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Thyroid disruption at birth due to prenatal exposure to β-hexachlorocyclohexane ☆

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Abstract

Objective: Thyroid hormones play an important role in human brain development, and some organochlorine compounds (OCs) act as thyroid disruptors. The objective of the present study was to evaluate the association between prenatal exposure to organochlorine compounds and thyroid function in newborns from a general population birth cohort in Menorca, with an a-priori specific focus on β-HCH.
Methods: Levels of polychlorinated biphenyls (PCB congeners 28, 52, 101, 118, 138, 153 and 180), hexachlorobenzene (HCB), beta-hexachlorocyclohexane (β-HCH), dichlorodiphenyl dichloroethylene (*p′p′*-DDE) and dichlorodiphenyl trichloroethane (*p′p*-DDT) in cord serum, and thyrotropin (TSH) concentration in plasma three days after birth were measured in 387 newborns from Menorca. The TSH concentration was categorized (high or low), except for 27 children whose TSH levels were quantified.
Results: Levels of β-HCH and PCB-153 were positively related to TSH concentrations (gestational age-adjusted coefficient (*p*-value): 0.26 ($p = 0.006$) and 0.31 ($p = 0.050$), respectively).
Conclusions: β-HCH is potentially a new thyroid disrupting compound, deserving special interest in future studies given its high body burden in humans.

Keywords: Hexachlorocyclohexane; Thyroid hormones; Organochlorine compounds; Newborns

1. Introduction

Organochlorine compounds (OCs) are highly lipophylic and chemically stable compounds that have been detected recently in human adipose tissue, milk and blood (Suzuki et al., 2005). Exposure to some OCs have been found to be associated with thyroid hormone concentrations in animals (Hallergen and Darnerud, 2002; Braathen et al., 2004) and humans (Hagmar, 2003). Given that thyroid hormones play an important role in human brain development and that the foetus can be exposed to these compounds through the placenta (Suzuki et al., 2005), the effects of OCs in human thyroid function have been studied mainly in newborns (Koopman-Esseboom et al., 1994; Longnecker et al., 2000; Sandau et al., 2002; Fiolet et al., 1997; Steuerwald et al., 2000; Takser et al., 2005; Wang et al., 2005;

Abbreviations: TH, thyroid hormones; TSH, thyrotropin or thyroid stimulating hormone; SE, standard error; OCs, organochlorine compounds; PCB, polychlorinated biphenyl; HCB, hexachlorobenzene; β-HCH, beta-hexachlorocyclohexane; *p′p′*-DDE, dichlorodiphenyl dichloroethylene; *p′p*-DDT, dichlorodiphenyl trichloroethane.

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Asawasinsopon et al., 2006). Most of these studies have evaluated the effects of PCBs and dioxins (Koopman-Esseboom et al., 1994; Longnecker et al., 2000; Sandau et al., 2002; Fiolet et al., 1997; Steuerwald et al., 2000; Wang et al., 2005), but other OCs such as beta-hexachlorocyclohexane (β-HCH) have been rarely studied. We have previously found an effect of β-HCH on TSH levels at birth in a small cohort of newborns from Ribera d'Ebre, Spain (Ribas-Fito et al., 2003). β-HCH is an isomer of the pesticide formulation of HCH, in which the active insecticidal ingredient is γ -HCH (lindane). β-HCH is the isomer most frequently found in human fat, blood and breast milk, due to its longer biological half-life in the body (Willet et al., 1998). The general population is exposed to HCH through the inhalation of ambient air and the consumption of contaminated food, and several toxic effects of β-HCH have been described in humans (ATSDR, 2005). However, few studies have assessed the effects of β-HCH on thyroid function in newborns or children.

The objective of this study was to assess the effect of prenatal exposure to a range of OCs, particularly β-HCH, on levels of TSH in newborns in a population birth cohort in Menorca, Spain.

2. Methods

2.1. Study population

This study is based on data from a birth cohort from the general population in the Spanish Balearic Island of Menorca, located in the northwest Mediterranean Sea. Children from the Menorca cohort were participants in the Asthma Multicenter Infant Cohort Study (AMICS), a European study assessing factors causing asthma in children (Polk et al., 2004). This cohort recruited all children born between July 1997 and December 1998, with a total of 482 children being enrolled. Of these children, 387 (80%) had OCs and TSH measured in cord blood and plasma samples, respectively. Written consent was obtained from parents and the study was approved by the ethics committee of the Institut Municipal d'Investigació Mèdica, Barcelona.

2.2. TSH measurement

TSH in newborn plasma was obtained from the national early screening programme of hypothyroidism. In this programme TSH is determined 3 days after birth using immunoassay (ELISA) with a detection limit of 10 mU/l (established to detect cases of hypothyroidism). Therefore, those children with TSH above 10 mU/l had TSH concentrations quantified. Prior to September 1997, a detection limit of 0.1 mU/l had been in use, thus an additional 22 samples from children with TSH concentrations below 10 mU/l were also quantified and are included in these analyses.

Table 1
Comparison of Ocs by low (<10 mU/l) and high (>=10 mU/l) TSH in 382 and 5 cord serum samples, respectively

	Geometric mean (95%IC)	
	low TSH (n=382)	high TSH (n=5)
HCB (ng/ml)	0.70 (0.66–0.74)	0.83 (0.32–2.14)
p, p'-DDE (ng/ml)	1.08 (0.98–1.18)	1.10 (0.47–2.57)
p, p'-DDT (ng/ml)	0.07 (0.05–0.08)	0.06 (0.02–0.18)
B -HCH (ng/ml)	0.24 (0.21–0.28)	0.48 (0.16–1.46)
PCB-138 (ng/ml)	0.12 (0.10–0.13)	0.19 (0.10–0.38)
PCB-180 (ng/ml)	0.10 (0.08–0.12)	0.15 (0.09–0.27)
PCB-153 (ng/ml)	0.16 (0.14–0.18)	0.24 (0.17–0.32)
PCB-118 (ng/ml)	0.03 (0.02–0.04)	0.08 (0.04–0.15)
PCBs (ng/ml)	0.70 (0.62-0.73)	0.87 (0.55–1.37)

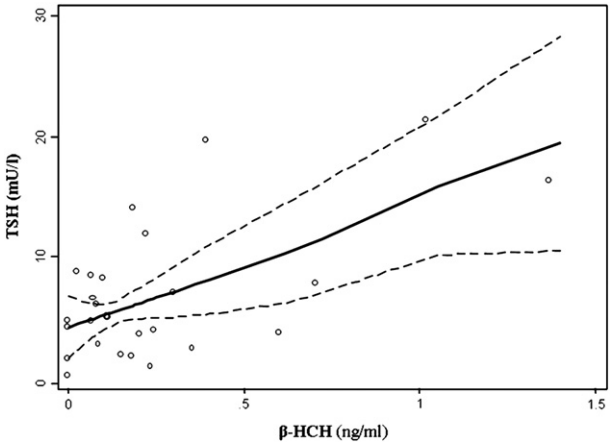

Fig. 1. Association between β-HCH and TSH (GAM models).

2.3. Organochlorine compounds

OCs (HCB, β-HCH, p,p'-DDT, p,p'-DDE, and PCB congeners 28, 52, 101, 118, 138, 153 and 180) were analysed in cord serum samples by gas chromatography (GC) with electron capture detection (Hewlett-Packard 6890N GC-ECD) and GC coupled to chemical ionisation negative-ion mass spectrometry (HP 5973 MSD) which has been previously described, as well as detection limits for all OCs (Carrizo et al., 2006).

2.4. Other variables

Information on paternal education, socioeconomic background, maternal disease and obstetric history, parity, gender and fetal exposure to alcohol and cigarette smoking was obtained through questionnaire. Information on gestational age and anthropometric measures at birth was available from clinical records.

2.5. Statistical analysis

TSH concentrations were categorized as high/low concentrations, taking the detection limit (10 mU/l) as a cut-off point. Levels of OCs were measured in each group of TSH. For a small subsample (n = 27) quantified concentration of TSH was available and Adjusted General Additive Models (GAM) models were used to evaluate the linearity of the relation between TSH concentration and levels of β-HCH. Subsequent linear regression models were run using the OC levels as independent variables, and the TSH concentration as the outcome (n = 27). OCs and TSH had a non-normal distribution and were log transformed before being included in the models. Normality and homoscedasticity of the residuals were checked using Shapiro–Wilk W test and Breusch–Pagan test, respectively. All models were adjusted by gestational age, mother's age and mother's smoking habits during pregnancy, as identified from the literature. No other variables (such as sex or mother's weight) were included in the models since the level of significance in the association with the outcome in the bivariate analysis was above 0.20. Statistical significance was set at a p-value <0.05. All analyses were conducted with the STATA 8.2 statistical software package.

3. Results

Table 1 describes the OCs concentrations (geometric mean and 95% IC) in each group of TSH (below and above the detection limit). Mann–Whitney test was used to compare the OCs concentrations between each group, however given that there were only 5 children