Environmental Research ∎ (∎∎∎∎) ∎∎∎–∎∎∎

Contents lists available at ScienceDirect

Environmental Research

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

Maternal serum perfluoroalkyl substances during pregnancy and duration of breastfeeding

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ARTICLE INFO

Article history:
Received 12 January 2016
Received in revised form
7 April 2016
Accepted 25 April 2016

Keywords:
Perfluoroalkyl substances
Perfluorooctanoic acid
Perfluorooctane sulfonic acid
Breastfeeding

ABSTRACT

Background: Perfluoroalkyl substances (PFAS) may affect breast development and decrease duration of breastfeeding, thus interfering with the health benefits of breastfeeding. We investigated the association between maternal PFAS exposure and breastfeeding duration.

Methods: We measured PFAS concentrations in maternal serum collected during pregnancy in 2003–2006. After delivery, women (n=336) completed standardized breastfeeding surveys every 3 months until ending breastfeeding or 36 months postpartum. We estimated relative risks (RRs) for ending any breastfeeding within 3–6 months postpartum by Poisson regression, adjusted for relevant confounding factors.

Results: Women in the 4th quartile of perfluorooctanoic acid (PFOA) serum concentration had 1.77 times the risk of ending any breastfeeding by 3 months (95% confidence interval (CI): 1.23, 2.54; p-trend=0.003) and 1.41 times the risk of ending any breastfeeding by 6 months (95%CI: 1.06, 1.87; p-trend=0.038), compared with women in the first quartile. Women in the 4th quartile of perfluorooctane sulfonic acid serum concentration had a marginally increased risk of discontinuing any breastfeeding by 3 months (RR=1.32; 95%CI: 0.97, 1.79; p-trend=0.065).

Conclusions: Maternal serum PFOA concentrations were inversely related to duration of any breastfeeding in this cohort, even after controlling for prior breastfeeding. These findings suggest that PFOA exposure may adversely affect breastfeeding duration and highlight the need to consider the potential adverse effects of maternal environmental chemical exposure on breastfeeding.

1. Introduction

The American Academy of Pediatrics (AAP) recommends 6 months of exclusive breastfeeding and continued partial breastfeeding for 12 months or longer (AAP, 2012) to promote numerous associated short and long term health benefits for both mother and child (Ip et al., 2007). However, in the United States (US) in 2012 only 29.2% of mothers continue any breastfeeding until 12 months (National Immunization Survey, 2015). Known barriers to breastfeeding include sociocultural, medical, nutritional, and infant level factors, including perceived inadequate milk supply, problems with latch, and insufficient support from health care providers, family, or workplace (Teich et al., 2014). However, exposure to environmental chemicals may interfere with hormones regulating initiation of lactation (e.g. prolactin) and milk production (e.g. oxytocin) (Lew et al., 2009; Rogan and Gladen, 1985).

Perfluoroalkyl substances (PFAS) are commonly used in oil and

Abbreviations: AAP, American Academy of Pediatrics; ANOVA, Analysis of Variance; CDC, Centers for Disease Control and Prevention; CI, Confidence interval; HOME, Health Outcomes and Measures of the Environment; IQR, Interquartile range; NHANES, National Health and Nutrition Examination Survey; NICU, Neonatal Intensive Care Unit; PFAS, Perfluoroalkyl substances; PFOA, Perfluorooctanoic acid; PFOS, Perfluorooctane sulfonic acid; PFNA, Perfluorononanoic acid; PFHxS, Perfluorohexane sulfonic acid; QC, Quality control; RR, Relative risk; US, United States

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http://dx.doi.org/10.1016/j.envres.2016.04.034
0013-9351/

water resistant consumer products (e.g. non-stick cookware, food container coatings, textile treatments), fire-fighting foam, and industrial surfactants (Buck et al., 2011; European Food Safety Authority Panel on Contaminants in the Food Chain, 2008). Four PFAS are nearly ubiquitous in sera collected from the US population: perfluorooctanoic acid (PFOA), perfluorooctane sulfonic acid (PFOS), perfluorononanoic acid (PFNA), and perfluorohexane sulfonic acid (PFHxS) (Jain, 2013; Woodruff et al., 2011). Toxicologic studies suggest that exposure to PFOA during pregnancy disrupts mammary gland differentiation and development (Tucker et al., 2015; White et al., 2007; Yang et al., 2009), delays epithelial involution (White et al., 2007), and may alter expression of placental prolactin-family hormone and milk protein genes (Suh et al., 2011; White et al., 2007). Only one prior epidemiologic study has assessed the effect of maternal PFOA and PFOS exposure on breastfeeding duration. Using data from the Danish National Birth Cohort, Fei et al. observed that greater concentrations of maternal plasma PFOA and PFOS during pregnancy were associated with shorter duration of breastfeeding among multiparous women (Fei et al., 2010). Collectively, these studies suggest that PFAS may have adverse effects, on duration of breastfeeding. However, Fei et. al did not control for prior breastfeeding duration (Fei et al., 2010), which is an important route of maternal PFAS excretion (Barbarossa et al., 2013; Mondal et al., 2014) and an important predictor of future breastfeeding success (Nagy et al., 2001; Whalen and Cramton, 2010).

We tested the hypothesis that greater maternal serum concentrations of PFAS during pregnancy are associated with a shorter duration of breastfeeding. We examined these associations, controlling for prior breastfeeding history, in a longitudinal cohort that had median serum PFOA concentrations about two-times higher than those of pregnant women who participated in the National Health and Nutrition Examination Survey (NHANES) (Braun et al., 2016), a nationally representative sampling of the US general population (Jain, 2013).

2. Materials and methods

2.1. Study population

We used data from the Health Outcomes and Measures of the Environment (HOME) Study, a prospective pregnancy and birth cohort designed to examine the impact of early life environmental chemical exposures (Braun et al., 2014; Geraghty et al., 2008). Pregnant women were recruited from nine prenatal clinics associated with three hospitals in the Cincinnati, Ohio area between March 2003 and January 2006. At baseline, women were eligible to participate if they were pregnant (16 ± 3 weeks gestation), ≥ 18 years old, English speakers, living in a home built before 1978, intending to continue prenatal care and deliver at a study-affiliated obstetric practice, and had no history of HIV infection. Women taking medication for seizures or thyroid disorders were not eligible to participate. All women provided written informed consent, and the institutional review boards of Cincinnati Children's Hospital Medical Center, the cooperating delivery hospitals, and the Centers for Disease Control and Prevention (CDC) approved the study protocol.

Of the 468 women who initially enrolled in the study, 67 dropped out before delivery. We excluded nine sets of twins, three stillborn children, and three children with congenital anomalies. Among the remaining 386 singleton births, 357 (93%) mothers provided serum samples; of these, 336 (87%) completed follow-up surveys regarding breastfeeding practices and had complete covariate information.

2.2. Serum PFAS concentrations

We collected blood samples from women at ~16 and ~26 weeks gestation and at delivery. For women who had insufficient serum volume to quantify PFAS concentrations in their 16 week sample, we used the 26 week (n=33, 10%), or delivery sample (n=16, 5%). We used online solid phase extraction coupled to high performance liquid chromatography-isotope dilution tandem mass spectrometry to measure serum PFOA, PFOS, PFNA, and PFHxS concentrations (Kato et al., 2011), which were detectable in all samples. The limits of detection were 0.1 ng/mL (PFOA, PFHxS), 0.2 ng/mL (PFOS), and 0.082 ng/mL (PFNA). Every analytic batch included reagent blanks and quality control (QC) materials. The coefficients of variation of repeated measurements of the QC materials were ~6%.

2.3. Duration of breastfeeding

After delivery, women completed standardized interviewer-administered surveys by phone about breastfeeding practices every 3 months until breastfeeding was discontinued or the child's third year birthday, whichever came first. The surveys included questions about the introduction of water, juice or other liquids, formula, non-human milk, and solid foods into the infant diet. Women also provided information about the duration of any breastfeeding of their previous children. We defined *any breastfeeding* as the duration in months that the mother reported any extent of breastfeeding, irrespective of supplementation with formula, liquids, or solid foods. We used the AAP guidelines to define *exclusive breastfeeding*, which indicate that breast milk may not be supplemented (including water, juice, non-human milk, formula, or solid foods) with the exception of vitamins, minerals, and medications (AAP, 2012). We set the duration of exclusive breastfeeding to each infant's age at the earliest of first use of formula, introduction of water, juice, or solid foods; we excluded 19 participants with missing data related to introduction of liquids and solid foods from the exclusive breastfeeding analyses. Our primary outcomes were the termination of *any breastfeeding* by 3 or 6 months postpartum and termination of *exclusive breastfeeding* by 3 months postpartum. We chose these cutoffs for our participants because relatively few infants were exclusively breastfed for ≥ 3 months (n=44) or continued to receive any breastmilk for ≥ 12 months (n=83) (AAP, 2012).

2.4. Covariates

During the second trimester, demographic, socioeconomic, perinatal, and behavioral factors, as well as reproductive and medical histories, were collected using a computer-assisted questionnaire administered by trained research staff.

2.5. Statistical analysis

First, we examined univariate statistics of PFAS concentrations, duration of any breastfeeding, and potential covariates. We then conducted bivariate analyses to assess associations among PFAS concentrations, breastfeeding duration, and covariates, applying a log(2) transformation to PFAS concentrations and a natural log transformation for duration of any breastfeeding, due to their skewed distribution. Second, because the outcome under study (ending breastfeeding) was not rare and data were collected prospectively, we used multivariable Poisson regression models with robust standard errors to estimate the relative risk (RR) (Zou, 2004) of ending any breastfeeding by 3 or 6 months and exclusive breastfeeding by 3 months. Potential confounding variables were initially identified based on known associations with either PFAS

Please cite this article as: Romano, M.E., et al., Maternal serum perfluoroalkyl substances during pregnancy and duration of breastfeeding. Environ. Res. (2016), http://dx.doi.org/10.1016/j.envres.2016.04.034