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Dietary benzo(a)pyrene intake during pregnancy and birth weight: Associations modified by vitamin C intakes in the Norwegian Mother and Child Cohort Study (MoBa)

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ABSTRACT

Background: Maternal exposure to polycyclic aromatic hydrocarbons (PAH) during pregnancy has been associated with reduced fetal growth. However, the role of diet, the main source of PAH exposure among non-smokers, remains uncertain.
Objective: To assess associations between maternal exposure to dietary intake of the genotoxic PAH benzo(a)pyrene [B(a)P] during pregnancy and birth weight, exploring potential effect modification by dietary intakes of vitamins C, E and A, hypothesized to influence PAH metabolism.
Methods: This study included 50,651 women in the Norwegian Mother and Child Cohort Study (MoBa). Dietary B(a)P and nutrient intakes were estimated based on total consumption obtained from a food frequency questionnaire (FFQ) and estimated based on food composition data. Data on infant birth weight were obtained from the Medical Birth Registry of Norway (MBRN). Multivariate regression was used to assess associations between dietary B(a)P and birth weight, evaluating potential interactions with candidate nutrients.
Results: The multivariate-adjusted coefficient (95%CI) for birth weight associated with maternal energy-adjusted B(a)P intake was −20.5 g (−31.1, −10.0) in women in the third compared with the first tertile of B(a)P intake. Results were similar after excluding smokers. Significant interactions were found between elevated intakes of vitamin C (>85 mg/day) and dietary B(a)P during pregnancy for birth weight ($P < 0.05$), but no interactions were found with other vitamins. The multivariate-adjusted coefficients (95%CI) for birth weight in women in the third compared with the first tertile of B(a)P intake were −44.4 g (−76.5, −12.3) in the group with low vitamin C intakes *vs.* −17.6 g (−29.0, −6.1) in the high vitamin C intake group.
Conclusion: The results suggest that higher prenatal exposure to dietary B(a)P may reduce birth weight. Lowering maternal intake of B(a)P and increasing dietary vitamin C intake during pregnancy may help to reduce any adverse effects of B(a)P on birth weight.

1. Introduction

Maternal diet during pregnancy is the main source of essential nutrients that are needed for optimal fetal and child development (Fenech, 2002; Godfrey and Barker, 2000). At the same time, however, it is also the main source of *in utero* exposure to contaminants, such as polycyclic aromatic hydrocarbons (PAH) (Agency for Toxic Substances and Disease, 1995; Phillips, 1999; Suzuki and Yoshinaga, 2007). PAHs cross the placenta barrier, and may therefore compromise fetal development (Autrup and Vestergaard, 1996; Perera et al., 1999; Sanyal et al., 2007). Benzo(a)pyrene [B(a)P] has been identified as a human mutagen, carcinogen, and endocrine disruptor, and has been widely used as a marker of exposure to total carcinogenic PAH (Agency for Toxic Substances and Disease, 1995). Oral exposure to B(a)P is known to induce developmental and reproductive toxicity in experimental studies in animals, including effects on fetal growth (Scientific Committee on Food, 2002).

Previous epidemiological studies suggest that prenatal exposure to airborne PAH or levels of bulky DNA adducts in white blood cells; a marker of overall PAH exposure; may be associated with adverse reproductive or child health outcomes, including reduced fetal growth and lower scores on childhood tests of neurodevelopment (Choi et al., 2006, 2008; Perera et al., 2005, 2006). Recently, we reported an association between dietary B(a)P intake during pregnancy and lower birth weight in a Spanish birth cohort study (Duarte-Salles et al., 2010, 2012).

Abbreviations: FFQ, food frequency questionnaire; MBRN, Medical Birth Registry of Norway; MoBa, the Norwegian Mother and Child Cohort Study; PAHs, polycyclic aromatic hydrocarbons; B(a)P, benzo(a)pyrene.

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Antioxidant nutrients such as vitamins C, E, and A, and carotenes, have been suggested to reduce DNA damage related to PAH exposure and could therefore help to protect against adverse health outcomes related to exposure to such contaminants, perhaps by inducing the activity of detoxifying enzymes such as GSTs (Bhuvaneswari et al., 2002; Kelvin et al., 2009; Mooney et al., 2005; Palli et al., 2000; Sram et al., 2009; van Lieshout et al., 1996). Moreover, maternal intake of antioxidant nutrients during pregnancy has been shown to modify the formation of DNA adducts in cord blood (Kelvin et al., 2009), although the effect of vitamin C has not been studied. To our knowledge only one previous study has examined whether antioxidant intakes modify associations between prenatal exposure to dietary PAH and fetal growth indicators (Duarte-Salles et al., 2012). That study was conducted in a Spanish population in which the consumption of fruit and vegetables was above the recommendations for pregnant women and higher than the consumption previously reported in Nordic countries (Boffetta et al., 2010). Additionally, opposite patterns of nutrient intakes have previously been reported between Mediterranean and Nordic countries (Freisling et al., 2010).

The present study aimed to assess associations between maternal dietary intakes of B(a)P during pregnancy and birth weight in a large population-based pregnancy cohort within The Norwegian Mother and Child Cohort Study (MoBa), and investigate whether the intake of maternal antioxidant vitamin intakes could impact the associations. The study also aimed to describe population characteristics as well as dietary aspects associated with higher intakes of B(a)P.

2. Methods

2.1. Population and study design

The Norwegian Mother and Child Cohort Study (MoBa) is a prospective population-based pregnancy cohort study conducted by the Norwegian Institute of Public Health (Magnus et al., 2006). Participants were recruited from all over Norway during 1999–2008, and 38.5% of invited women consented to participate. The cohort now includes 108,000 children, 90,700 mothers and 71,500 fathers. Follow-up is conducted by questionnaires at regular intervals and by linkage to national health registries. The current study is based on version 5 of the quality-assured data files released for research on June 2010. Informed consent was provided by each MoBa participant upon recruitment. The study was approved by The Regional Committee for Medical Research Ethics in South-Eastern Norway.

Women were eligible for the present analysis if they were recorded in the Medical Birth Registry of Norway (MBRN) and had singleton births. They completed questionnaires 1 and 3 (in weeks 17 and 30 of pregnancy, respectively), baseline MoBa questionnaires covering information on sociodemographic characteristics, exposure to tobacco smoke during pregnancy, and general health; questionnaire 2 (during weeks 23–24 of pregnancy), which covered dietary information; and questionnaire 4 (when the child was 6 months of age), which collected information on maternal health at time of delivery, including maternal weight gain during pregnancy (n = 62,124). We then excluded women if they participated in MoBa with multiple pregnancies (n = 6604), if gestational age at the child's birth was <28 weeks or >42 weeks (n = 385), if data were missing on birth weight (n = 22) or maternal smoking during pregnancy (n = 817), or if the mother's estimated energy intake was <4500 kJ or >20,000 kJ (n = 796). In addition, we excluded women with missing (n = 2386) or improbable values for weight gain during pregnancy (<−30 kg or >50 kg) (n = 463), leaving a study sample of 50,651 women. Since smoking is negatively associated with birth weight and is a significant source of B(a)P exposure, we performed additional analyses (n = 46,420) excluding women who reported any smoking during pregnancy (n = 4231).

2.2. Dietary assessment and B(a)P intakes

The MoBa FFQ (downloadable at http://www.fhi.no/dokumenter/011fbd699d.pdf) was used for calculation of B(a)P and nutrient intake. This FFQ is a semi-quantitative questionnaire designed to provide information on dietary habits and intake of dietary supplements during the first four to five months of pregnancy (Meltzer et al., 2008). It has been thoroughly validated with regard to foods and nutrients (Brantsaeter et al., 2008). For each of the 255 food and beverage items, the frequency of consumption was reported by selecting one of 8–10 possible frequencies, ranging from never to several times monthly, weekly or daily. Energy intake was calculated from the FFQ using FoodCalc (Lauritsen 2005) and the Norwegian Food Composition table (Rimestad 2005). Plausibility of energy intake was identified using published equations to calculate total estimated energy requirements among pregnant women (Huang et al., 2005; Institute of Medicine, 2005); women reporting intakes below or above 2 SDs of the requirements were defined as under-reporters and over-reporters, respectively.

To calculate B(a)P intake a database was prepared containing values of B(a)P concentration for each food item in the questionnaire. First, a compilation of all available data on food concentrations of B(a)P was undertaken to construct a food composition table. Exclusion criteria for the selection of eligible values applicable to this study includes: (i) values published before 1990, (ii) values from potentially highly polluted settings (e.g.: foods locally produced in Kuwait) (Husain et al., 1997), (iii) extreme outliers, and (iv) values for heterogeneous food groups instead of food items. Examples of assigned values for each food item have been published previously (Duarte-Salles et al., 2010). When a published value was below the limit of detection/not detectable, the value assigned was the half of the detection limit. Average concentrations for B(a)P in each food were calculated using all available data for that food item. When no data was available for a food item in the FFQ, concentrations of B(a)P were imputed from similar food items (e.g.: values for skimmed milk were imputed from semi-skimmed milk). Finally, daily intake of B(a)P was estimated by multiplying food item concentrations of B(a)P by intake in grams for each woman. Total dietary intake of B(a)P was assessed by summing intakes for all food items and expressed as nanograms (ng) per day. In order to identify the main food contributors to B(a)P intake, the 255 food items in the FFQ were condensed into food groups based on nutrient profiles, culinary usage or known B(a)P levels.

2.3. Birth outcomes and other variables

Birth weight and birth length were measured by the midwife who attended the birth and reported to MBRN (Irgens 2000). Gestational age was calculated on the basis of first trimester ultrasound in 98.2% of MoBa participants. In the event of a missing ultrasound measure, gestational age was calculated from last menstrual period. Preterm birth was defined as born before week 37.

Parity was classified based on data from both MoBa and MBRN and categorized as primiparous or multiparous. Data on maternal education attainment (≤12, 13–16 and 17+ years), age, and smoking were collected from questionnaires. Smoking during pregnancy was categorized as non-smoker, occasional smoker and daily smoker. Participants with unknown/missing values for education or father's smoking were grouped in a “missing” category; results were not meaningfully different when these subjects were excluded from the analysis sample in a complete case analysis (not shown). Pre-pregnant weight and height were self-reported at week 17 of pregnancy and used to calculate pre-pregnant body mass index (BMI, kg/m^2), which was categorized as underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), or obese (≥30.0 kg/m^2). Sex of the child and weight of the mother at the time of delivery (kg) were collected from questionnaire 4. Maternal weight gain during pregnancy (kg) was