CONDITION OF THYROID HORMONE SYSTEM IN 10-MONTH-OLD JAPANESE INFANTS PERINATALLY EXPOSED TO ORGANOCHLORINE PESTICIDES, PCBs AND DIOXINS

Junya Nagayama [1)], Takao Iida [2)], Reiko Nakagawa [2)], Takahiko Matsueda [2)], Hironori Hirakawa [2)],
Erni Tri Astuti [3)], Takashi Yanagawa [3)], Jun'ichiro Fukushige [4)] and Tadayoshi Watanabe [5)]

1) Laboratory of Environmental Health Sciences, School of Health Sciences, Kyushu University, Fukuoka 812-8582, Japan; 2) Department of Environmental Sciences, Fukuoka Institute of Health and Environmental
Sciences, Fukuoka 818-0135, Japan; 3) Department of Mathematical Statistics, Graduate School of
Mathematics, Kyushu University, Fukuoka 812-8581, Japan; 4) Fukuoka Children's Hospital, Fukuoka 810-0063, Japan; 5) Watanabe O.B.G.Y. Clinic, Fukuoka 813-0044, Japan

Introduction

Foods in Japan have been polluted with some organochlorine compounds such as pesticides, polychlorinated biphenyls (PCBs) and dioxins [1] and Japanese people have also been contaminated with these compounds [2, 3, 4]. Consequently, some pesticides such as hexachlorocyclohexanes (HCHs), 1,1,1-trichloro-2,2-bis-(4-chlorophenyl)-ethane (DDT), dieldrin and heptachlor epoxide (HCE), and PCBs have been determined in Japanese breast milk and their mean or median concentrations on fat weight basis were about 420, 330, 3, 4 and 110 ppb, respectively [4, 5, 6]. Their levels, however, were still 100 to 10,000 times higher than those of dioxins, that is, polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and coplanar polychlorinated biphenyls (Co-PCBs) in 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) toxic equivqlent (TEQ) value as a whole in the breast milk of Japan [5]. Therefore, we should give due attention to possible health consequences of these organochlorine pesticides and PCBs as well as dioxins in Japanese infants.

We have already reported effects of perinatal exposure to these compounds on the thyroid and related hormone statuses in the peripheral blood of Japanese infants [6, 7, 8, 9]. In this study, their effects on them were investigated more in detail in the same infants.

Materials and Methods

One hundred and twenty four mothers volunteered to participate in all in this study. Pregnancy and delivery were completed without overt signs of serious illness or complications. Only babies born at term (37 to 42 weeks of gestation) without congenital anomalies or diseases were included. Breast milk (50~100 ml), sampled 2 to 4 months after childbirth, was employed to determine the concentrations of organochlorine pesticides and PCBs by ECD gas chromatographic method [5, 10] and dioxins by high resolution GC/MS method [5].

About 1 year after birth, 5 to 10 ml of peripheral blood samples were individually obtained from 101 infants. These blood samples were used to determine serum concentrations of triiodothyronine (T_3), thyroxine (T_4) and thyroid stimulating hormone (TSH) by radioimmunoassay methods using commercially available kits [11].

In order to conduct more reliable and robust statistical analysis, data were categorized into two groups. According to concentrations of the organochlorine pesticides, PCBs and dioxins, which were adjusted for years, and serum levels of T_3, T_4 and TSH, donated by 0 (less than the mean value including minimum one) and 1 (the last quartile including maximum value). Then, we examined the relationship between contamination levels of the organochlorine compounds and serum levels of the three hormones by simple logistic regression analysis, and calculated odds ratios. In addition, multiple logistic regression analysis was done to compute the joint effect of every two organochlorine compounds, each of which showed less than 0.300 of *p*-value in simple logistic regression analysis, on the thyroid hormone system.

Results and discussion

Concentrations of the organochlorine compounds in Japanese breast milk are shown in Table 1. Contamination level of ß-HCH or DDT was about 100 times greater than that of dieldrin or HCE. Median concentrations of chlordane and PCBs were 68 and 110 ng/g lipid, respectively, and 20 to 40 times higher than those of dieldrin and HCE. In dioxins, their TEQ levels were calculated by using 1998 WHO toxic equivalency factor (TEF) values [12] and the median concentration was 23 pg-TEQ/g lipid, which was about 130 times less than those of dieldrin and HCE.

Table 1. Contamination levels of organochlorine pesticides, PCBs and dioxins in the breast milk of Japanese mother

Compound	Concentration		
	Median	Min	Max
Organochlorine pesticide (ng/g lipid)			
ß-HCH	334	39	1,229
Dieldrin	3.0	n.d.	27
DDT*	286	52	1,348
HCE	3.0	n.d.	23
Chlordane**	68	10	454
PCBs (ng/g lipid)	110	20	545
Dioxins***(pg-TEQ/g lipid)	23	3.4	49

n.d. : Less than the detection limit
* : Sum of *p, p'*-DDE and *p, p'*-DDT
** : Sum of oxychlordane, *trans*-nonaclor and *cis*-nonaclor
*** : Sum of PCDDs, PCDFs and Co-PCBs

Table 2. Thyroid and related hormone statuses in the peripheral blood of Japanese infants

Hormone	Median (min. ~ max.)	Normal Range*
T_3 (ng/ml)	1.99 (1.00 ~ 2.50)	0.8 ~ 1.8
T_4 (_g/dl)	11.3 (7.7 ~ 16.7)	4.6 ~ 12.6
TSH(_U/ml)	2.58 (0.56 ~ 8.51)	0.34 ~ 3.5

* : Determined by the biggest center of clinical examinations in Japan, SRL Corp., Tokyo, Japan for adults

As indicated in Table 2, higher levels of T_3, T_4 and TSH in the serum of Japanese infants were greater than their upper limits of Japanese adults. These hormones play vital roles in an early stage of human life and therefore obviously they are required more in fetuses and infants than in adults.

Results of simple and multiple logistic regression analyses concerning effects of the organochlorine compounds on the thyroid hormone system are shown in Tables 3 and 4, respectively.

In simple logistic regression analysis, significant negative odds ratios (less than 1.0) were seen between DDT and T_3, and between HCE and TSH. We observed significant negative correlation between DDT and T_4 and also positive correlation between DDT or dioxins and TSH in our previous studies [7, 8]. According to the robustness and reproducibility of the present statistical analysis, results of this study seem more reliable.

In multiple logistic regression analysis, DDT and PCBs jointly affected the serum T_3 levels and significantly lowered the odds ratio. Same kind of joint effect of HCE and chlordane was also observed on the serum TSH levels, and they decreased the odds ratio more than each of them did. We, however, do not know the clinical significance of these effects observed in this study for the present.

Table 3. Relationship between thyroid hormone system in the peripheral blood of Japanese infants and perinatal exposure to organochlorine pesticides, PCBs or dioxins by simple logistic regression analysis (p-value_0.250)

	Exposure Variable (Odds Ratio, p-value)
Response Variable	Organochlorine pesticides, PCBs and Dioxins
T_3	**DDT (0.57, 0.081)**
T_4	—
TSH	Dioxins (1.48, 0.212), DDT (1.56, 0.158) **HCE (0.52, 0.059)**, Chlordane (0.70, 0.250)

Boldface indicates statistically significant exposure variable (p-value<0.100).

Table 4. Joint effects of two perinatally exposed compounds on thyroid hormone system in the peripheral blood of Japanese infants by multiple logistic regression analysis

	Exposure Variable (Organochlorine pesticides, PCBs and Dioxins)			
Response Variable	X_1	X_2	Odds Ratio	*p*-value
T_3	**DDT (0.88)**	**PCBs (0.50)**	**0.44**	**0.066**
T_4				
TSH	Dioxins (1.30)	DDT (1.14)	1.48	0.650
		HCE (0.54)	**Chlordane (0.80)**	
	0.43	**0.097**		

Number in parenthesis is odds ratio of the single compound.
Boldface shows statistically significant joint effect of the two compounds (X_1, X_2) at *p*-value less than 0.100.

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