Environmental Research 154 (2017) 212–221

Contents lists available at ScienceDirect

Environmental Research

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

Serum perfluoroalkyl substances in children exposed to the world trade center disaster☆

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ARTICLE INFO

Keywords:
Perfluoroalkyl substances
Children
World Trade Center disaster
Dust cloud
Home dust exposure

ABSTRACT

The World Trade Center (WTC) disaster released large amounts of various chemical substances into the environment, including perfluoroalkyl substances (PFASs). Yet, no studies have examined exposures in children living or attending schools near the disaster site. We measured serum PFASs in WTC Health Registry (WTCHR) respondents who were ≤8 years of age on September 11, 2001 and a sociodemographically-matched comparison group. We also examined the relationship of PFASs levels with dust cloud exposure; home dust exposure, and with traumatic exposure, the latter to take into account differences related to possible mental health consequences and associated behavioral problems. Serum samples, collected between 2014 and 2016, were analyzed from 123 WTCHR participants and from 185 participants in the comparison group. In the WTCHR group, median perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS) levels were 1.81 ng/mL and 3.72 ng/mL, respectively. Controlling for sex, caloric intake, race/ethnicity, and date of birth, significant increases among WTCHR participants compared with the matched comparison group were detected for perfluorohexanesulfonate (0.23 ng/mL increase or 0.24 log unit increase, p=0.006); PFOS (0.86 ng/mL increase or 0.16 log unit increase, p=0.011); PFOA (0.35 ng/mL increase or 0.18 log unit increase, $p < 0.001$); perfluorononanoic acid (0.12 ng/mL increase or 0.17 log unit increase, p=0.003); perfluorodecanoic acid (0.06 ng/mL increase or 0.42 log unit increase, $p < 0.001$); and perfluoroundecanoic acid (0.03 ng/mL increase or 0.32 log unit increase, p=0.019). Stronger associations were identified for home dust exposures and traumatic exposures than dust cloud. These findings highlight the importance of conducting longitudinal studies in this population to assess possible cardiometabolic and renal consequences related to these exposures.

1. Introduction

The World Trade Center (WTC) disaster released large amounts of particulate matter, heavy metals and persistent organic pollutants (POP) (Landrigan et al., 2004). Among various POPs, elevated exposure to perfluoroalkyl substances (PFASs) in personnel responding to the WTC disaster site has been reported among New York State employees and National Guard personnel 5–26 months after the disaster (Tao et al., 2008), with a twofold higher concentration of perfluoroocatnoic acid (PFOA) (mean 8.88 ng/mL) and perfluorohex-

Abbreviations: BMI, Body Mass Index; HDL, High-density lipoprotein; LODs, Limits of Detection; N-MeFOSAA, N-methylperfluoro-1-octanesulfonamidoacetic acid; N-meFOSAA, N-methyl perfluorooctanesulfonamido acetic acid; NYSDOH, New York State Department of Health; NYC DOHMH, NYC Department of Health & Mental Hygiene; PFASs, Perfluoroalkyl substances; PFDS, Perfluorodecane sulfonate; PFDA, Perfluorodecanoic acid; PFDoDA, Perfluorododecanoic acid; PFHpA, Perfluoroheptanoic acid; PFHxS, Perfluorohexanesulfonic acid; PFNA, Perfluorononanoic acid; PFOSA, Perfluorooctane sulfonamide; PFOS, Perfluorooctanesulfonic acid; PFOA, Perfluorooctanoic acid; PFUnDA, Perfluoroundecanoic acid; WTC, World Trade Center; WTCHR, WTC Health Registry

☆ Clinical trials identifier: NCT02068183.

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http://dx.doi.org/10.1016/j.envres.2017.01.008
Received 15 December 2016; Received in revised form 6 January 2017; Accepted 8 January 2017

anesulfonate (PFHxS, mean 3.70 ng/mL) compared to nationally representative samples (4.6 and 1.9 ng/mL, respectively) (Tao et al., 2008). In addition to acute dust cloud exposures, local residents experienced significant subchronic exposures from fires and resuspended dust, which entered homes and schools through windows and air shafts (Friedman et al., 2011a). Furthermore, a particular concern remains regarding combustion products released by fires burning for more than 3 months after the event (Landrigan et al., 2004).

PFASs are used as surfactants and stain-resistant coatings on many products, including upholstery, carpet, nonstick cookware (Kotthoff et al., 2015; Trier et al., 2011), and building and construction material (Becanova et al., 2016). In addition, PFASs are also found in fire-fighting material used for fire suppression (Moody and Field, 2000). Since the disaster, laboratory studies have identified PFASs to disrupt metabolic, cardiovascular and renal functions. PFASs interact with alpha- and gamma-peroxisome proliferator activated receptors, which play key roles in lipid and carbohydrate metabolism (Zhang et al., 2014). In cell culture studies using the 3T3-L1 preadipocyte system, several PFASs altered gene expression associated with adipocyte differentiation and lipid metabolism (Watkins et al., 2015), and developmental PFAS exposures in mice have resulted in increased leptin and insulin levels in midlife (Hines et al., 2009). Microvascular endothelial cell culture studies have shown that PFAS exposure increases reactive oxidative species and induces endothelial permeability (Qian et al., 2010), which plays a critical role in ischemic renal injury (Sutton et al., 2003). While not all results from experimental studies have been confirmed in humans, some important effects have been reported in human studies. A positive association has been detected between concentrations of perfluorooctanesulfonic acid (PFOS), perfluorooctanoic acid (PFOA) and perfluorononanoic acid (PFNA), and total and non-high-density cholesterol in National Health and Nutrition Examination Survey (NHANES) participants aged 20–80 years, despite the relatively low level of exposure (Nelson et al., 2009). In adolescents, PFOA and PFOS have been found to be significantly associated with dyslipidemia (Geiger et al., 2014). PFOS and PFNA concentrations have also been shown to be associated with lower levels of insulin growth factor-1 (IGF-1) in children (Lopez-Espinosa et al., 2016) and, among 12–19 year olds in NHANES 2003–2010, those with the highest quartile of serum PFC had significantly lower renal glomerular function compared to those in the lowest quartile (Kataria et al., 2015), although the possibility of reverse causation cannot be excluded in this cross-sectional study.

A particular concern about early life WTC-related chemical exposure is that childhood represents a uniquely susceptible period for developmental metabolic programming, which can result in adverse health consequences in later life. A previous study examining a population of children with clinical concerns relating to the WTC disaster identified reductions in high density lipoprotein (HDL) and elevations in triglycerides among those with (subchronic) home dust exposure, although in this study no specific chemical compounds were examined (Trasande et al., 2013). To further examine the plausible role of specific chemical exposures that could potentially contribute to cardiometabolic alterations in exposed children, we compared serum PFAS levels in a sample of WTC-exposed children with levels in a matched comparison group, and examined the relationship of serum PFAS levels with dust cloud (acute), home dust (subchronic), and traumatic exposures.

2. Methods

2.1. Population

The study population consisted of: (1) a cohort of New York City residents enrolled in the World Trade Center Health Registry (WTCHR) with dates of birth on or between September 11, 1993 and September 10, 2001 and (2) a comparison cohort of individuals born during the same time period, who were ineligible for enrollment in the WTCHR because they either did not reside south of Canal Street, did not attend school south of Canal Street, and were not present south of Canal Street on the morning of 9/11 (Friedman et al., 2011b).

To enroll members of the WTCHR cohort in the present study, WTCHR staff of the New York City Department of Health (NYCDOHMH) who were fluent in English, Spanish, Mandarin, or Cantonese attempted contacts by mail, email, phone and in-person visits. Both a hard-copy letter and brochure describing the study were mailed to each potential participant. Two weeks after the mailing, phone calls were initiated to individuals who had not responded to the mailed invitation to participate. Calls were made to all known telephone numbers, and calls were attempted at different hours of the day and evening, and on different days of the week. Emails were sent to potential participants who did not respond to mail or telephone contacts. If there was no response to emails, then Lexis-Nexis (RELX Group: New York City, NY) search tools were used to identify new contact information. If new contact information was identified, then telephone and/or email contact were reinitiated. If no new contact information was obtained from tracing, two WTCHR staff members attempted a home visit to the last known place of residence. In all methods of contact, WTCHR staff described the study and invited individuals to call the WTCHR or NYU School of Medicine staff to further discuss study details and make an appointment. For participants less than 18 years of age a parent or guardian was required to schedule an appointment and be available and present to authorize participation on the scheduled visit date.

For our comparison group, we recruited individuals who were not eligible for enrollment in the WTCHR. To maximize comparability between the two study populations we developed a table of the desired frequencies of controls by date of birth (0–2, 3–5 or ≥6 years-old on 9/11/2001), sex, race (White, African-American, Asian, other), ethnicity (Hispanic, non-Hispanic) and income (< $25,000, ≥$25,000), assuming that the enrolled group of WTCHR participants would reflect participants in the WTCHR's most recent (2011-12) survey cycle. Three modes of recruitment were employed to recruit the frequency-matched comparison group: (1) well visits at pediatric clinics affiliated with NYU School of Medicine; (2) contact through health fairs, youth organizations, and postings in areas where youth congregate, posting and advertisements at local colleges; and (3) social media outreach by West Coast Clinical Trials (WCCT) Global, a contract research organization. Participants' eligibility and ability to fill slots in the frequency-matching table were assessed using a screening questionnaire, which staff conducted over the phone or in person. Individuals were excluded from the present study as matched comparisons if they would have qualified for WTCHR enrollment because of place of residence or school, or having been in the vicinity of the WTC towers on 9/11/2001.

The study was reviewed and approved by the NYU School of Medicine Institutional Review Board, as well as research committees at Bellevue and Gouverneur Hospital Centers. The NYCDOHMH Institutional Review Board identified this study not to involve human subject activity by NYCDOHMH staff. In addition to parental consent on behalf of minors, assent was obtained from adolescents prior to initiation of the study procedures. A Certificate of Confidentiality was obtained to protect participant privacy. The study was approved by New York State Department of Health (NYSDOH) for the analysis of serum samples.

2.2. Sociodemographic and exposure variables

Demographic variables such as age, sex, race/ethnicity and family annual income (categorized as < $25,000 or ≥$25,000) were documented for each participant. Age groups were categorized as 0–2, 3–5 or ≥6 years old on 9/11/2001. Dust cloud (acute) and home dust (subchronic) exposure information was collected from both study participants and parent/guardian, if applicable. Dust cloud exposure was assessed categorically as present or absent with the question: