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The effect of drinking water contaminated with perfluoroalkyl substances on a 10-year longitudinal trend of plasma levels in an elderly Uppsala cohort

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ABSTRACT

Background: In 2012, drinking water contaminated with per- and polyfluoroalkyl substances (PFASs), foremost perfluorooctanesulfonic acid (PFOS) and perfluorohexanesulfonic acid (PFHxS) at levels over 20 ng/L and 40 ng/L, respectively, was confirmed in Uppsala, Sweden.

Objectives: We assessed how a longitudinally sampled cohort's temporal trend in PFAS plasma concentration was influenced by their residential location and determined the plausible association or disparity between the PFASs detected in the drinking water and the trend in the study cohort.

Methods: The Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) cohort provided plasma samples three times from 2001 to 2014. Individuals maintaining the same zip code throughout the study (n = 399) were divided into a reference (no known PFAS exposure), low, intermediate and high exposure area depending on the proportion of contaminated drinking water received. Eight PFASs detected in the majority (75%) of the cohort's plasma samples were evaluated for significant changes in temporal PFAS concentrations using a random effects (mixed) model.

Results: PFHxS plasma concentrations continued to significantly increase in individuals living in areas receiving the largest percentage of contaminated drinking water ($p < 0.0001$), while PFOS showed an overall decrease. The temporal trend of other PFAS plasma concentrations did not show an association to the quality of drinking water received.

Conclusions: The distribution of contaminated drinking water had a direct effect on the trend in PFHxS plasma levels among the different exposure groups, resulting in increased concentrations over time, especially in the intermediate and high exposure areas. PFOS and the remaining PFASs did not show the same relationship, suggesting other sources of exposure influenced these PFAS plasma trends.

1. Introduction

Per- and polyfluoroalkyl substances (PFASs) are a class of environmentally persistent man-made chemicals that have been produced since the 1950s (Buck et al., 2011). Today PFASs are used in various industrial processes and applications including stain and soil repellents, hydraulic fluids, and aqueous fire-fighting foams (AFFFs) (Buck et al., 2011; Calafat et al., 2007). Consequently, PFASs have been universally detected in the environment and in human blood since the 1990s and early 2000s, respectively (Calafat et al., 2007; Giesy and Kannan, 2001; Kannan et al., 2004). Epidemiological studies have shown associations between exposure to some PFASs and negative health effects including diabetes, serum lipids, atherosclerosis, ulcerative colitis, early menopause, thyroid function in women, and osteoarthritis (Frisbee et al., 2009; Innes et al., 2011; Lind et al., 2014, 2017; S. Knox et al., 2011; Steenland et al., 2013, 2009b). In order to decrease environmental and

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human PFAS exposure, restrictions have been implemented to reduce their global emission, including the voluntary phase out of perfluorooctane sulfonic acid (PFOS) and like substances by 3 M in 2000 (USEPA, 2000), the addition of PFOS and PFOS precursors to the Stockholm Convention in 2009 (UNEP, 2010), the 2010/2015 perfluorooctanoic acid (PFOA) and higher homologue perfluorocarboxylic acids (PFCAs) Stewardship (USEPA, 2016), of which included PFOA precursors, and the recent EU ban of many fluoride based substances (Kemikalieinspektionen, 2016). Despite these efforts, humans are still exposed to present and historical PFAS production, due to their persistent characteristics. Some examples of common exposures include degradation of precursor fluorotelomer alcohols, fluorotelomer-based fluorosurfactants and other fluoropolymers (D'eon and Mabury, 2011; Fraser et al., 2012; Olsen et al., 2012; Yeung et al., 2013a), and production of replacement chemicals such as perfluorobutane sulfonic acid (PFBS) (Olsen et al., 2009). Another important contributor includes the continued leaching of PFASs into land and water surrounding PFAS point sources like production facilities or military airports which used AFFFs containing PFOS and/or other PFASs (Gyllenhammar et al., 2015; Hu et al., 2016; Hölzer et al., 2008; Steenland et al., 2009a; Weiß et al., 2012).

A number of studies have been carried out world-wide in order to monitor the levels of PFASs in our environment (Ahrens et al., 2015; de Solla et al., 2012; Eriksson et al., 2016; Filipovic et al., 2015; Gebbink et al., 2016; Gewurtz et al., 2014; Hloušková et al., 2014; Kärrman et al., 2011; Pan et al., 2014). Unfortunately, in some cases, high levels of PFASs have been determined years after a contamination began. Two separate investigations, showed drinking water in Uppsala, Sweden was contaminated with perfluorohexane sulfonic acid (PFHxS), PFOS, PFBS, perfluorohexanoic acid (PFHxA), and PFOA in 2012 (Glynn, 2012; Gyllenhammar et al., 2015). In the 2012 pilot study, the highest concentrations of PFHxS and PFOS in drinking water was above 40 ng/L and 20 ng/L, respectively (Glynn, 2012). In a later study when drinking water samples were collected between 2012 and 2014, the median concentration of PFHxS and PFOS measured in the drinking water was 25 ng/L and 13 ng/L, respectively (Gyllenhammar et al., 2015). The frequency in detection and concentration of PFBS, PFHxA, and PFOA in the drinking water samples were noticeably lower than PFHxS and PFOS (Glynn, 2012; Gyllenhammar et al., 2015). The contamination was traced back to a groundwater well field located downstream from a military airport, where AFFFs containing PFASs were used from 1985 to 2003 (Bergström, 2014; Gyllenhammar et al., 2015). Analysis of biobanked serum showed significantly increased levels of PFHxS and PFBS, which suggests that the drinking water was contaminated with PFASs at least from the mid-1990s (Glynn et al., 2012; Gyllenhammar et al., 2015). Increased concentrations of PFHxS in plasma samples from the Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) cohort, were also observed (Stubleski et al., 2016). A previously developed model simulation predicted that between 1996 and 2004, people living in the southern and western parts of the city were most heavily affected by PFAS contaminated drinking water from the groundwater well field, which was shut down in 2004 (Gyllenhammar et al., 2015). In 2007, the water flowing from the groundwater well field was redirected into a drinking water treatment plant (WTP) where the contaminated water was diluted approximately 60% with other incoming water sources (Gyllenhammar et al., 2015). The diluted PFAS contaminated water was then distributed to the eastern, western and southern parts of the city. Since 2014, activated carbon filters have also been used at the WTP to remove PFASs from the water (Uppsala Vatten, 2016). A timeline detailing the years where changes in the drinking water distribution occurred, the restrictions in PFAS production and use were implemented, use of AFFFs containing PFASs during military training, and the years the PIVUS cohort was sampled is shown in Fig. S1.

The relationship between PFAS contaminated drinking water and consequent levels in humans has been previously researched (Emmett et al., 2006; Hoffman et al., 2011; Hurley et al., 2016; Hölzer et al., 2008; Steenland et al., 2009a), with correlations to the longitudinal trend in PFAS serum or plasma concentrations being very limited (Brede et al., 2010; Fitz-Simon et al., 2013). Cross sectional studies monitoring the change in human levels of PFASs in Uppsala, Sweden have been conducted in the past and are still ongoing (Glynn et al., 2015b, 2012). However, to the best of our knowledge, the correlation of the longitudinal trend in PFAS concentrations in a large population-based cohort and the distribution of PFAS contaminated drinking water has not yet been studied. Longitudinal investigations are ideal for observing individual-based trends over time and reduce the variation in exposure within the study population (Glynn et al., 2012).

The aims of this study were to assess how the exposure to PFAS contaminated drinking water influenced the initial PFAS plasma concentration and longitudinal change over time in the PIVUS cohort. First, a cross-sectional analysis was used to compare the levels of PFASs between the individuals living in areas receiving high, intermediate (IM) and low proportions of contaminated drinking water (n = 1016) during the first sampling period (2001–2004). Second, we used a longitudinal design to investigate how the residential area affected PFAS levels over 10 years in the 399 participants of the PIVUS cohort that were present in three repeated plasma sample collections, from 2001 to 2004, 2006 to 2009 and 2011 to 2014, and who had not changed their residential area during the study period.

2. Materials and methods

2.1. Sample collection

The study participants were chosen from the general population register and invited via mail to participate in the PIVUS study. About half of the invited subjects participated. In total, plasma samples from 1016 70 year-old participants (50% women) living in Uppsala, Sweden were collected between April 2001 and June 2004 (Lind et al., 2006). The total sample of 1016 investigated individuals was used in the cross-sectional analysis performed at age 70 (Table 1). A repeated sample collection was performed twice for the same remaining participants when they turned 75 years old (sampled from 2006 to 2009) and again at 80 years old 2011–2014).

The 399 subjects whose plasma was present in all three collections and who had retained the same zip code from 2001 to 2014 were included in the longitudinal analysis (Table 2). All plasma samples were collected in the morning after an over-night fast and the samples were stored at − 70 °C until analysis. The study was approved by the Ethics Committee of the University of Uppsala and the participants gave a written informed consent.

2.2. Sample preparation and instrumental analysis

The sample preparation and instrumental analysis methods used in this study were previously developed and validated in terms of recovery, accuracy and precision (Salihovic et al., 2013). Fourteen target PFASs: perfluoropentanoic acid (PFPeA), PFHxA, perfluoroheptanoic acid (PFHpA), PFOA, perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUnDA), perfluorododecanoic acid (PFDoDA), perfluorotridecanoic acid (PFTrDA), PFBS, PFHxS, linear isomer of PFOS (L-PFOS), perfluorodecane sulfonic acid (PFDxS), and perfluorooctane sulfonamide (FOSA) were extracted from 150 µL of plasma or serum using protein precipitation and filtered through an Ostro (Waters corp.) 96 well-plate. The samples were then analyzed with an Acquity UPLC coupled to a Quattro Premier XE tandem mass spectrometry (MS/MS) system (Waters Corporation, Milford, USA) operating in negative electrospray ionization. The PFAS concentrations were quantified via isotope dilution.

Quality assurance and quality control measures implemented throughout the analyses including: a matrix matched calibration curve,