SHORT REPORT

Organochlorine compounds and concentrations of thyroid stimulating hormone in newborns

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Aims: To assess the association between prenatal exposure to organochlorine compounds and thyroid status in newborns from an area with high levels of hexachlorobenzene (HCB).
Methods: A total of 98 mother-infant pairs (83.1% of all children born during the period 1997–99 in a specific area polluted with HCB) were recruited. Levels of organochlorine compounds were measured in 70 cord serum samples. Concentrations of thyroid stimulating hormone (TSH) were measured in plasma of all newborns three days after birth.
Results: All newborns had concentrations of TSH within the range of normal reference values (<25 mU/l). Dichlorodiphenyl dichloroethylene (p,p'DDE), beta-hexachlorocyclohexane (β-HCH), polychlorinated biphenyl (PCB) 138 and 118 were related to higher concentrations of TSH, although only significant for β-HCH. Levels of HCB were not associated with TSH.
Conclusions: Although this community is highly exposed to HCB, no association was found between this organochlorine and TSH concentrations at birth.

Exposure to some organochlorine compounds, such as polychlorinated biphenyls (PCBs), has been associated with alterations in thyroid hormone status in adult humans and animals.[1] In infants, an association of background level perinatal PCB exposure with increased thyroid stimulating hormone (TSH) concentrations at birth has been reported.[2]

In a rural village of 5000 inhabitants located in the vicinity of an electrochemical factory (Flix, Catalonia, Spain), unusually high atmospheric levels of hexachlorobenzene (HCB) were detected. The factory is the only one in the village. It was built in 1898 and has been producing volatile chlorinated solvents over the past four decades. HCB is released to the environment as a byproduct. Adult inhabitants studied in 1994 had the highest serum HCB levels ever found, and levels of HCB in the cord serum of newborns from this population are among the highest ever reported in the 1990s in western countries.[3] The aim of the present study was to assess the association of prenatal exposure to organochlorine compounds with concentrations of TSH at birth.

SUBJECTS AND METHODS

The study area included the village of Flix and all the nearby towns of the same health area (12 000 inhabitants). A total of 110 children were born between March 1997 and December 1999 in the main hospital of the study area (93% of all children born in the study area). Children presented no congenital anomalies or diseases. Two non-Caucasian infants and two twins were excluded. A total of 98 infants born in the main hospital of the study area were finally recruited after giving written consent. The ethical committee of the Institut Municipal d'Investigació Mèdica approved this study.

Organochlorine compounds were measured in 70 cord serum samples by gas chromatography (GC) coupled to electron capture detection and GC coupled to chemical ionisation negative-ion mass spectrometry. From the remaining newborns no information was available because of the small volume of the obtained samples. We present results for the most prevalent compounds found in sera samples: HCB, dichlorodiphenyl dichloroethylene (p,p'DDE), beta-hexachlorocyclohexane (β-HCH), and PCBs. Because the sum of PCB 118, 138, 153, and 180 represented 91% of total PCBs in cord serum, we also provide results of these four congeners. Detection limits for HCB, β-HCH, and p,p'-DDE were 0.03, 0.15, and 0.09 respectively; and for the individual PCB congeners 28, 52, 101, 118, 138, 153, and 180, were 0.17, 0.15, 0.09, 0.11, 0.15, 0.12, and 0.10 ng/ml respectively. A value of 0.01 ng/ml was given for the non-detectable levels and a value of 0.05 ng/ml for those detectable but not quantifiable. The lipid content of each serum sample was not measured because the sample volume was insufficient.

Concentrations of thyroid stimulating hormone (TSH) in plasma of 3 day old newborns are routinely measured in Spanish hospitals for the early screening of hypothyroidism. TSH was measured at the Clinical Biochemistry Institute by immunoassay (ELISA). The detection limit for TSH was 10 mU/l. Laboratory personnel were unaware of the degree of organochlorine exposure of the newborns.

Information on socioeconomic background, maternal history, parity, gender, anthropometrics, and fetal exposure to alcohol and cigarette smoking was obtained through a questionnaire prepared ad hoc for this study and from clinical records. There were no significant differences in these covariates between those mother-infant pairs with biological samples and those without.

Cord serum organochlorine concentrations were normalised by base 2 logarithmic transformation since their distribution was skewed to the right. PCB congeners were only analysed as categorical variables given the high proportion of non-quantifiable values.

TSH concentrations were dichotomised in high/low concentrations, taking the detection limit as a cut off point. Multiple logistic regression was used for analysing the associations of organochlorine compounds with concentrations of TSH. Potential confounding variables were considered for inclusion in the regression based on the literature. Selection of variables in the final regression model was data driven; only variables

Abbreviations: p,p'DDE, dichlorodiphenyl dichloroethylene; β-HCH, beta-hexachlorocyclohexane; HCB, hexachlorobenzene; PCB, polychlorinated biphenyl; TSH, thyroid stimulating hormone

Table 1 Association of organochlorine compounds (ng/ml) in cord serum and TSH levels at birth

		Crude association*		
		TSH <10 mU/l (n=60)	TSH ⩾10 mU/l (n=10)	Gestational age adjusted odds ratio of having TSH ⩾10 mU/l OR (95% CI) n=70
	Median	*Geometric mean (range)*	*Geometric mean (range)*	*Doubling the dose*
HCB	1.14	1.14 (0.96–1.35)	1.14 (0.71–1.84)	1.15 (0.48 to 2.76)
p,p'DDE	0.85	0.81 (0.64–1.02)	1.20 (0.60–2.39)	1.60 (0.87 to 2.92)
β-HCH	0.54	0.23 (0.14–0.37)	0.86 (0.52–1.40)‡	1.81 (1.06 to 3.11)‡
ΣPCBs†	0.27	0.34 (0.28–0.42)	0.44 (0.23–0.82)	1.38 (0.75 to 2.57)
		% Quantifiable	*% Quantifiable*	*Quantifiable v non-quantifiable*
PCB 138		25.0%	40.0%	2.54 (0.58 to 11.18)
PCB 180		23.33%	20.0%	0.97 (0.17 to 5.47)
PCB 153		21.67%	20.0%	0.90 (0.16 to 5.04)
		% Detectable	*% Detectable*	*Detectable v non-detectable*
PCB 118		45.0%	70.0%	2.76 (0.62 to 12.31)

*Student's *t* test on base 2 log transformed variables.
†Sum of the individual congeners 28, 52, 101, 118, 138, 153, and 180.
‡p=0.03.

with associations at $p < 0.20$ with the outcome variable after inclusion of the potential confounders were selected. All statistical analyses were conducted with the SPSS and STATA packages. The criterion of statistical significance was $p < 0.05$.

RESULTS

All newborns had concentrations of TSH within the range of normal reference values (<25 mU/l). A total of 89% of the newborns had concentrations of TSH lower than 10 mU/l. Newborns with concentrations of TSH higher than 10 mU/l had a higher gestational age than those with lower concentrations of TSH ($p < 0.05$). Levels of HCB were not associated with TSH (odds ratio 1.15, 95% confidence interval 0.48 to 2.76). However, p,p'DDE, β-HCH, and PCB 138 and 118 were related to higher concentrations of TSH. Multiple regression analyses adjusting for gestational age showed that for each doubling of a dose of β-HCH there was an increase of the risk of having higher concentrations of TSH of 1.81 (table 1). This association was not modified after adjusting for the other organochlorine compounds.

DISCUSSION

These results suggest that in this cohort, conformed by a high proportion of the infants born in an HCB polluted area, there is no evidence to suggest that exposure to this chemical is associated with TSH concentrations at birth. However, those infants with higher concentrations of TSH had higher concentrations of β-HCH.

PCBs have been associated with TSH in newborns,[2 4] although some authors state that the association with PCBs may be due to chance.[5] Levels of PCBs in this study were lower than in other populations.[6] However, the lack of significant association with PCB 118 and PCB 138 could be the result of a lack of statistical power. The observed association between prenatal exposure to β-HCH with concentrations of TSH in this study was unexpected and has to be considered carefully.

In this study only concentrations of TSH were measured, but no data on total thyroxine or free thyroxine were available. In a previous study on adults of the same population, an association was observed between exposure to HCB and PCBs and an increase of total thyroxine, but no association was observed with TSH or free thyroxine.[7] A study on 1 year old Japanese infants showed decreased values of thyroxine and triiodothyronine, depending on the concentrations of PCBs in maternal milk, whereas TSH values were also unaffected.[8]

The influence of organochlorine compounds on the hypothalamic-pituitary-thyroid axis might become more pronounced later in life. In Germany, a statistically significant positive association was found between PCB 118 and TSH, and a negative relation of other congeners with triiodothyronine in children 7–10 years of age.[9] However, a study on 12 hospitalised children aged 7–14 years, who had raised concentrations of β-HCH, p,p'DDE, and PCBs, did not reveal any associations with total thyroxine or TSH.[10] This population will be followed up to 4 years of life and specific thyroid hormones will be measured.

There is a need for further studies in other populations to assess the specific effects of these organochlorines on thyroid hormones at birth and at later ages. Because of possible adverse effects of these compounds on growth and development, it is also important to observe the relation between brain development and thyroid function.

Main messages

- Organochlorine compounds may affect thyroid functioning.
- HCB levels are not associated with TSH concentrations in this highly exposed population.
- Reassessment, measuring all thyroid hormones at older ages is required.

Policy implications

- There is a need for further studies in both general and specifically exposed populations.
- Because of possible adverse effects it is important to observe the relation between brain development and thyroid function.

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REFERENCES

1 **Brouwer A**, Morse DC, Lans MC, *et al*. Interactions of persistent environmental organohalogens with the thyroid hormone system: mechanisms and possible consequences for animal and human health. *Toxicol Ind Health* 1998;**14**:59–84.
2 **Koopman-Esseboom C**, Morse DC, Weisglas-Kuperus N, *et al*. Effects of dioxins and polychlorinated biphenyls on thyroid hormone status of pregnant women and their infants. *Pediatr Res* 1994;**36**:468–73.
3 **Sala M**, Ribas-Fitó N, Cardo E, *et al*. Levels of hexachlorobenzene and other organochlorine compounds in cord blood: exposure across placenta. *Chemosphere* 2001;**43**:895–901.
4 **Longnecker MP**, Gladen BC, Patterson DG Jr, *et al*. Polychlorinated biphenyl (PCB) exposure in relation to thyroid hormone levels in neonates. *Epidemiology* 2000;**11**:249–54.
5 **Vulsma T**. Impact of exposure to maternal PCBs and dioxins on the neonate's thyroid hormone status. *Epidemiology* 2000;**11**:239–41.
6 **Korrick SA**, Altshul LM, Tolbert PE, *et al*. Measurement of PCBs, DDE, and hexachlorobenzene in cord blood from infants born in towns adjacent to a PCB-contaminated waste site. *J Expo Anal Environ Epidemiol* 2000;**10**:743–54.
7 **Sala M**, Sunyer J, Herrero C, *et al*. Association between serum concentrations of hexachlorobenzene and polychlorobiphenyls with thyroid hormone and liver enzymes in a sample of the general population. *Occup Environ Med* 2001;**58**:172–7.
8 **Nagayama J**, Okamura K, Iida T, *et al*. Postnatal exposure to chlorinated dioxins and related chemicals on thyroid hormone status in Japanese breast-fed infants. *Chemosphere* 1998;**37**:1789–93.
9 **Osius N**, Karmaus W, Kruse H, *et al*. Exposure to polychlorinated biphenyls and levels of thyroid hormones in children. *Environ Health Perspect* 1999;**107**:843–9.
10 **Mazhitova Z**, Jensen S, Ritzen M, *et al*. Chlorinated contaminants, growth and thyroid function in schoolchildren from the Aral Sea region in Kazakhstan. *Acta Paediatr* 1998;**87**:991–5.

ECHO

Educational level may affect mortality among working Koreans

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An epidemiological study in South Korea has shown that education is a primary influence on mortality, in contrast to studies of more developed populations.

The researchers studied deaths in the South Korean working population aged 20–64 years, as recorded on the death certificates of the Korean National Statistics Office, and obtained information on occupation and education from next of kin. They derived denominators from a 10% stratified random sample from the 1995 census.

Their data covered 287 000 deaths in nearly 17 million people. Death rates adjusted for age were greater in manual versus non-manual occupations and with lower levels of education in men (1.65 *v* 1.00; 5.11 *v* 1.00 respectively) and women (1.48 *v* 1.00; 3.42 *v* 1.00 respectively).

The relation was abolished in men (1.65 *v* 0.94) and more or less in women (1.48 *v* 1.17 when rates were adjusted for sex and education, but remained similar when educational level was adjusted for occupation.

These class differences in deaths are greater than in the west. They may reflect a huge investment in education to assure national economic survival or may be a phenomenon that has already peaked and levelled off in western populations. However, the researchers are anxious not to overstate their case. "The effects of education predominate, but the close association of the two variables, and data limitations, suggest a cautious interpretation."

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