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Exposure to organochlorines and mercury through fish and marine mammal consumption: Associations with growth and duration of gestation among Inuit newborns☆,☆☆

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ABSTRACT

Background: Several studies have reported negative associations of polychlorinated biphenyls (PCBs), hexachlorobenzene (HCB) and mercury (Hg) with duration of gestation and fetal growth in fish eating populations. Docosahexaenoic acid (DHA) from fish, seafood and marine mammal intake has been reported to be positively related with pregnancy duration and fetal growth. So far, it remains unclear, however, if the associations of environmental contaminants (ECs) with growth are direct or mediated through their relation with the duration of gestation and the degree to which DHA intake during pregnancy attenuates the negative association of ECs with fetal growth.
Objectives: To investigate direct and indirect associations of in utero exposure to ECs with fetal growth and pregnancy duration while taking into account the possible positive effects of DHA.
Methods: Pregnant Inuit women ($N = 248$) from Arctic Quebec were recruited and cord blood samples were analyzed for PCBs, HCB, Hg and DHA. Anthropometric measurements were assessed at birth. Path models were used to evaluate direct and indirect associations.
Results: Cord concentrations of PCB 153, HCB and Hg were significantly associated with shorter duration of pregnancy (β varying from −0.17 to −0.20, $p < 0.05$). Path models indicated that the associations of PCBs, HCB and Hg with reduced fetal growth (β varying from −0.09 to −0.13, $p < 0.05$) were mediated through their relations with shorter gestation duration. Cord DHA was indirectly related to greater growth parameters (β varying from 0.17 to 0.20, $p < 0.05$) through its positive association with gestation duration.
Conclusion: Prenatal exposure to ECs was associated with reduced gestation duration, which is a recognized determinant of fetal growth. DHA intake during pregnancy appeared to have independent positive association with fetal growth by prolonging gestation. Whether these associations are causal remains to be elucidated.

1. Introduction

Benefits and risks associated with consumption of fish, seafood and marine mammals is a public health issue of great relevance for many populations around the world. These food sources often contain environmental contaminants (ECs) that cross the placenta, thereby exposing the embryo and the fetus during conception and prenatal development, periods of well-documented vulnerability to exogenous chemicals. On the other hand, fish, seafood and marine mammals are good sources of nutrients, such as n−3 polyunsaturated fatty acids (n−3 PUFAs), for which there is increasing evidence of positive effects on fetal growth and length of gestation in term infants (Makrides et al., 2006; Olsen et al., 1986; Szajewska et al., 2006).

ECs of concern for pregnant women and women of childbearing age that are consuming fish, seafood and marine mammals include methylmercury (MeHg) and organochlorine chemicals (OCs), such as

Abbreviations: DHA, docosahexaenoic acids; ECs, environmental contaminants; HCB, hexachlorobenzene; Hg, mercury; MAR, missing at random; MeHg, methylmercury; n−3 PUFAs, n−3 polyunsatured fatty acids; OCs, organochlorine compounds; Pb, lead; PCBs, polychlorinated biphenyls; Se, selenium.

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☆☆ Ethics: The participation of human subjects did occur after informed consent was obtained. The research procedures were approved by the human subjects committees of Laval University and Wayne State University.

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polychlorinated biphenyls (PCBs) and hexachlorobenzene (HCB). OCs are a family of persistent hydrocarbon compounds used extensively in North American and European industry and agriculture from 1930 through the mid-1980s. Due to their high lipophilicity and resistance to biodegradation, OCs bioaccumulate in fatty tissues of organisms and are biomagnified through the food chain (Dewailly et al., 1993a). In the aquatic environment, mercury (Hg), which comes from both natural and anthropogenic sources, is transformed by bacteria into methylmercury (MeHg) and accumulates in seafood.

Relationships between prenatal exposure to background levels of OCs and MeHg with fetal growth and duration of gestation have been studied in several prospective and retrospective cohort studies of fish eating populations. To date, ten PCB studies have been conducted with frequent consumers of fish and/or marine mammals (Bjerregaard and Hansen, 2000; Dewailly et al., 1993b; Fein et al., 1984; Grandjean et al., 2001; Karmaus and Zhu, 2004; Murphy et al., 2010; Rylander et al., 1998; Vartiainen et al., 1998; Weisskopf et al., 2005; Wojtyniak et al., 2010). PCB exposure was associated with smaller birth weight in five of those studies (Fein et al., 1984; Karmaus and Zhu, 2004; Murphy et al., 2010; Rylander et al., 1998; Wojtyniak et al., 2010). Dewailly et al. (1993b) have found shorter body length among boys, without association with head circumference. However, smaller head circumference was observed in Fein et al. (1984) study. Shorter gestation was found to be related to cord PCB concentrations in one study (Fein et al., 1984), but not with maternal preconceptional PCB concentrations in the New York anglers study (Murphy et al., 2010). The association of in utero exposure to HCB with fetal growth was reported only in one fish eating cohort (Dewailly et al., 1993b), where this OC was related to shorter body length.

Six studies in fish-eating populations have focused on in utero Hg exposure relationships with birth weight (Bjerregaard and Hansen, 2000; Drouillet-Pinard et al., 2010; Foldspang and Hansen, 1990; Lee et al., 2010; Mendez et al., 2010; Ramon et al., 2009), two on body length (Drouillet-Pinard et al., 2010; Ramon et al., 2009), one on head circumference (Drouillet-Pinard et al., 2010) and four on gestation duration (Bjerregaard and Hansen, 2000; Drouillet-Pinard et al., 2010; Foldspang and Hansen, 1990; Xue et al., 2007). Significant associations were reported with smaller birth weight in four studies, and with reduced birth length in one of the Spanish cohorts (Ramon et al., 2009). Newborn head circumference was not related to maternal Hg levels in hair among French pregnant women (Drouillet-Pinard et al., 2010). In the Pregnancy Outcome and Community Health (POUCH) study, increasing risk of preterm delivery was reported among women with hair Hg concentrations above the 90th percentile (Xue et al., 2007), while the other studies did not evaluate or find a relation between Hg exposure and pregnancy duration.

Several randomized controlled trials have documented benefits of prenatal n−3 PUFAs, particularly docosahexaenoic acid (DHA), on gestation duration, reduced risk of preterm deliveries (Olsen et al., 2000) and in some instances fetal growth (Campoy et al., 2012; Helland et al., 2001; Olsen et al., 1992). Although the hypothesis that the adverse reproductive effects of OCs and MeHg might be attenuated by a high maternal intake of n−3 PUFAs was formulated two decades ago, it has received little direct scientific scrutiny. The vast majority of cohort studies conducted to date have focused either on ECs or n−3 PUFAs and did not obtain biomarkers of both. Moreover, in observational studies, a failure to control for prenatal n−3 PUFAs could lead to an underestimation of the toxicity of ECs on the outcomes of interest (Choi et al., 2008; Davidson et al., 2008).

We conducted a prospective longitudinal study to examine the potential associations of pre- and postnatal exposures to moderately high levels of OCs and Hg on duration of gestation, physical growth as well as cognitive and behavioral development in a sample of Inuit infants in Northern Quebec, Canada (Jacobson et al., 2008; Muckle et al., 2001). This paper focuses specifically on the associations of prenatal exposure to OCs and Hg with fetal growth and duration of pregnancy and addresses two research questions: If EC concentrations are negatively associated with growth parameters, are the associations direct or mediated through shortened duration of gestation? Are n−3 PUFA levels positively related to gestation duration and fetal growth, and if so, do they mitigate the potential negative effects of ECs on gestation duration and growth?

2. Materials and methods

2.1. Population

Pregnant Inuit women from the Arctic Quebec region known as Nunavik were invited to participate in a study focusing on infant health and development. Nunavik is a region located north of the 55th parallel, in which 10 000 Inuit live in 14 villages scattered along a 2000-km coastline on the Hudson Bay, Hudson Strait, and Ungava Bay. Participants were recruited from the three largest communities on the Hudson Bay coast.

2.2. Procedures and variables

From November 1995 to November 2001 pregnant women in these communities were invited to participate in the study at their first prenatal visit to the village nursing station. The recruitment procedure has previously been described (Muckle et al., 2001). A detailed informed consent was obtained from each participating mother. The research procedures were approved by the human subject committees of Laval University and Wayne State University. Maternal interviews were conducted in the community's nursing station at mid-pregnancy and at 1-month postpartum by trained research assistants to assess the mothers' socioeconomic and personal characteristics. Among the 417 Nunavik women invited to participate in this study, 47 were excluded because a newborn from the same mother had been previously recruited, 9 could not be contacted by our research assistants to schedule the prenatal interview, and 110 refused to participate. Among the 251 women interviewed prenatally, 3 were subsequently excluded due to miscarriage or perinatal or postnatal mortality. Overall, the participation rate for the study was 69%, for a total of 248 pregnant women and their newborns for whom we have information regarding environmental exposure and/or growth parameters.

2.3. Biomarkers and laboratory procedures

A 30-mL blood sample was drawn from the umbilical cord after it was severed. Concentration of the 14 most prevalent PCB congeners (IUPAC nos. 28, 52, 99, 101, 105, 118, 128, 138, 153, 156, 170, 180, 183, 187) and HCB, were measured in cord plasma samples. The detection limit was 0.02 μg/L for all compounds. Hg concentrations were determined in cord whole blood, as well as in the maternal hair sample collected postnatally, which was cut into three segments of 3 cm, each corresponding to a trimester of pregnancy. The detection limits were 1.0 nmol/L and 1.0 nmol/g for blood and hair Hg analysis, respectively. Fatty acids including n−3 PUFAs and DHA were determined in cord plasma phospholipids and expressed as percentages of all fatty acids from C14:0 to C24:1 (% weight). Total cholesterol, free cholesterol, triglycerides, and phospholipids in plasma were also determined. Concentrations of total plasma lipids were estimated according to the formula developed by Akins et al. (1989). Detailed laboratory procedures for ECs, n−3 PUFAs and lipid quantification and quality control data have been described previously (Jacobson et al., 2008; Muckle et al., 2001).

2.4. Outcomes

Weight, length, and head circumference at birth were measured by a midwife or nurse, who had been trained by the investigators to follow a standard protocol. Two measurements were performed for each growth