

Thyroid ultrasound volume, structure and function after long-term high exposure of large population to polychlorinated biphenyls, pesticides and dioxin

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Abstract

We examined 2046 adults (834 males and 1212 females aged 20–75 years) from polluted district in East Slovakia (POLL) and two neighboring upstream and upwind located districts of background pollution (BCGR). By ultrasound we estimated the thyroid volume (ThV), hypoechogenicity (HYE), nodules and cysts. Serum levels of thyrotropin (TSH), thyroperoxidase antibodies (TPOab) and thyroglobulin were estimated by electrochemiluminiscent assay and these of 15 PCB congeners, *p,p'*-DDE, *p,p'*-DDT, hexachlorobenzene (HCB) and hexachlorocyclohexane by high-resolution gas chromatography. In 320 subjects also selected hydroxylated and methylsulfonated PCB metabolites, polychlorinated dibenzo-dioxins (PCDDs), -furans (PCDFs), five dioxin-like coplanar and eight mono-ortho PCB congeners were estimated. Urinary iodine was measured by automatic microplate method. Reciprocal positive association was found between three major POPs (PCBs, DDE and HCB), the levels of these and also PCDDs plus PCDFs in polluted area being considerably higher than in background pollution area. ThV in groups of males and females from POLL with high PCBs level was significantly higher ($p < 0.001$ by *t*-test) than in age and sex matched groups from BCGR with low PCBs level. In 1048 males and females aged <60 years with serum PCBs level >1000 ng g⁻¹ lipid (median = 1756 ng g⁻¹) a significant effect of age on ThV was found ($p < 0.01$ by ANOVA), while in 921 respective subjects with PCBs level <1000 ng g⁻¹ (median = 661 ng g⁻¹) it was not. These findings supported the view on the additional effect of PCBs on ThV other than that of age. Since the urinary iodine in both districts showed optimal range, any interfering effect of unsatisfactory iodine intake on ThV may be excluded. The frequency of autoimmune thyroiditis signs such as HYE, increased serum level of TPOab and TSH resulting in subclinical or overt thyroid hypofunction was positively associated with sex, age and organochlorine levels. The increase of such frequency in males with POPs levels was much more abrupt than that in females. No considerable differences in the frequency of thyroid nodules as related to PCBs level were found.

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1. Introduction

Because of remarkable structural similarity of some organochlorinated pollutants (POPs) such as dioxins, polychlorinated biphenyls (PCBs), pesticides etc. and thyroid hormones, attention has been focused to possible effects of these toxicants on the thyroid gland as reviewed by Brucker-Davis (1998), Hagmar (2003), Langer and Michajlovskij (1992), Langer (2005) or discussed at several workshops (Kavlock et al., 1996; DeVito et al., 1999).

In East Slovakia, chemical factory Chemko produced about 22000 tons of PCBs in 1955–84. Since no preventive measures were taken due to serious environmental negligence, factory employees and the population were exposed to heavy professional and environmental pollution by PCBs and pesticides (due to unlimited agricultural use of the latter) for a half of century. High levels of POPs in environmental and human samples were previously found (Kočan et al., 1994) and they are still persisting (Kočan et al., 2001; Chovancová et al., 2005; Jursa et al., 2006; Petřík et al., 2006).

Any activities related to such pollution were strictly banned until 1990. However, in 1994 we found increased thyroid volume by ultrasound and increased frequency of thyroid antibodies in Chemko employees and adolescents from polluted area (Langer et al., 1998). Within the next survey also the mean PCBs level of 7300 ng g⁻¹ was found in Chemko employees (Langer et al., 2003b). After comparing such level to the average of 1000–2000 ng g⁻¹ found in Baltic fishermen (Johansen et al., 1996; Kiviranta et al., 2002; Hagmar, 2003), of about 4000 ng g⁻¹ in exposed Inuits in arctic Quebec (Ayotte et al., 1997), to 95th centile of 2643 ng g⁻¹ in the population of Brescia (Italy) living around PCBs producing factory (Apostoli et al., 2005) or to median value of 5900 ng g⁻¹ in very few sea food consuming females from Faroe Islands (Fangström et al., 2002), it was concluded that the levels found in the area around Chemko belong to the highest ever reported.

Since this population has been exposed also to several other POPs, such type of unique multiple exposure offered the opportunity to search for some conclusive data on the adverse effects on human health.

2. Materials and methods

2.1. Subjects

A total of 2046 adults was examined consisting of 834 males (248 aged 19–40 years, median 27 and 586 aged 41–75 years, median 51) and 1212 females (330 aged 19–40 years, median 28 and 882 aged 41–75 years, median 50). The subjects were recruited from East Slovakian districts of Svidník, Stropkov and Michalovce, a major part of the latter being previously found heavily polluted by PCBs and other POPs (see below). Virtually all residents had a primary care physician assigned to them based on their residence, providing a direct link from physician's

practice to a geographic area of the district. Each of 28 a priori selected local physicians has been instructed to divide the alphabetical list of subjects under their care into centiles and then to call randomly one subject per each centile to fulfil the final aim to recruit about 30% of subjects <40 years and 70% between 41 and 75 years, while the ratio of males to females should be kept about 40/60%. By such a way about 60–100 subjects were finally recruited by each physician and examined in his office by the research staff. The examination consisted of previously obtained questionnaire data, physical examination, thyroid ultrasound examination, obtaining 20 ml of blood and spot urine samples from all participants after signing an informed consent document. In 320 willing subjects 90 ml of blood was obtained for the estimation of dioxins, PCB metabolites etc. (see below). The procedure was approved by Institutional Review Board and by anonymous reviewers of European Commission.

Blood was withdrawn by the vacutainer, centrifuged in a refrigerated centrifuge and the serum and urine aliquots were transported in portable freezer to the laboratory and kept frozen at –20 °C until assayed.

2.2. Thyroid ultrasound examination

This was carried out by a single observer with two decades of thyroid ultrasound experience (M.T.). Intra-observer variation was 3.9 ± 3.5% (as estimated by three subsequent measurements of 50 thyroid volumes ranging from 3.0 to 20.5 ml, median 6.2 ml and calculating the mean ± SD of deviations from the means of each set of three measurements). ThV was measured by real time sonography using the method by Brunn et al. (1981) with the aid of portable apparatus Aloka (Japan) and 7.5 MHz linear transducer.

Simultaneously, thyroid hypoechogenicity (HYE) of all thyroids was also determined as based on the comparison of thyroid image density with that of surrounding muscles (Fig. 1), both the homogenous and non-homogenous HYE being considered as the same category. If some nodules or cysts were detected, their three dimensions were measured.

2.3. Hormones, antibodies and lipids

The levels of thyrotropin (TSH), thyroglobulin (TG) and thyroperoxidase antibodies (TPOAb) were estimated by highly sensitive electrochemiluminiscent immunoassay using automatic system Elecsys (Roche, Germany). For TPOab we used cut/off level of 37 IU/ml.

2.4. Polychlorinated biphenyls and pesticides

Fifteen PCBs congeners (IUPAC numbers 28, 52, 101, 105, 114, 118, 123, 138⁺¹⁶³, 153, 156⁺¹⁷¹, 157, 167, 170, 180 and 189) and also *p,p'*-DDE (2,2'-bis(4-chlorophenyl)-1,1-dichloroethylene), *p,p'*-DDT (2,2'-bis(4-chlorophenyl)-1,1,1-trichloro-ethane), hexachlorobenzene (HCB) as well

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