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Exposure of Norwegian toddlers to perfluoroalkyl substances (PFAS): The association with breastfeeding and maternal PFAS concentrations

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ABSTRACT

High exposure to perfluoroalkyl substances (PFASs) has been associated with adverse health effects in children. PFASs exposure pathways of toddlers might differ from those of infants and adults, and the investigations on determinants of PFASs exposure in early childhood are scarce. Our aims were to examine the PFAS blood concentrations in Norwegian toddlers and to assess their relationship with maternal PFAS concentrations in pregnancy and breastfeeding duration. We determined PFAS concentrations in 112 plasma samples of 3-year-old children collected at 2010–2011 and 99 maternal serum samples collected around delivery at 2007–2008. PFAS concentrations in children were regressed on duration of breastfeeding, and the effect modification by maternal prenatal PFAS concentrations was examined in 55 mother-child pairs. Six PFASs were quantifiable in >50% of both maternal and children samples. Positive and significant correlations ranging between 0.50 and 0.66 were found between maternal and child concentrations of the same PFAS congeners. Nevertheless, toddlers had higher total PFAS blood concentrations than their mothers, due to higher concentrations of PFOA, PFNA and PFHxS. Every month of breastfeeding was associated with an increase of 3.3% (95% Confidence Intervals (CI): 0.8–5.8) for PFOS, 4.7% (95%CI: 2.8–6.6) for PFOA and 6.1% (95% CI: 2.6–9.7) for PFHpS in toddlers' plasma and a dose-response association was found, after adjustment for confounders. However, PFNA and PFUnDA concentrations in children were not associated with either maternal concentrations or breastfeeding duration. Our findings suggest that transplacental transfer, prenatally, and breastfeeding, postanatally, are among the main determinants of PFOS, PFOA, PFHxS and PFHpS concentrations in toddlers, while that was not the case for PFNA and PFUnDA. Nevertheless, due to the small number of mother child-pairs in our study, our results should be interpreted with caution.

1. Introduction

Perfluoroalkyl substances (PFASs) are synthetic fluorinated organic compounds used in industrial and consumer products over the last 50 years due to their chemical and thermal stability and water and oil repellency (Buck et al., 2011). Adults are exposed to PFASs through ambient indoor air, house dust and drinking water, though the main route is through food (Jain 2014; Vestergren et al., 2012). During pregnancy, maternal PFASs are transferred through the placenta resulting in prenatal exposure of the fetus (Gutzkow et al., 2012). According to previous reports comparing PFAS concentrations in paired samples of maternal and cord serum, the transfer efficiency of PFOS is approximately 30–36% and for PFOA 63–80% (Beesoon et al., 2011; Fromme et al., 2010; Gutzkow et al., 2012; Kim et al., 2011; Lee et al., 2013). PFOS and PFOA are highly persistent, have half-lives from 3.8 to 5.4 years (Olsen et al., 2007), and are currently the main contributors to the total PFAS concentrations in maternal, cord and infant blood and breast milk (Fromme et al., 2010; Gutzkow et al., 2012; Karrman et al., 2007; Thomsen et al., 2010).

The developing fetus is vulnerable to environmental toxicants. Several epidemiological studies have demonstrated that high prenatal exposure to PFASs is associated with restricted fetal growth; namely high prenatal PFOA exposure has been associated with a reduction in birth weight of up to 250 g (Bach et al., 2015; Olsen et al., 2009). Additionally, high prenatal PFOS exposure has been related to high risk of low birth weight and small for gestational age neonates (Chen et al., 2012; Stein et al., 2009). Further, there is epidemiological evidence of immunotoxic and neurotoxic effects in children associated with high prenatal PFASs exposure (Grandjean et al., 2012; Granum et al., 2013; Hoyer et al., 2015; Liew et al., 2014; Okada et al., 2012; Wang et al., 2015).

After birth, the breastfed infant is continuously exposed to PFASs through consumption of breast milk (Kim et al., 2011). Even though the PFAS concentrations in breast milk are one to two orders of magnitude lower than in maternal serum (Karrman et al., 2007; Kim et al., 2011), 6 months of breastfeeding can substantially increase the PFAS

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body burden of the infant. It has been shown that 90% of infant's PFAS exposure can be attributed to breastfeeding (Haug et al., 2011). Maternal PFAS concentrations are positively correlated with PFAS concentrations in cord blood, newborn blood and breast milk and this has been well documented for the most abundant congeners. However, the relationship between maternal PFASs and PFAS concentrations in young children is scarcely studied (Mondal et al., 2012, 2014). Infants (0–1 year) and toddlers (1–3 years) have been exposed to PFASs both in-utero and postnatally through breastfeeding, while other postnatal exposure patterns, through diet, indoor air and dust, might also occur for toddlers and the main sources of exposure to PFAS for toddlers has not been well documented. Toddlers' PFAS levels can be related to levels in childhood and adolescence, while exposure in this age might be important as this is a critical developmental window. Some studies have been focusing specifically in PFAS exposure during early childhood (5–9 years) and related health outcomes reporting immunotoxic and endocrine diruptive effects, (Grandjean et al., 2012; Lopez-Espinosa et al., 2016; Stein et al., 2013) while no evidence exist on the association between PFAS levels in younger children and contemporary and long-term health outcomes. Given the emerging evidence of adverse health effects related to high PFASs exposure of children, it is important to report the PFAS concentrations in toddlers and investigate the determinants of PFASs exposure in this age group.

The aims of this study are to examine the PFAS blood concentrations in Norwegian toddlers and to assess the relationship with maternal PFAS levels in pregnancy and breastfeeding duration.

2. Methods

2.1. Study population

The Norwegian birth cohort BraMat is a sub-cohort of the Norwegian Mother and Child Cohort Study (MoBa). MoBa is a prospective population-based pregnancy cohort study conducted by the Norwegian Institute of Public Health (Magnus et al., 2006; Ronningen et al., 2006). Participants were recruited from all over Norway from 1999 to 2008. The women consented to participation in 40.6% of the pregnancies. The cohort now includes 114,500 children, 95,200 mothers and 75,200 fathers. Eligible participants in the BraMat sub-cohort were women with singleton pregnancies, already recruited in the MoBa study and who were scheduled to give birth at the Oslo University Hospital Ullevål or the Akershus University Hospital, in Oslo area, Norway (Stolevik et al., 2011). Out of the 820 mothers eligible and invited to participate, 205 were recruited in BraMat (25%). The recruitment took place between April 2007 and March 2008 and women were contacted at the 37th week of pregnancy, thus only full-term pregnancies were included (37th–42nd week of pregnancy). Exclusion criteria in the BraMat cohort were: autoimmune diseases of the mother and use of steroids, anti-inflammatory, epileptic drugs during pregnancy. The main aim of the BraMat sub-cohort was to investigate the relationship of prenatal exposure to environmental contaminants and immunotoxic effects in children (Granum et al., 2013; Stolevik et al., 2011).

The BraMat study was approved by the Norwegian Regional Committee for Medical and Health Research Ethics and the Data Inspectorate. Written informed consents were obtained from the mothers who agreed to participate.

2.2. Blood collection and PFASs determination

Blood samples were collected from 205 mothers around delivery (0–3 days after birth) and 112 (56%) children at the age of three years. This study includes 99 mothers and 112 3-year old children (mean age: 34.4 months, SD: 2.5), of whom 55 are mother-child pairs, with enough blood sample volume available to perform PFAS analyses. Blood collection is described in details by Granum et al. (2013). Concentrations of nineteen PFASs were investigated in maternal plasma and children's serum samples, using high-performance tandem mass spectrometry at the Norwegian Institute of Public Health by a previously described method (Haug et al., 2009). In brief, 150 μL of sample was transferred to a centrifugation tube, added internal standards and methanol to make up a total volume of 150 μL methanol for precipitation of proteins, and then mixed using a whirl mixer. The samples were subsequently centrifuged and the supernatant was transferred to a glass autosampler vial, added 500 μL 0.1 M formic acid and mixed on a whirl mixer. The samples were analyzed by injection of 400 μL extract on a column switching liquid chromatography (LC) system coupled to a triple quadrupole mass spectrometer (MS). For quantification of PFOS, the total area of the linear and branched isomers was integrated. Eleven PFASs were determined in the samples, three from the group of perfluoroalkyl sulfonates: perfluorohexanesulfonate (PFHxS), perfluoroheptanesulfonate (PFHpS) and perfluorooctanesulfonate (PFOS), seven from the group of perfluoroalkyl carboxylates: perfluoroheptanoic acid (PFHpA), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUnDA), perfluorododecanoic acid (PFDoDA) and perfluorotridecanoic acid (PFTrDA) and one from the group of perfluoroalkyl sulfonamides: perfluorooctane sulfonamide (PFOSA). For quantification of PFOS, the total area of linear and branched isomers was integrated. The limit of quantification (LOQ) was 0.05 ng/mL for all measured PFASs. Statistical analyses were limited to six PFASs that were quantifiable in >50% of both maternal and children samples. The compounds finally included in our study were: PFHxS, PFHpS, PFOS, PFOA, PFNA, and PFUnDA. Values below LOQ were replaced with LOQ divided by the square root of two for further statistical analysis.

2.3. Maternal and pregnancy related characteristics

Several maternal and pregnancy related characteristics including maternal age and education, pre-pregnancy body mass index (BMI), parity, history of breastfeeding in previous pregnancies and type of delivery have been identified as determinants of PFAS blood concentrations in mothers and can have a potential relationship with toddlers' PFASs levels (Brantsaeter et al., 2013). This information was retrieved through questionnaires administered at 15th and 30th week of gestation (version 5 of the quality-controlled data files of MoBa) and the Medical Birth Registry of Norway. Child's gender, gestational age and birth weight were also included as potential predictors of PFAS blood concentrations in children (Mondal et al., 2012, 2014). Information on duration of breastfeeding and attendance to day-care center were obtained by questionnaires administered at the follow-up of the BraMat study at 3-years of age, as proxies of postnatal exposure pathways.

2.4. Statistical analysis

The blood concentrations of PFASs in maternal and children samples as well as the child: mother ratios of PFASs were summarized by descriptive statistics. The contribution of each of the 6 PFAS congeners to total PFASs concentrations in samples from mothers and children was presented graphically. All PFASs distributions failed the Shapiro-Wilk test of normality, thus the logarithm (base 10) of the values was used in subsequent analyses. We estimated the Spearman's correlation coefficients for the log-transformed values of PFASs in mother-child pairs and we presented the associations between paired PFAS measurements in scatter plots. Maternal PFAS levels measured after birth are highly correlated with maternal PFAS concentrations during pregnancy even if the measurement is taken 3 weeks after birth; (Glynn et al., 2012) hence the measured maternal PFAS around birth can reflect prenatal exposure of the fetus and they are referred to also as “prenatal exposure” throughout the manuscript.

We clarify that the description of the PFAS levels in toddlers, the identification of important predictors and the multivariate association