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Maternal serum concentrations of per- and polyfluoroalkyl substances and their predictors in years with reduced production and use

Vivian Berg [a,b,c,*], Therese Haugdahl Nøst [a,b,c], Sandra Huber [a,b], Charlotta Rylander [c], Solrunn Hansen [c], Anna Sofía Veyhe [c], Ole Martin Fuskevåg [a], Jon Øyvind Odland [c], Torkjel Manning Sandanger [b,c]

[a] Department of Laboratory Medicine, Diagnostic Clinic, University Hospital of Northern Norway, Sykehusveien 38, NO-9038 Tromsø, Norway
[b] Department of Environmental Chemistry, Norwegian Institute of Air Research, Fram Centre, Hjalmar Johansens Gate 14, NO-9296 Tromsø, Norway
[c] Department of Community Medicine, Faculty of Health Sciences, University of Tromsø – The Arctic University of Norway, Hansine Hansens veg 18, NO-9019 Tromsø, Norway

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ABSTRACT

Determining maternal concentrations of per- and polyfluoroalkyl substances (PFASs) and the relative impact of various demographic and dietary predictors is important for assessing fetal exposure and for developing proper lifestyle advisories for pregnant women.

This study was conducted to investigate maternal PFAS concentrations and their predictors in years when the production and use of several PFASs declined, and to assess the relative importance of significant predictors.

Blood from 391 pregnant women participating in The Northern Norway Mother-and-Child Contaminant Cohort Study (MISA) was collected in the period 2007–2009 and serum analyses of 26 PFASs were conducted. Associations between PFAS concentrations, sampling date, and demographic and dietary variables were evaluated by multivariate analyses and linear models including relevant covariates.

Parity was the strongest significant predictor for all the investigated PFASs, and nulliparous women had higher concentrations compared to multiparous women (10 ng/mL versus 4.5 ng/mL in median PFOS, respectively). Serum concentrations of PFOS and PFOA of women recruited day 1–100 were 25% and 26% higher, respectively, compared to those women recruited in the last 167 days of the study (day 601–867), and the concentrations of PFNA, PFDA and PFUnDA increased with age. Dietary predictors explained 0–17% of the variation in concentrations for the different PFASs. Significantly elevated concentrations of PFOS, PFNA, PFDA and PFUnDA were found among high consumers of marine food. The concentrations of PFHxS, PFHpS and PFNA were also increased in high consumers of game and elevated concentrations of PFHpS and PFOS were detected in high consumers of white meat. Study subjects with a high intake of salty snacks and beef had significantly higher concentrations of PFOA.

The present study demonstrates that parity, sampling date and birth year are the most important predictors for maternal PFAS concentrations in years following a decrease in production and use of several PFASs. Further, dietary predictors of PFAS concentrations were identified and varied in importance according to compound.

1. Introduction

Per- and polyfluoroalkyl substances (PFASs) are fluorinated aliphatic substances, widely used in consumer products like textiles, paper products and lubricants (Lehmler, 2005). The most studied compounds to date are perfluoroalkyl carboxylic acids (PFCAs), like perfluorooctanoate (PFOA) and perfluoroalkyl sulfonic acids (PFSAs), like perfluorooctane sulfonate (PFOS) (D'eon and Mabury, 2011; Martin et al., 2010). Several PFASs are persistent substances that have been directly emitted to the environment during their production and use (Prevedouros et al., 2006). PFASs have been produced since the 1950s with increasing intensities from 1966 to the 1990s. The production remained constant

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Abbreviations: ANCOVA, analysis of covariance; BMI, body mass index; FFQ, food frequency questionnaire; FOSA, perfluorooctane sulphonamide; LOD, limit of detection; MISA, The Northern Norway Mother-and-Child Contaminant Cohort Study; PFAS, per- and polyfluoroalkyl substance; PFCA, perfluoroalkyl carboxylic acid; PFDA, perfluorodecanoate; PFDoDA, perfluorododecanoate; PFHpA, perfluoroheptanoate; PFHpS, perfluoroheptane sulfonate; PFHxS, pefluorohexane sulfonate; PFNA, perfluorononanoate; PFOA, perfluorooctanoate; PFOS, perfluorooctane sulfonate; PFSA, perfluoroalkyl sulfonic acid; PFUnDA, perfluoroundecanoate; PLS, partial least square; POP, persistent organic pollutant; SRM, standard reference material; UHPLC-MS/MS, ultra-high pressure liquid chromatography triple–quadrupole mass-spectrometry.

* Corresponding author at: Department of Laboratory Medicine, Diagnostic Clinic, University Hospital of Northern Norway, Sykehusveien 38, NO-9038 Tromsø, Norway. Tel.: +47 77750393.

E-mail address: vivian.berg@uit.no (V. Berg).

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from 1990 to 2000 until a phase-out was announced in 2000, resulting in a rapid drop of PFOS related compounds from the year 2002 (Paul et al., 2009).

Concerns about the persistence of PFASs in the environment, bioaccumulation potential and risk for toxicological effects in animals and humans have classified PFOS as a persistent organic pollutant (POP) (Stockholm convention, 2009). Restricted use of PFOS was implemented in Europe from June 2008 (European Parliament, 2006) and in the US in 2001 (Paul et al., 2009). In addition, the US launched the "PFOA Stewardship Program" (US EPA, 2006) where eight of the major PFOA-producing companies committed to reduce emissions of PFOA and related chemicals by 95% by 2010. In Norway, the ban of PFOA in Norwegian consumer products by 1st of June 2014 was recently announced (Miljøverndepartementet, 2013).

Following the regulatory initiatives, a decrease in PFOS and PFOA has been observed in humans in later years (Calafat et al., 2007; Glynn et al., 2012; Haug et al., 2009; Schroter-Kermani et al., 2012). Conversely, a decreasing time trend has not been observed for longer chained PFCAs (Buck et al., 2011). Still, there are concerns about potential human health effects of PFASs such as hormonal changes, hepatotoxicity, developmental toxicity and immunotoxicity (Grandjean and Budtz-Jorgensen, 2013; Grandjean et al., 2012; Lau et al., 2007). PFASs are transferred from the mother to the fetus via the placenta during pregnancy and from mothers milk postpartum (Liu et al., 2011). Fetuses and infants are thereby exposed to these compounds at critical developmental stages.

Diet is currently suspected to be the major on-going exposure route of PFASs for humans (Fromme et al., 2009; Haug et al., 2011a; Vestergren and Cousins, 2009). In addition, these chemicals are passed to humans through air, house dust, drinking water and water based beverages (Eschauzier et al., 2013; Haug et al., 2011a, 2011b; Ullah et al., 2011). Elevated concentrations of PFASs have been associated with consumption of marine food (Berger et al., 2009; Haug et al., 2010b; Rylander et al., 2009; Vestergren et al., 2012), but also to consumption of red meat, animal fat and snacks (Halldorsson et al., 2008; Haug et al., 2010a; Noorlander et al., 2011; Ostertag et al., 2009; Vestergren et al., 2012).

Cross-sectional population studies of polychlorinated biphenyls have demonstrated increasing concentrations with age that reflect birth year dependent past exposures due to time-variant emission (Alcock et al., 2000; Moser and McLachlan, 2002; Nost et al., 2013; Ritter et al., 2009). Similar relationship of individual exposures and to historic production and use could be expected for PFAS concentrations in the general population. We hypothesize that individual maternal PFAS exposures are largely influenced by variables such as sampling date, dietary habits, birth year, parity and breastfeeding. Further, concentrations of PFASs in maternal blood during pregnancy are relevant as indicator of the exposure experienced by the fetus (Verner et al., 2009). Therefore, the aims of the study were to investigate maternal PFAS concentrations and their predictors in years when production and use of several PFASs declined, and to assess the relative importance of significant predictors.

2. Materials and methods

2.1. Study participants and collection of blood samples

The selected subjects in the present study represent the 391 women who completed The Northern Norway Mother-and-Child Contaminant Cohort Study (MISA) which consists of 515 enrolled pregnant women, recruited from June 2007 to October 2009 (recruitment period; 867 days). All participants answered a detailed questionnaire about diet and lifestyle at enrolment, and donated a blood sample at three time points (around gestational week 20, 3 days after delivery and 6 weeks after delivery). Detailed information about the study group characteristics, ethical approvals, the food frequency questionnaire (FFQ), dietary calculations and the blood collection procedures have been reported elsewhere (Hansen et al., 2010; Veyhe et al., 2012). Blood samples donated at mean gestational week 18.6 (9–36) were analyzed for a variety of PFASs. Thirteen women did not complete the food frequency questionnaire adequately, thus the total number included in the statistical analyses was 378.

2.2. Chemical analyses

A total of 26 PFASs, thirteen PFCAs (C_4-C_{14}, C_{16}, C_{18}), six PFSAs (C_4-C_8, C_{10}), three phosphonic acids (C_6, C_8, C_{10}), three fluortelomer sulfonates (4:2, 6:2, 8:2) and one perfluroalkyl sulfonamide (C_8), were initially screened for in a sub-group of 50 serum samples. PFASs detected (>LOD) in more than 20% of the samples were further quantified in the remaining serum samples ($N = 391$). Analytes were determined in serum samples using sonication-facilitated liquid–liquid extraction, activated ENVI-carb clean-up (Powley et al., 2005) and analyzed by ultrahigh pressure liquid chromatography triple–quadrupole mass-spectrometry (UHPLC-MS/MS). The sample preparation, treatment and extraction were performed as described by Hanssen et al. (2013) except for the volumes used; 25 μL of an 0.1 ng/μL internal standard mixture was added to 0.25 mL serum before the addition of 1 mL methanol. 20 μL of a 0.1 ng/μL branched PFDA solution was added as the recovery standard. Prior to analysis, an aliquot of 100 μL extract was transferred to a vial and mixed with an equal amount of 2 mM aqueous ammoniumacetate (NH_4OAc, ≥99%, Sigma-Aldrich, St. Louis, MO, USA). The analytical method, reagents and instrumentation are described in detail by Hanssen et al. Briefly, 10 μL was injected on a Acquity UPLC HSS T3 column (2.1 × 100 mm, 1.8 μm) (Waters Corporation, Milford, MA, USA) coupled to an Acella 1250 UHPLC pump and a TSQ Vantage (Thermo Fisher Scientific Inc., Waltham, MA, USA). Details on compounds analyzed, analytical conditions, the parent ions, monitored transitions, collision energies and S-lens settings are provided in the supplemental material Table S1. Quantification was conducted using the LCQuan software from Thermo Scientific (Thermo Fisher Scientific Inc., Waltham, MA, USA; Version 2.6).

2.3. Quality control

Quantification of the contaminants was performed by the internal-standard addition method with isotope-labeled PFASs (Hanssen et al., 2013). Concentrations of PFASs in all samples were within the linear range of the instrument and the calibration curve. For each compound in the mass spectrometry analyses, a second mass transition served to confirm compound specificity. The quality of the analysis was assured through repetitive analysis of blank samples and reference samples. One standard reference material (SRM1957® from the National Institute of Standards and Technology, Gaithersburg, MD, USA; $N = 31$), one bovine serum blank and one water blank were prepared for each batch of 30 samples. Validation data (recoveries, LODs and linear regression values for the calibration curves) and analytical uncertainties for certified concentrations in SRMs are available in the supplemental material Tables S2, S3 and S4. Additionally, our laboratory participates in the Artic Monitoring and Assessment Programme ring test for POPs in human serum, an international comparison program, organized by Institut National de Santé Publique du Québec, Canada (Institut national de santé publique du Québec, 2014). Interlaboratory comparisons indicate that the uncertainties of our analysis are within ±15–20% of the assigned values. The linear PFOS isomers was chromatographically separated from the branched isomers and quantified separately. The coelution of branched isomers (quantified as one peak) was not structurally elucidated but rather identified as eluting earlier than the linear PFOS as described elsewhere (Rylander et al., 2009). The internal standard for linear PFOS was used for quantification of the branched isomers as well (Arsenault et al., 2008). When