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Postnatal weight growth and trihalomethane exposure during pregnancy

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ABSTRACT

Background: Impaired postnatal growth after chloroform exposure in utero has been observed in rodents without an effect on birth weight. We aimed to study the relationship between exposure to trihalomethanes (THMs) during pregnancy and postnatal weight growth during infancy.
Methods: We analysed 2216 mother–child pairs recruited in Gipuzkoa, Sabadell, Valencia (Spain, INMA Project, enrolment: 2003–2008) and Crete (Greece, RHEA Study, enrolment: 2007–2008). Drinking water habits and water-related activities ascertained through personal interviews were combined with THM measurements in drinking water to estimate THM exposure through different exposure routes during pregnancy. Weight measurements during the first year of life were used to fit postnatal weight growth curves from birth to one year and to predict weight at six months. Multiple linear regression was used to evaluate the relationship between six months weight gain and interquartile range (IQR) increase in THM exposure adjusting for confounders.
Results: Average weight gain at six months ranged from 4325 g (Gipuzkoa) to 4668 g (Crete). Median residential THM levels ranged from 1 μg/l (Crete) to 117 μg/l (Sabadell). No significant association was observed overall (−24.4 g [95% CI −78.8, 30.0] for an IQR increase in total residential uptake). A negative relationship was observed in Sabadell (−148 g [95% CI −282, −13.7]) for an IQR increase in ingestion THM uptake.
Conclusions: No consistent evidence of an association between THM exposure during pregnancy and postnatal growth was observed. The novelty of the hypothesis and the negative trend observed in the region with the highest levels warrants the replication in future studies.

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1. Introduction

The evidence that early life factors including environmental exposures may have effects on pregnancy outcomes and childhood diseases has become strong (Gluckman et al., 2005). Some exposures occurring during pregnancy (e.g. alcohol, glycaemia) have

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been shown to affect the growth and development in utero and/or during early postnatal life (Swanson et al., 2009; Regnault et al., 2010; Boekelheide et al., 2012), and a number of complex epigenetic mechanisms have been invoked (Boekelheide et al., 2012).

Disinfection-by-products (DBPs) are chemicals occurring in drinking water as a result of the treatment process. Among more than 700 DBPs identified, trihalomethanes (THMs) are some of the most abundant (Nieuwenhuijsen, 2003). They mainly include chloroform (trichloromethane, TCM), bromodichloromethane (BDCM), chlorodibromomethane (CDBM) and bromoform (tribromomethane, TBM). Exposure can occur through water ingestion, inhalation and dermal absorption when showering or bathing. Meta-analyses (Grellier et al., 2010; Nieuwenhuijsen et al., 2009) and recent studies conducted in Brittany (France), Kaunas (Lithuania) and Quebec (Canada) (Grazuleviciene et al., 2011; Costet et al., 2012; Levallois et al., 2012) have shown evidence for an association between THM exposure and born small for gestational age (SGA) and foetal growth restriction, whereas others did not show such associations (Villanueva et al., 2011; Patelarou et al., 2011). Genetic polymorphism of glutathione S-transferases could partially explain the heterogeneity of the results (Danileviciute et al., 2012).

An increasing number of epidemiological studies are showing associations between exposure to environmental contaminants during pregnancy, especially those with an endocrine disrupting activity, and postnatal growth. For instance, prenatal exposure to organochlorine pesticides was associated with an increased risk of overweight in children (Valvi et al., 2012). On the contrary, prenatal exposure to bisphenol A has been negatively associated with body mass index (BMI) in a population of 9 years old girls (Harley et al., 2013).

To our knowledge, the effect of THM exposure during pregnancy on postnatal growth has not been studied in humans so far. Experimental evidence in rodents showed that offspring of dams exposed to chloroform in utero had a significantly impaired postnatal weight growth until weaning at day 21 but did not show a lower birth weight (Lim et al., 2004). No underlying mechanism of such relationship has been settled, although an endocrine disrupting activity has been mentioned (Klinefelter et al., 2004) as well as a possible epigenetic activity (Coffin et al., 2000; Pereira et al., 2001).

We postulated that the effect of THM exposure during pregnancy could arise after birth and aimed to evaluate in term newborns the relationship between exposure to THMs during pregnancy and postnatal weight gain between birth and six months in a prospective cohort study.

2. Methods

2.1. Study population

The Infancia y Medio Ambiente (INMA) and RHEA (Mother–child cohort in Crete) Projects are two mother–child cohort studies, respectively conducted in Spain and Crete, Greece (Guxens et al., 2011; Chatzi et al., 2009). In the present analysis we only used cohorts with detailed postnatal weight data available (Gipuzkoa, Sabadell and Valencia from INMA, and RHEA). Study subjects from the general population were recruited from week 10 to 13 in both cohorts, at the time of the first major ultrasound examination. Inclusion criteria were being 16 years or older, residence in the study area, planning to deliver at the study hospitals, no communication handicap and, for INMA only, not having followed an assisted reproduction programme and singleton pregnancy. Twins from the RHEA study were then excluded. The study sample was representative of the target population in terms of prenatal care attendance in the public health system (used by more than 80% of the pregnant women) for INMA, and representative of all the population of pregnant women (from public hospitals and private maternity clinics) in Heraklion prefecture for the RHEA study.

Enrolment periods were November 2003 to June 2005 in Valencia, June 2004 to July 2006 in Sabadell, May 2006 to February 2008 in Gipuzkoa and February 2007 to February 2008 in Heraklion, Crete (Guxens et al., 2011; Chatzi et al., 2009). Study subjects were followed until delivery and during the postnatal period. From the initial sample, 611 (96%) in Gipuzkoa, 620 (94%) in Sabadell, 787 (92%) in Valencia and 1371 (82%) in Crete were followed at delivery. To fit individual weight growth trajectories adequately, at least four measures of weight between birth and one year were required, leading to 450, 533, 645 and 873 term newborns in Gipuzkoa, Sabadell, Valencia, and Crete, respectively. Estimates of THM exposure during pregnancy were available for, respectively, 567, 559, 720 and 782 subjects. Both exposure and growth data were available for 421, 487, 594 and 772 subjects in Gipuzkoa, Sabadell, Valencia, and Crete, respectively. Finally, considering the missing data for adjustment variables (parity: $n=26$, maternal smoking: $n=26$, paternal anthropometry: $n=25$, maternal education: $n=10$, maternal weight: $n=5$, maternal age: $n=4$), the study sample was 2216: 407 (67%), 473 (76%), 594 (75%) and 742 (54%) in Gipuzkoa, Sabadell, Valencia, and Crete, respectively. The excluded population was not significantly different from the final population in terms of exposures, outcomes and potential confounders.

The Ethical Committees of each centre approved the studies and all subjects were given written informed consent before participating.

2.2. Exposure assessment

Details about data collection and exposure assessments have been published elsewhere (Villanueva et al., 2011; Patelarou et al., 2011).

Water use habits during pregnancy were ascertained through personal interviews at recruitment (before week 15) in Crete and at week 32 of gestation in Spain. The same questions were used in all cohorts and included the type of water (municipal/bottled/private well) consumed at home and outside the home, the type of water used to cook, the use of filters for drinking and cooking, the frequency and duration of showering, bathing and swimming pool attendance. A food frequency questionnaire at week 12 and 32 in Spain and during the 2nd trimester in Crete was used to obtain extensive information on water-based fluids consumption (coffee, tea, herbal drinks). In Crete, an additional questionnaire at the third trimester of pregnancy included questions on average daily consumption of water during the third trimester of pregnancy.

Chlorine was the main disinfectant used for drinking water in all the study areas, and water source was ground in Rhea and rural municipalities in Valencia and surface in Gipuzkoa, Sabadell and the urban municipalities in Valencia. The THM levels were lower in Gipuzkoa compared to Sabadell because in that region, the water is collected from rivers that contains a lower amount of organic matter (Ventura and Rivera, 1985; Ibarluzea et al., 1994). Residential levels of THMs (TCM, BDCM, CDBM and TBM) were measured through sampling campaigns in the tap water in selected public buildings covering the study areas and from routine monitoring data in the Sabadell cohort, at the tap. THMs were determined in 421 samples in Gipuzkoa, 198 in Sabadell (148 own sampling, 50 regulatory), 162 in Valencia and 72 in RHEA. In Gipuzkoa and Sabadell, data were available almost every month over the period of pregnancies, and in Valencia and Crete, data were available at three and four time points respectively, allowing

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