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Effects of maternal diet and environmental exposure to organochlorine pesticides on newborn weight in Southern Spain

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HIGHLIGHTS

- We analyzed prenatal exposure to OCPs and its relationship with newborn weight.
- We determined OCPs in serum from umbilical cord blood.
- We measured anthropometric variables in mothers and newborn.
- OCPs were detected in 95% of umbilical cord serum samples from the 320 newborns.
- Prenatal exposure to OCPs had an impact on the weight of healthy full-term newborns.

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ABSTRACT

An appropriate eating pattern is essential during childbearing years and pregnancy to ensure a healthy pregnancy and newborn. Our group developed a Mediterranean Diet Score for Pregnancy (MDS-P) based on the MD and the specific need of pregnant women for Fe, Ca, and folic acid. Humans are daily exposed to endocrine disruptors, which may alter body weight and hormone system regulation. This study analyzed the relationship of maternal diet and *in utero* exposure to organochlorine pesticides (OCPs) with newborn weight in mothers and newborns from Southern Spain. Higher MDS-P score, folic acid supplementation, and greater *in utero* exposure to endosulfan-diol and endosulfan-1 were related to higher newborn weight. MDS-P score was not associated with maternal weight gain during pregnancy (above or below 12 Kg). Residues from one or more OCPs were detected in 96.5% of umbilical cord serum samples from 320 newborns. The most frequent residues were endosulfans (96.5%). The presence of endosulfan-diol, endosulfan-I, p-pDDT, folic acid supplementation, and a higher MDS-P (>8) were predictive factors for newborn overweight (>3500 g). Conversely, smoking during pregnancy, shorter gestation time (32–36 *vs.* 37–39 weeks), and lesser maternal weight gain during pregnancy predicted lower newborn weight (<2500 g). These results indicate prenatal exposure to OCPs in Southern Spain and its possible impact on the weight of healthy full-term newborns. Further studies are warranted to interpret the consequences of this exposure and identify preventive measures. Adherence to the MD and folic acid supplementation during pregnancy emerged as predictive factors for overweight in newborns.

1. Introduction

An appropriate eating pattern is essential throughout childbearing years and during pregnancy to ensure a healthy pregnancy and baby (Pick et al., 2005). Pregnant women require more energy and nutrients to meet the demands of the developing fetus (Scholl, 2008). Numerous authors have pointed out the importance of

Abbreviations list: BMI, Body Mass Index; DDD, Dichlorodiphenyldichloroethane; DDE, Dichlorodiphenyldichloroethylene; DDT, Dichlorodiphenyltrichloroethane; EDCs, Endocrine Disrupting Chemicals; FFQ, Food Frequency Questionnaire; GC/ECD, Gas Chromatography and Electron-Capture Detection; GC/MS, Gas Chromatography and Mass Spectrometry; MD, Mediterranean Diet; MDS-P, Mediterranean Dietary Score-Pregnant; OCPs, Organochlorine pesticides; RDI, Reference Dietary Intakes for Spanish population.

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supplementing the diet of pregnant women with different micronutrients, especially Fe and folates (Ramakrishnau et al., 2004; Harvey et al., 2007; Bojar et al., 2012), and some have even related folic acid or folic acid plus Fe supplementation with a reduced risk of a low-weight birth (Palma et al., 2008). It is important to take account of the lifestyle and particularities of a given country or population in the evaluation of diet quality. Thus, besides addressing specific nutritional requirements, it is necessary to evaluate the foods consumed and the frequency with which they follow the daily diet of the target population. The population of interest in the present study is under the influence of the Mediterranean diet (MD).

In general, the population of Southern Spain follows the MD (Hernandez-Elizondo et al., 2009; Rivas et al., 2009; Monteagudo et al., 2015), characterized by: a high intake of vegetables, pulses, fruit, nuts, and cereals (largely unrefined in the past); a high intake of olive oil and low intake of saturated lipids; a moderately high intake of fish (depending on the proximity to the sea); a low-to-moderate intake of dairy products (mostly cheese or yoghurt); a low intake of meat and poultry; and a regular but moderate intake of wine, generally during meals (Trichopoulou et al., 2003; Monteagudo et al., 2015). Various indexes have been developed to assess diet quality in the Mediterranean area (Kennedy et al., 1995; Kant, 1996; Drewnowski et al., 1997; Mariscal-Arcas et al., 2009 Mariscal-Arcas et al., 2010a,b). Our group developed a diet quality index based on the traditional MD (Trichopoulou et al., 2003) and on the specific need during pregnancy for Fe, Ca, and folic acid, designated the Mediterranean Diet Score for Pregnancy (MDS-P) (Mariscal-Arcas et al., 2009).

Humans are daily exposed to endocrine disruptors (EDCs), chemical substances of natural or artificial origin that have been found to alter the regulation of body weight and hormone system, among other effects (Casals-Casas, 2011). They include organochlorine pesticides (OCPs), which were widely used in agriculture and, although now banned in many countries, are still manufactured for export and are highly persistent in the environment (UNEP-POP, 2011; EFSA, 2010). Studies on human exposure to OCPs in Southern Spain reported their presence in almost all adults studied (Cerrillo et al., 2006; Jimenez Torres et al., 2006; Carreno et al., 2007) and in a large proportion of the children (Lopez-Espinosa et al., 2008). A study of OCP residues in human placentas also indicated a high exposure of mother-child pairs in the same geographical area (Lopez-Espinosa et al., 2007).

Accumulation of these compounds in fat tissue during the life of the mother may be a major source of exposure for offspring, both during gestation and via breast-feeding (Cerrillo et al., 2005; LaKind et al., 2009; Elserougy et al., 2012; Dewan et al., 2013). Exposure of pregnant women to OCPs is largely dietary but can also derive from environmental, occupational, and other sources (Fernandes et al., 2011; Perelló et al., 2012). *In utero* exposure to EDs has been related to the development of obesity and related diseases (Newbold et al., 2007a,b, 2008; Legler et al., 2011; Legler, 2013). It has also been proposed that transient environmental exposures during development can alter long-term weight or adiposity regulation through epigenetic changes that affect gene expression or protein regulation, i.e., the so-called “environmental obesogen” hypothesis (Heindel & vom Saal, 2009; Lee et al., 2010b).

The objectives of this study were to analyze the relationship of maternal diet and *in utero* exposure to OCPs with newborn weight.

2. Material and methods

2.1. Study design

A cohort of mother-son pairs was established at the San Cecilio University Hospital of Granada to investigate chronic exposure to endocrine disrupting chemicals (QLK 4-CT-2002-00603). Inclusion criteria for mothers were delivery at the hospital and written consent to participate in the study and complete a questionnaire. Exclusion criteria were: presence of chronic disease (e.g., diabetes, hypertension or thyroid pathology), development of pregnancy complications that could affect fetal growth or development, and non-residence in the area served by the hospital. Data were gathered over a period of one year.

The investigation was approved by the Ethics Committee of San Cecilio University Hospital of Granada and all subject data were coded to maintain confidentiality. The present study reports on the chemical analysis of 320 umbilical cord serum samples randomly selected from the cohort.

Participants completed a prenatal questionnaire on their medication, drug and alcohol consumption, smoking, disease history, reproductive characteristics, social and working environment, residential area, diet, and cosmetic use.

2.2. Nutritional survey

Before delivery, trained researchers conducted structured face-to-face interviews, gathering data on diet, including medically recommended nutritional supplements or specific diets. All study participants completed a semi-quantitative food frequency questionnaire (FFQ) validated by our research group (Rivas et al., 2009; Mariscal-Arcas et al., 2011; Handam et al., 2014), which includes foods commonly consumed in the Mediterranean area, recording the frequency of consumption of the food items over the previous 12 months. Daily consumption in g or mL was calculated from the FFQ by multiplying the standard serving size of each one defined in the questionnaire by the value corresponding to each consumption frequency (Monteagudo et al., 2015). Twelve main food groups were then created (i.e., dairy products, eggs, meat, fish, cereals, legumes, vegetables, fruits, sweets, fats and oils, non-alcoholic beverages, and alcoholic beverages) (Willett, 1998; Hamdan et al., 2014).

Foods were converted into nutrients by using the DIAL 1.0 computer program (© 2008 Alce Ingenierías). The questionnaire design took account of the eating habits of the Spanish population. The mean portions consumed by the study population were estimated using habitual domestic measurements, e.g., spoons, glasses, cups, etc. Food intake (in g/d) was calculated from the frequency and weight (in g) of each portion, as reported by the women, or in some cases according to the usual average portion in Spain (Moreiras et al., 2013).

2.2.1. MDS-P estimation

The MDS-P (Mariscal-Arcas et al., 2009) was calculated by evaluating compliance with eight typical components of the MD: high consumption (median intake) of vegetables, fruit and nuts, pulses, cereals, and fish; a high MUFA:SFA ratio; low consumption of meat and dairy products; and the Spanish recommended daily intake (RDI) of selected micronutrients (folic acid, Fe, and Ca) (Moreiras et al., 2013), considering two-thirds of the RDI for pregnant women as the cut-off point, in common with some other indexes (Tur et al., 2005; Mariscal-Arcas et al., 2007; Bach et al., 2006). A moderate alcohol intake, also typical of the MD, was not considered in calculating the index in this group of women, who reported no alcohol consumption due to their pregnancy.

Anthropometric variables, including newborn weight (nearest gram) and length (nearest 0.1 cm), were measured at birth by staff trained in using standard protocols (Lohman et al., 1988). The height of the mothers (nearest 0.5 cm) was recorded using a model 872 Seca digital floor scale (Seca Medical Scales and Measuring