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Maternal diet, prenatal exposure to dioxins and other persistent organic pollutants and anogenital distance in children

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HIGHLIGHTS

- "High-fat-diet" score was positively related to maternal dioxin-like activity.
- "High-fat-diet" score was positively related to maternal PCB and HCB blood levels.
- "High-fat-diet" score was associated with shorter genitalia distance in newborn boys.
- "High-fat-diet" score was associated with longer genitalia distance in newborn girls.
- No association between "high-fat-diet" score and genitalia distances in young children

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ABSTRACT

We investigated the potential endocrine disruptive effect of prenatal exposure to persistent organic pollutants (POPs) through maternal diet, by measuring anogenital distance in newborns and young children. We included 231 mothers and their newborns measured at birth from the Rhea study in Crete, Greece and the Hmar study in Barcelona, Spain and 476 mothers and their children measured between 1 and 2 years from the Rhea study. We used food frequency questionnaires to assess maternal diet and estimated plasma dioxin-like activity by the Dioxin-Responsive Chemically Activated LUciferase eXpression (DR-CALUX®) and other POPs in maternal samples. We defined a "high-fat diet" score, as a prenatal exposure estimate, that incorporated intakes of red meat, processed meat, fatty fish, seafood, eggs and high-fat dairy products during pregnancy. Increasing maternal "high-fat diet" score was related to increasing dioxin-like activity and serum concentrations of lipophilic persistent organic pollutants in maternal blood. An inverse dose–response association was found between "high-fat diet" score and anoscrotal distance in newborn males. The highest tertile of the maternal score was associated with −4.2 mm (95% CI −6.6 to −1.8) reduction in anoscrotal distance of newborn males, compared to the lowest tertile. A weak positive association was found between the "high-fat diet" score and anofourchetal distance in newborn females. In young children we found no association between maternal "high-fat diet" score and anogenital distances. In conclusion, maternal high-fat diet may be linked to high prenatal exposure to persistent organic pollutants and endocrine disruptive effects, resulting to phenotypic alterations of the reproductive system.

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1. Introduction

Maternal diet during pregnancy is crucial because it provides essential nutrients to the developing fetus (Chatzi et al., 2012; Knudsen et al., 2008). However, the fetus is also exposed through the mother to persistent organic pollutants (POPs) (Liem et al., 2000). Human exposure to POPs such as dioxins, biphenyls (PCBs) and organochlorine pesticides occurs mainly through diet. Studies combining food consumption and contamination levels have identified seafood, meat, eggs and dairy products as main sources of dietary exposure to POPs (Darnerud et al., 2006; De Mul et al., 2008; Perello et al., 2012; Tard et al., 2007).

Diet of pregnant women is associated with levels of lipophilic organochlorine contaminants in maternal and cord blood as well as in the placenta (Glynn et al., 2007; Halldorsson et al., 2008; Huang et al., 2007; Llop et al., 2010). During pregnancy, absorbed compounds pass through the placenta and reach the fetus (Lopez-Espinosa et al., 2007; Suzuki et al., 2005). After birth, exposure continues through breast-feeding and concentrations of POPs in maternal blood have been related to concentrations in breast milk (Solomon and Weiss, 2002). Therefore, maternal body burden of POPs is important because of potential health effects in the fetuses.

Organochlorine contaminants can disrupt normal endocrine function and in-utero exposures have been linked to several adverse health effects (Lundqvist et al., 2006; Wigle et al., 2008). In animals, prenatal exposure to organochlorine contaminants may induce anti-androgenic effects and alterations in the reproductive system of offspring, including a reduction in anogenital distance (Gray et al., 2001; Ohsako et al., 2002). Anogenital distance, measured from the anus to the genitalia, is used as a marker of prenatal exposure to androgens. Additional post-natal androgen production does not affect anogenital distance in animals and may assist as a predictor of androgen responsive outcomes in adulthood (McIntyre et al., 2002; van den Driesche et al., 2011).

In humans, prenatal exposure to phthalates, which can act as hormone disrupters, has been linked to shorter anogenital distance mainly in boys (Huang et al., 2009; Suzuki et al., 2012; Swan et al., 2005). Two studies have investigated the association between prenatal exposure to DDE and anogenital distance in children and reported inconsistent results (Longnecker et al., 2007; Torres-Sanchez et al., 2008). Our research group recently showed that high dioxin-like activity in maternal blood was associated with a reduction in anogenital distance of newborn boys (Vafeiadi et al., 2013). There is no study on the effect of maternal diet, as a source of exposure to POPs, on anogenital distance of children. In adult men, shorter anogenital distance predicted poorer semen quality and hypogonadal testosterone levels, while prostate cancer patients had shorter anogenital distances than healthy adult men (Castano-Vinyals et al., 2012; Eisenberg et al., 2012a; Mendiola et al., 2011). Anogenital distance in humans has been also suggested as a novel marker of adult testicular function (Eisenberg et al., 2012a, 2012b, 2012c).

We examined the association between prenatal exposure to organochlorine compounds, through maternal high-fat diet, and anogenital distance measured in males and females, in two mother–child cohorts in Greece and Spain.

2. Methods

2.1. Study population

Mothers and their children included in this analysis were from the mother–child cohort in Crete, Greece ("Rhea study") and the Hospital del Mar cohort in Barcelona, Spain ("Hmar study"). The Rhea study examines prospectively a population-based cohort of pregnant women and their children at the prefecture of Heraklion, Crete, Greece (Chatzi et al., 2009). Women were recruited within a year (from February 2007) at around 12 weeks of gestation. The inclusion criteria were: to be residents of the study area, to be more than 16 years old, to have the 1st visit at hospitals or private clinics at 10–13 weeks of gestation for the first major ultrasound examination and to have no communication handicap. The Hmar study includes women with singleton pregnancies enrolled at delivery in a public hospital of Barcelona, Spain, from October 2008 to March 2010. Women less than 18 years old, with multiple pregnancies or with pregnancy complications (HIV/B hepatitis/C hepatitis infections, urgent C-sections, postpartum excessive hemorrhage) were excluded.

In the Rhea study, 795 (49.4% of the total "Rhea study" population) women with singleton pregnancies agreed to participate in the anogenital measurement protocol of their children and 647 children were measured. In the Hmar study, 187 (66.5% of the total "Hmar study" population) newborns were measured and 127 mother–newborn pairs were eligible for this analysis with complete maternal dietary information. In both studies, 34 women were excluded due to missing information on maternal socio-demographic characteristics and 33 women were excluded due to implausible maternal energy intake (outside the range of 4184–16,736 kJ/day) (Davey et al., 2003). Hence, 231 mothers with their newborns (n = 128 from the Rhea study, n = 103 from the Hmar study) and 476 mothers with their children measured between 1 and 2 years (all from Rhea study) were included in our analysis.

All procedures of the study were approved by the ethical committee of the University Hospital in Heraklion, Crete, Greece and by the Clinical Research Ethical Committee at Hospital del Mar (CEIC), Barcelona, Spain. Written informed consent was obtained from all women participating in the studies concerning themselves as well as their children.

2.2. Dietary assessment and maternal "high-fat diet" score

In the Rhea study, a validated food frequency questionnaire (FFQ) was used to assess dietary habits over pregnancy. It was administered by trained research nurses between 14 and 18 weeks of gestation (Chatzi et al., 2011). Frequency of intake was obtained for 250 food items. The FFQ used by the Hmar study was adapted by the INMA (INfancia y Medio Ambiente) Project and it has been validated for use among adults living in Spain (Guxens et al., 2012). Women completed the FFQ after delivery and were asked to report the frequency of intake for 100 food items during the whole period of their pregnancy.

A "high-fat diet" score was created to estimate prenatal exposure to organochlorine contaminants from maternal diet. Foods of animal origin with high fat content, recognized as dietary sources of organochlorine compounds are included in this score as 6 food groups: red meat, processed meat, seafood, fatty fish, eggs and high fat dairy products (EFSA, 2012, 2006a, 2006b). Each food group was formed as a summary of the weekly frequency of intake of specific food items. The group of "red meat" included: pork, beef, lamb, goat, pork and beef burgers and minced meat. The group of "processed meat" included: cured meat (ham, sausage, salami, mortadella, smoked turkey), bacon and boiled turkey. Tuna (canned and fresh) and salmon were included in the "fatty fish group", as well as smaller species of fatty fish (i.e. sardines, mackerel). The group of "seafood" included: shrimps, squid and shellfish. The "eggs" food group was a summary of intake of boiled eggs, fried eggs and omelets. Finally, "high-fat dairy products" included: whole milk, high-fat cheese, whole yogurt, ice cream and whipped cream. Liver and offal were not included in the "high-fat diet" score because many women reported no intake of such foods (Rhea study: liver 74.7% and offal 85.7% of no intake; Hmar study: liver 63.1% and offal 80.6% of no intake).

Each food group was categorized in tertiles and a value was assigned in each woman, according to her level of intake, as follows: 0 for the lower tertile, 1 for the middle tertile and 2 for the upper tertile. The summary of those values was the "high-fat diet" score of each woman. Many women reported no intake of seafood (n = 406, 56%), thus we used 2 values for seafood intake. A value of 0 was assigned for no intake and 1 for intake. Hence, the "high-fat" score ranged from 0 to 11 and represents the cumulative weekly intake of 6 food groups (in times/week).