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Shorter duration of breastfeeding at elevated exposures to perfluoroalkyl substances

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ABSTRACT

The aim of this study was to determine whether maternal exposure to persistent perfluoroalkyl substances (PFASs) affect the capability to breastfeed.

In two Faroese birth cohorts (N = 1130), concentrations of five PFASs were measured in maternal serum during pregnancy or two weeks after term. Duration of breastfeeding was assessed by questionnaire and clinical interview. In adjusted linear regression models, a doubling of maternal serum PFASs was associated with a reduction in duration of both total and exclusive breastfeeding, most pronounced for perfluorooctane sulfonic acid (PFOS) where a doubling was associated with a reduction in total breastfeeding of 1.4 (95% CI: 0.6; 2.1) months and perfluorooctanoic acid (PFOA) where a doubling was associated with a reduction in exclusive breastfeeding of 0.5 (0.3; 0.7) months. The associations were evident among both primiparous and multiparous women, and thus cannot be explained by confounding from previous breastfeeding.

1. Introduction

Breastfeeding has many positive effects on the infant as well as the mother [1]. Thus, the World Health Organization (WHO) recommends that infants are breastfed exclusively for the first six months of life and partially up to two years or beyond [2]. However, globally only 38% of infants are exclusively breastfed as recommended [3].

Initiation and duration of breastfeeding is thought to depend mainly on individual choice and societal factors [4], but recent research shows that nearly half of the mothers in a US cohort study experienced early undesired weaning [5]. Inadequate milk supply is frequently reported to be one of the leading causes for early weaning [6–8]. Although the perception of inadequate milk supply is often attributed to social and psychological factors, insufficient supply may also be real and caused by physiological factors [9].

Still, little is known about the physiological reasons for insufficient milk production, and the focus has been on hormonal abnormalities, maternal disease and contraindications [10]. Persistent environmental chemicals could potentially result in endocrine disruption that could affect the hormonal processes responsible for maternal breast milk production. For example, dichlorodiphenyldichloroethylene (DDE) has been associated with reduced duration of breastfeeding in studies carried out in the United States [11] and in Mexico [12]. In the Mexican study, differences remained after censoring of women who ceased breastfeeding for known external causes. However, the associations were confined to those who had previously breastfed, which suggests that at least some of the effect could be a result of confounding from

Abbreviations: BMI, body mass index; DDE, dichlorodiphenyldichloroethylene; DAG, directed acyclic graph; LOD, limit of detection; PFAS, perfluoroalkyl substance; PFDA, perfluorodecanoic acid; PFHxS, perfluorohexane sulfonic acid; PFNA, perfluorononanoic acid; PFOS, perfluorooctane sulfonic acid; PFOA, perfluorooctanoic acid; PCB, polychlorinated biphenyl; WHO, world health organization.

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previous breastfeeding. Thus, women who had previously breastfed for a longer period would both have lowered their current DDE concentrations and be more likely to breastfeed longer again, as compared to women who had previously breastfed only shortly [12].

Also of possible concern are the perfluoroalkyl substances (PFASs), a group of highly persistent chemicals frequently used in consumer products [13], and which are ubiquitously present in humans [14–16]. Duration of breastfeeding in Danish women was found to decrease with increasing serum-concentrations of PFASs, but since the findings were seen only in multiparous women, previous breastfeeding could have confounded the association [17].

Using data from two Faroese cohorts we aimed to examine whether exposure to the five most common PFASs was associated with the duration of breastfeeding among primiparous and multiparous women.

2. Methods

2.1. Study design

Two birth cohorts were formed in 1997–2000 [18–20] and in 2007–2009 [21] in the Faroe Islands. Located in the North Atlantic, the Faroe Islands is a self-governing marine community within the Danish kingdom. This Nordic population is approximately 50,000, rather homogenous, and has free access to health care, including obstetric care. The birth cohorts were formed to examine associations between environmental chemical exposures and adverse health outcomes. The hypothesis being tested in the present study was formulated after data collection, as triggered by a recently published study [17].

A blood sample was obtained from the mother between week 34 and 36 of pregnancy (older cohort) or two weeks after their term date (younger cohort). Background and medical information about the mother, the gestational period and the childbirth was recorded at recruitment and at subsequent follow-up. At age 5, parents of both cohorts filled out a questionnaire followed by an interview by a research nurse. The younger cohort additionally filled out a questionnaire followed by an interview at age 18 months in which information about breastfeeding (yes/no), duration of exclusive breastfeeding, and breastfeeding in addition to formula or other food sources (mixed breastfeeding) was obtained (in terms of number of months). Total duration of breastfeeding was calculated as the sum of exclusive and mixed breastfeeding. Information about total duration of breastfeeding was, however, replaced with information from the questionnaire at age 5 years if the mother stated that the child had been breast-fed for more than 18 months. In the older cohort, information about duration of total and exclusive (no other food) breastfeeding was obtained from the 5-year questionnaire only. The WHO definition of exclusive breastfeeding states that no other liquids (including water) and solids are given [22]. We did, however, not inquire about supplementation with water; only trace amounts of PFASs have been detected in Faroese water samples [23].

Information retrieved from the hospital records included maternal age (maternal birthday – child birthday), parity (zero/at least one previous birth), pregnancy smoking (none/any), pregnancy alcohol intake (none/any), pre-pregnancy body mass index (BMI: weight/height^2), education (none/any education above primary school), and employment (employed including maternity leave/unemployed, under education, home maker, early retirement or sick leave). Furthermore, in the younger cohort, more detailed information about education was also obtained in a questionnaire to the mothers two weeks after their term date. If information about education was missing from the hospital records, we used information from the subsequent maternal questionnaire. Twins were excluded from our analyses.

Written informed consent was obtained from all women included in the study. The Faroese cohort study was performed in accordance with the Helsinki declaration and was approved by the Faroese ethical review committee and the institutional review board at Harvard T.H. Chan School of Public Health.

2.2. Exposure assessment

The five most common PFASs, i.e., perfluorohexane sulfonic acid (PFHxS), perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), and perfluorodecanoic acid (PFDA) were measured in maternal serum along with *p,p'*-DDE and polychlorinated biphenyls (PCBs). Quantitation of PFAS was carried out by isotope dilution and online solid-phase extraction followed by analysis using high-pressure liquid chromatography with tandem mass spectrometry [24]. PFOS was quantified by integration of two adjacent peaks, which represent the branched isomers and the linear isomer. The limit of detection (LOD) was 0.03 ng/mL. Values below LOD were assumed to be 0.015 ng/mL. The accuracy of the method was assessed by regular participation in the German Quality Assessment program (G-EQUAS) organized by the German Society of Occupational Medicine. The between batch-imprecision during the analysis of the samples were <7.7% for the older cohort and <5.0% for the younger cohort.

DDE and PCB serum analyses were conducted as previously described [18,24]. The accuracy for this analysis was also assessed by participation in the G-EQUAS program. Use of quality control samples verified that the results from the two cohorts were comparable. A simplified ΣPCB concentration was calculated as the sum of congeners CB-138, CB-153, and CB-180 multiplied by 2.

The population distribution of PFASs, DDE and ΣPCB concentrations is skewed to the right, and these measures were therefore log-transformed using log10 in order to reduce the influence of outlying values when they were used as predictors and to avoid violating model assumptions when performing analyses of associations with PFASs as the outcome.

2.3. Statistical analysis

Women who had not provided information about duration of breastfeeding or provided a blood sample for PFAS analysis were compared to those who had provided the information using unadjusted logistic regression models, and the two cohorts were compared with regard to exposures, outcomes and covariates using Wilcoxon's rank-sum test (continuous variables) or Chi squared test (categorical variables). Confounding was identified using a directed acyclic graph (DAG, Fig. 1) based on existing literature about predictors for breastfeeding and pregnancy serum-PFAS concentrations. Maternal smoking [6,7,9], maternal alcohol intake [10], high maternal BMI [7,9], low maternal age [6–9], low maternal education [6–9], maternal employment [6], and primiparity [6,8] have all been associated with reduced duration of breastfeeding. These factors might also be associated with PFAS exposure [25–29], although only the association between higher parity and reduced serum-PFAS concentrations is consistent across studies [25–27,29]. Confounding was identified as backdoor paths between maternal serum-PFAS concentrations and breastfeeding [30], and these paths were blocked by conditioning on one of the variables on each path if information was available [31].

Since knowledge about sources of PFAS exposure is limited and results from existing studies of predictors are inconsistent [25–29], we also tested associations between potential confounding variables and the log-transformed serum-PFAS concentrations in linear regression models adjusted for cohort, and the estimates

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