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Prenatal and postnatal insecticide use and infant neuropsychological development in a multicenter birth cohort study

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ABSTRACT

There is little evidence about exposure to currently used insecticides during early life periods and adverse effects on child neuropsychological development. The aim of this study is to examine the association between residential insecticide use during pregnancy and infancy, and the development of children.

Study subjects were participants in the INMA (Environment and Childhood) Project, a Spanish multicenter birth cohort study. Prenatal and postnatal use of indoor insecticides and other variables were obtained from personal interview during pregnancy and infancy. Mental and psychomotor development was assessed around 14 months using the Bayley Scales of Infant Development. The associations were analyzed by linear regression models.

54% of women used indoor insecticides at home during pregnancy and 47% postnatally. 34% of women used insecticide sprays and 33% used plug-in devices during pregnancy. During infancy, the percentage of women who used insecticide sprays decreased (22%), but the use of plug-in devices was similar to the prenatal period (32%). The use of insecticide sprays during pregnancy was associated with a decrement in psychomotor development ($\beta = -1.9$; 95%CI: −3.4, −0.5) but postnatal use did not associate with mental and psychomotor development. The negative effect was enhanced according to some modifying factors, such as being female, higher levels of prenatal exposure to PCB and mercury and belonging to the lowest social class.

We found certain evidence about the adverse effect of using insecticide sprays during pregnancy on the psychomotor development of children. Some socio-demographic factors and other exposures could enhance that effect.

1. Introduction

Insecticides are very widely used in the domestic setting. Studies conducted in the USA have shown that a high percentage (80–95%) of the population used some type of insecticide at home, even during pregnancy and in dwellings with young children (Adgate et al., 2000; Davis et al., 1992; Whyatt et al., 2002; Wu et al., 2011). The most frequently used were spray insecticides (Wu et al., 2011). In Bristol (UK), results from ALSPAC study (Avon Longitudinal Study of Parents and Children) showed that 93% of parents used domestic insecticides in dwellings with school age children, and 76% used two or more products (Grey et al., 2006). In Spain, 54% of the pregnant women of the INMA (Environment and Childhood) cohort used at least one type of insecticide (Llop et al., 2013).

Human exposure to insecticides may start during the uterine life period by transplacental transfer (Bradman et al., 2003). The developing brain is particularly susceptible to the adverse effects of environmental toxicants, since the blood–brain barrier, which protects the adult brain

Abbreviations: BSID-I, Bayley Scales of Infant Development; CI, Confidence intervals; EPA, Agency of Environmental Protection; RfD, reference dose; Hg, mercury; PCB, Polychlorobiphenyl; ALSPAC study, Avon Longitudinal Study of Parents and Children; CHAMACOS, Center for the Health Assessment of Mothers and Children of Salinas; CCCEH, Columbia Center for Children's Environmental Health.

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from many toxic agents, is not completely formed until 6 months after birth (Bradman et al., 2003; Grandjean and Landrigan, 2006). Furthermore, fetuses and children are especially vulnerable to insecticide exposure due to their immature detoxification and immune systems. All these factors may increase the risk of developing chronic diseases later in life (Landrigan et al., 2004).

Cognitive delays produced by the exposure to organophosphate during pregnancy have mainly been studied by three birth cohorts conducted in the USA. The Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) was a prospective cohort study that investigated the association between long-term pesticide exposure and the health of pregnant women and their children living in the agricultural area of Salinas Valley, California (Castorina et al., 2003). Urinary metabolites of organophosphate pesticides measured during pregnancy associated with mental development and pervasive developmental problems at 24 months of age (Eskenazi et al., 2007), problems of attention at age of 5 years (Marks et al., 2010), and poorer scores in working memory, processing speed, verbal comprehension, perceptual reasoning, and full-scale intelligence quotient at 7 years (Bouchard et al., 2011). Regarding the postnatal exposure to organophosphate pesticides, the authors did not find any significant association with a delay in child neurodevelopment (Young et al., 2005).

The Columbia Center for Children's Environmental Health (CCCEH) examined the effects of prenatal exposure to pesticides on children's neurodevelopment among minority communities in New York City (Perera et al., 2003). They found that higher prenatal levels of chlorpyrifos associated with mental and psychomotor delays, attention problems, and pervasive developmental disorder problems at 3 years of age (Rauh et al., 2006), however they did not observe a relation with prenatal permethrin exposure and adverse neurodevelopment (Horton et al., 2011).

Finally, in the birth cohort of Mount Sinai Hospital in New York City an association between prenatal exposure to malathion and abnormal reflexes in neonates was observed (Engel et al., 2007), as well as between some organophosphate metabolites levels and abnormal reflexes in neonates and a decrement in mental development at 12 months (Engel et al., 2011).

All these studies reported some evidence of adverse effects produced on neurodevelopment by prenatal exposure to organophosphate pesticides. However, there are certain contradictions and inconsistencies with regard to postnatal exposure to these compounds and also to prenatal and postnatal exposure to pyrethroids (Koureas et al., 2012), the group of insecticides most frequently used in domestic settings, so it would be necessary to conduct more epidemiologic studies in humans, and particularly in children.

The aim of the present study is to examine the association between residential insecticide use during pregnancy and infancy, both obtained by personal interview, and a possible delay in the neuropsychological development of children during the second year of life in a multicenter Spanish birth cohort.

2. Material and methods

2.1. Study population

Study subjects were participants in the INMA (Environment and Childhood) Project, a multicenter cohort study which aims to investigate the effect of environmental exposures and diet during pregnancy on fetal and child development in different geographical areas of Spain (http:www.proyectoinma.org). The study protocol has been reported elsewhere (Guxens et al., 2012; Ribas-Fito et al., 2006). Briefly, the original population in this study consisted of 2644 women recruited at the 1st trimester of pregnancy (November 2003–February 2008) in four regions of Spain: Sabadell (Catalonia), Gipuzkoa (Basque Country), Asturias and Valencia. Excluding women who withdrew from the study, were lost to follow-up, or had induced or spontaneous abortions or fetal deaths, a total sample of 2506 (95%) women were followed up until delivery (May 2004–August 2008). Their children were enrolled at birth, and were followed up until they were 30 months of age (n: 2360, 89%). The final study population consisted of mother–child pairs ($n = 1980$) with complete data on prenatal and postnatal insecticide use and for whom neuropsychological test scores were available during the second year of child's life. Women participating in the study signed an informed consent form in each phase and the Ethics Committees of the centers involved in the study approved the research protocol.

2.2. Exposure assessment

Information about prenatal and postnatal use of insecticides was obtained using a questionnaire during pregnancy and infancy. These questionnaires were administered by trained interviewers in the reference hospitals or in the primary attention centers.

The use of indoor insecticides during pregnancy (no, yes) was obtained at the third trimester (weeks 28–32). Method of application was also requested (sprays [no, yes], plug-in devices [no, yes] and other types [no, yes]). In a subsequent interview (11–30 months of age of children), we obtained information about the use of indoor insecticides during the first year of life of children (no, yes), as well as the use of insecticide sprays (no, yes), plug-in devices (no, yes) and other types (no, yes). The use of insecticide sprays and plug-in devices are not mutually exclusive and there were some women who used both applications. The prevalence of using other types of insecticides among the women was very low (2%) (Llop et al., 2013), therefore, it has been not used in the analysis.

2.3. Other variables

Socio-demographic, environmental and life-style information was obtained using questionnaires during pregnancy and infancy. The first questionnaire was administered during the first trimester of pregnancy. The variables used in this study were: maternal age, educational level (primary or no education, secondary, university), country of birth (Spain, other), and body mass index before pregnancy (underweight, healthy, overweight, obese). The second questionnaire was administered during the third trimester of pregnancy. We obtained information about: smoking habit during pregnancy (yes, no), maternal employment status (employed, unemployed), parity (0, 1, ≥2), having a garden or yard at home (no, yes) and residential proximity to an agricultural area (no, yes).

In a subsequent interview, when the children were between 11 and 30 months of age, we obtained other covariates: duration of breastfeeding (0, >0–16, >16–24, >24 weeks), main child-care provider (mother, mother with help from father, grandparent or others, other combinations without mother), child care attendance (no, yes), number of siblings (0, 1, ≥2), maternal employment status (employed, unemployed), and parental smoking habit (smoker, non smoker). Breastfeeding was defined as receiving breast milk and allowing supplementation of any food or liquid including nonhuman milk. Information related to the child's gestational age (weeks), sex, anthropometric measures, type of delivery, and the Apgar score at birth was obtained from clinical records. Low birth weight was defined as less than 2500 g, and small for gestational age (SGA) in length was defined as measuring below percentile 10. Preterm birth was considered to be less than 37 weeks of gestation.

We defined parental social class based on maternal or paternal occupation during pregnancy, whichever corresponded to the highest class among them, using a widely used Spanish adaptation of the international ISCO88 coding system (Domingo-Salvany et al., 2000). Class I included managerial jobs, senior technical staff, and commercial managers; class II included skilled non-manual workers; and class III, manual workers.