–2014. We used on-line solid-phase extraction coupled to isotope dilution-high performance liquid chromatography-tandem mass spectrometry; limits of detection were 0.1 ng/mL for all analytes. We calculated geometric mean concentrations, determined weighted Pearson correlations, and used linear regression to evaluate associations of sex, age (3–5 vs 6–11 years), race/ethnicity (Hispanic vs non-Hispanic), household income, and body mass index with concentrations of PFAS detected in more than 60% of participants. We detected PFOS, PFOA, PFHxS, and PFNA in all children at concentrations similar to those of NHANES 2013–2014 adolescents and adults, suggesting prevalent exposure to these PFAS or their precursors among U.S. 3–11 year old children, most of whom were born after the phase out of PFOS in the United States in 2002. PFAS concentration differences by sex, race/ethnicity, and age suggest lifestyle differences that may impact exposure, and highlight the importance of identifying exposure sources and of studying the environmental fate and transport of PFAS.

1. Introduction

Per- and polyfluoroalkyl substances (PFAS) have been in use for over 60 years in a variety of industrial and commercial applications, such as surfactants, lubricants, paper and textile coatings, polishes, food packaging, and fire-retarding foams (ATSDR, 2015; DeWitt, 2015; Lau et al., 2007; Prevedouros et al., 2006). Because of their chemical inertness and heat stability, several PFAS persist and bioaccumulate in the environment, and certain PFAS, such as perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS), are ubiquitous contaminants detected worldwide in occupationally exposed workers and general populations, as well as in wildlife (ATSDR, 2015; DeWitt, 2015).

Considerable amount of animal data suggest potential adverse health effects related to exposure to PFOA and PFOS (other PFAS have not been evaluated as extensively) including hepatotoxicity, tumor induction, developmental toxicity, immunotoxicity, neurotoxicity, and endocrine disruption (Corsini et al., 2012, 2014; DeWitt, 2015; Kennedy et al., 2004; Lau et al., 2004, 2007). However, the relevance of these animal data for human health is somewhat unclear because of the much shorter half-life of PFAS in animals compared to humans, and the possible dependence of toxicity on a peroxisome proliferation mechanism likely to be not as important in humans (DeWitt, 2015; Grandjean and Clapp, 2014; Steenland et al., 2010). Because animals and humans sometimes process chemicals differently, additional research will help scientists fully understand how PFAS may affect human health.

Epidemiologic research findings on the potential health effects from exposure to PFAS in humans, albeit inconsistent, cover a wide spectrum of outcomes, mainly associated with exposures to PFOA and PFOS, including increased serum cholesterol, low-density lipoprotein and uric acid, thyroid, cardiovascular and kidney diseases, altered liver enzyme activities, lengthened time-to-pregnancy, early onset of menopause,

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delays in age of menarche, abnormal fetal growth and development, attention deficit hyperactivity disorder, and reduced immune responses in children, (Apelberg et al., 2007; ATSDR, 2015; DeWitt, 2015; Fei et al., 2007, 2008, 2010; Granum et al., 2013; Gump et al., 2011; Hamm et al., 2010; Lopez-Espinosa et al., 2011; Nolan et al., 2009; Olsen et al., 2009; Stein et al., 2014; Stein and Savitz, 2011; Washino et al., 2009). These inconsistencies among human studies stress the need for additional research to assess the potential impact of exposures to PFAS, especially in children, a vulnerable segment of the population.

Dietary intake, indoor air and house dust, drinking water, and use of products containing PFAS are potential sources of exposure to these compounds (ATSDR, 2015; DeWitt, 2015). Of late, PFAS have been detected increasingly in drinking water supplies around the world including the United States (Boiteux et al., 2012; Ericson et al., 2009; Filipovic et al., 2015; Hoffman et al., 2011; Hu et al., 2016; Post et al., 2012, 2013; Sun et al., 2016; Thompson et al., 2011; Weiss et al., 2012; Wilhelm et al., 2010), and in 2016, the U.S. Environmental Protection Agency (EPA) established a 70 parts per trillion drinking water health advisory level of PFOS and PFOA (U.S.EPA, 2016). Health advisories, which are non-enforceable and non-regulatory, provide technical guidance to state, local and tribal governments and drinking water system operators so that they can determine if concentrations of chemicals in tap water from public utilities are safe for drinking and other use. Under the U.S. EPA Unmonitored Contaminant Monitoring Rule, from 2013 to 2016 all U.S. public water systems (PWS) serving 10,000 or more customers (and a representative sample of those serving ≤10,000 people) tested their supplies for six PFAS including PFOA, and PFOS. As of January 2017, of 4920 PWS with results for PFOS and PFOA, 46 (for PFOS) and 13 (for PFOA) serving millions of Americans had detections at or above the EPA's health advisory level (U.S.EPA, 2016). These findings have contributed, at least in part, to increased interest in PFAS-related research in recent years.

Assessing human exposure to PFASs can provide information useful for understanding their potential adverse health effects. Yet, PFAS data among young children (Gump et al., 2011; Harris et al., 2017; Kim et al., 2014; Pinney et al., 2014; Schecter et al., 2012; Stein and Savitz, 2011; Toms et al., 2009; Wu et al., 2015; Zhang et al., 2010), albeit important because of children's potential vulnerability to environmental insults, are not as common as data in adults. Until now, information on the extent of PFAS exposure among children in the United States was limited to a convenience group of 200 Texas children (0 to < 13 years of age) sampled in 2009 (Schecter et al., 2012), and children who participated in epidemiological studies conducted to evaluate the potential health impacts of exposure to environmental contaminants, including PFAS (Gump et al., 2011; Harris et al., 2017; Pinney et al., 2014; Stein and Savitz, 2011; Wu et al., 2015).

PFAS have been measured in the U.S. National Health and Nutrition Examination Survey (NHANES) for participants 12 years of age and older since 1999–2000 (CDC, 2017). However, because the volume of serum collected from preadolescents is limited, NHANES PFAS exposure data among persons younger than 12 years are limited to one report of concentrations using pooled sera collected in NHANES 2001–2002 from children 3–11 years old (Kato et al., 2009). Having nationally-representative exposure information among young children is of public health interest in view of the recent detection of some PFAS in drinking water systems (Hu et al., 2016), and in residents, including children, of affected communities throughout the United States (Hoffman et al., 2011; Landsteiner et al., 2014; New Hampshire Department of Environmental Services, 2017; Vermont Department of Health, 2017). Therefore, we quantified PFAS in NHANES 2013–2014 children sera, and report here the first nationally representative data on the serum concentrations of 14 PFAS in the U.S. general population 3–11 years of age, stratified by age group, sex, and race/ethnicity.

2. Materials and methods

2.1. Survey design

NHANES, conducted by the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention (CDC), is an ongoing survey designed to measure the health and nutritional status of the civilian noninstitutionalized U.S. population (CDC, 2014). The survey includes household interviews, standardized physical examinations, and collection of medical histories and biologic specimens, some of which are used to assess exposure to environmental chemicals (CDC, 2014). The NCHS Research Ethics Review Board reviewed and approved the NHANES study protocol. Parents or guardians provided written consent for all participants < 18 years of age (CDC, 2014).

For this study, we quantified 14 PFAS in serum, originally collected for the measurement of cotinine, from a random one-third subsample of 639 NHANES 2013–2014 participants 3–11 years of age. Because the subsample was random, the representative design of the survey was maintained. The sera had been shipped on dry ice to CDC's National Center for Environmental Health where it was stored at or below −20 °C until analysis.

2.2. Laboratory method

We used a modification of a published on-line solid-phase extraction coupled to high-performance liquid chromatography–isotope dilution–tandem mass spectrometry (on-line SPE-HPLC–MS/MS) approach (CDC, 2016) to quantify the following 14 PFAS: perfluorooctane sulfonamide (FOSA, PFOSA), 2-(*N*-methyl-perfluorooctane sulfonamido) acetic acid (MeFOSAA, Me-PFOSA-AcOH), 2-(*N*-ethyl-perfluorooctane sulfonamido) acetic acid (EtFOSAA, Et-PFOSA-AcOH), perfluorobutane sulfonic acid (PFBS), perfluorohexane sulfonic acid (PFHxS), perfluoroheptanoic acid (PFHpA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUnDA), perfluorododecanoic acid (PFDoDA), linear PFOA (n-PFOA), sum of branched isomers of PFOA (Sb-PFOA), linear PFOS (n-PFOS), and sum of perfluoromethylheptane sulfonate isomers (Sm-PFOS). Briefly, after dilution with formic acid and addition of stable isotope internal standards, one aliquot of 50 µL of serum was injected into a commercial on-line SPE Symbiosis system (Spark Holland, Plainsboro, NJ) for the preconcentration of the analytes on a HySphere C8-SE (7 µM) cartridge (i-Chrome solutions, Plainsboro, NJ). The analytes were then back-eluted onto a pair of Chromolith® HighResolution RP-18e columns (4.6 × 100 mm, Merck KGaA, Germany) for HPLC separation, and detected by negative-ion TurboIonspray-MS/MS on an ABSciex 5500 or ABSciex 6500 Q trap mass spectrometer (Applied Biosystems, Foster City, CA). The limits of detection (LODs) were 0.1 ng/mL for all analytes. The method accuracy, calculated from the recovery at three spiking levels, ranged from 90% to 113%. We prepared low-concentration and high-concentration quality control materials (QCL and QCH, respectively) after spiking pools of commercial calf serum, and analyzed these QCs with standards, reagent and serum blanks, and NHANES samples. The precision of the measurements, expressed as the relative standard deviation of inter- and intra-day measurements of those QCs in a period of approximately 6 months, varied from 7.4% to 15.8% (QCL) and 6.3% to 11.9% (QCH), depending on the analytes. Adequate performance and accuracy of the method have been further confirmed by successful ongoing participation in two international interlaboratory comparison programs, namely the German External Quality Assessment Scheme (G-EQUAS) for PFOS and PFOA in serum, organized and managed by the Institute and Outpatient clinic for Occupational, Social and Environmental Medicine of the University of Erlangen-Nuremberg in Germany (since 2006), and the Arctic Monitoring and Assessment Program (AMAP) Ring Test, conducted by the Institut National de Santé Publique du Québec in Canada, for several PFAS, including PFHxS, PFOS, PFOA, and PFNA, in serum (since 2010).