Effects of perinatal exposure to organochlorine pesticides, PCBs and dioxins on lipid weight basis on immune response and thyroid hormone systems in 10-month-old Japanese Infants

Junya Nagayama[1], Hiroshi Tsuji[2], Takao Iida[3], Reiko Nakagawa[3], Takahiko Matsueda[3], Hironori Hirakawa[3], Takashi Yanagawa[4], Jun'ichiro Fukushige[5], Tadayoshi Watanabe[6]

[1]Laboratory of Environmental Molecular Epidemiology, School of Health Sciences, Faculty of Medicine, Kyushu University
[2]Kitakyushu-Tsuyazaki Hospital
[3]Department of Environmental Sciences, Fukuoka Institute of Health and Environmental Sciences
[4]Biostatistical Center, Kurume University
[5]Fukuoka Children's Hospital
[6]Watanabe O.B.G.Y. Clinic

Introduction

Organochlorine pesticides such as hexachlorocyclohexanes (HCHs), dichlorodiphenyltrichloroethane (DDT), dieldrin, heptachlor and chlordane, and polychlorinated biphenyls (PCBs) have been banned to use in late 1960s and in early 1970s in Japan, because of their persistence and bioaccumulation in the environment, their appearance in animal and human tissue, and their toxicity. However, these chemicals and their metabolites still have been contaminating our environment, food and human beings [1, 2, 3]. Polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and coplanar PCBs (Co-PCBs), highly toxic organochlorine compounds and so-called dioxins, are also determined in human beings [1, 3, 4]. Consequently, the chemicals mentioned above and their metabolites have been measured in Japanese breast milk [5, 6, 7], which indicates Japanese mothers are also contaminated with these compounds.These compounds in Japanese mothers may cause some deleterious effects on immune response and thyroid hormone systems of Japanese infants through the placenta and/or breast milk. Therefore, we investigated the effects of perinatal exposure to the organochlorine pesticides, PCBs and dioxins on lipid weight basis on these biological systems at about 10 months of age in Japanese male and female infants.

Materials and Methods

In this study, one hundred and twenty-four mothers (mean age : 29 years old and the range : 24 ~ 38 years old) volunteered to participate in all. 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 at 2 to 4 months after childbirth, was used to determine concentrations of organochlorine pesticides and PCBs by ECD gas chromatographic method [6, 8] and dioxins by high resolution GC/MS method [6]. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD) toxic equivalent (TEQ) concentrations of dioxins were calculated by using 1998 WHO TCDD toxic equivalency factor values [9]. At around 10 months of age, 5 to 10 ml of peripheral blood samples was individually obtained from 100 infants (57 males and 43 females). These blood samples were employed to measure lymphocyte subsets by indirect immunofluorescence using monoclonal mouse anti-human antibodies against CD3 for mature T cells, CD4 for helper/inducer T cells, CD8 for suppressor/cytotoxic T cells, CD4 and CD8 double positive (CD4+8+) cells, CD16 for natural killer T cells, CD20 for B cells and HLA-DR for activated T cells (Ortho Pharmaceutical Corp., Raritan, NJ and Becton-Dickinson, Mountain View, CA) [10]. Then the relative population densities of the lymphocyte subsets were calculated. These blood samples were also used to determine the serum concentrations of T_3, T_4, TSH and TBG by radioimmunoassay methods using commercially available kits [11]. We are studying the relative risks of toxic chemicals to these biological systems, but not their causality. For this purpose and in order to conduct reliable and robust analysis, the concentrations of the organochlorine compounds, the percentages of the lymphocyte subsets, as well as CD4+/CD8+ ratio, and the serum levels of thyroid related chemicals were categorized into two groups ; namely, the measurements which were less than the mean and equal to or over the mean in each year set by 0 and 1,

respectively. Then, Fisher's exact test was applied to the resulted fourfold tables and odds ratios were computed from the tables by logistic regression to evaluate the relative risks. In this study, less than 10 percent of *p*-value was considered as statistically significant.

Results and Discussion

Mean concentrations (male and female infant groups) of HCH, dieldrin, DDT, HCE, chlordane, PCB and dioxins on lipid weight basis were 368 and 440 ng/g, 2.9 and 5.0 ng/g, 277 and 355 ng/g, 4.5 and 4.7 ng/g, 76 and 81 ng/g, 128 and 114 ng/g, and 23.1 and 23.3 TEQ-pg/g, respectively, as indicated in Table 1. Contamination levels of HCH, dieldrin and DDT were somewhat higher in the female infant group than in the male one.

Table 1. Concentrations of organochlorine pesticides, PCBs and dioxins in the mother's milk of male and female infants

	Concentration on Lipid Weight Basis*	
Compound	Male Infants	Female Infants
Organochlorine Pesticides (ng/g)		
HCH	368 ± 267	440 ± 298
Dieldrin	2.9 ± 2.5	5.0 ± 5.8
DDT	277 ± 147	355 ± 251
HCE	4.5 ± 4.6	4.7 ± 4.1
Chlordane	76 ± 45	81 ± 69
PCB (ng/g)	128 ± 69	114 ± 58
Dioxins (TEQ-pg/g)	23.1 ± 8.5	23.3 ± 8.2

*: Mean ± Standard Deviation

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 sucklings than in adults.

Table 2. Effects of perinatal exposure to organochlorine pesticides, PCBs and dioxins on lipid weight basis on the lymphocyte subsets in the blood of Japanese male and female infants

	Male		Female	
Compound	Odds Ratio	90%C.I	Odds Ratio	90%C.I
CD4+				
PCBs	**0.18**	**0.06 ~ 0.49**	2.50	0.84 ~ 7.83
CD8+				
HCH	1.11	0.43 ~ 2.85	**0.30**	**0.02 ~ 0.91**
HCE	1.79	0.69 ~ 4.72	**3.75**	**1.19 ~13.1**
CD4+/CD8+				
Dieldrin	0.67	0.20 ~ 2.14	**8.17**	**1.92 ~ 45.6**
PCBs	**0.30**	**0.11 ~ 0.78**	2.50	0.84 ~ 7.83
CD3+				
HCE	**3.10**	**1.17 ~ 8.69**	2.29	0.75 ~ 7.40
Chlordane	**3.90**	**1.43 ~ 11.6**	0.60	0.20~ 1.75
CD20+				
Dioxins	**2.42**	**0.97 ~ 6.21**	1.23	0.41 ~ 3.80
DDT	**2.75**	**1.09 ~ 7.16**	1.37	0.48 ~ 4.03
HCE	0.73	0.28 ~ 1.87	**0.31**	**0.10 ~ 0.96**

As indicated in Table 2, perinatal higher exposure to PCBs decreased the CD4+ lymphocytes in the blood of male infants, but not in the female infants. HCH and HCE lowered and enhanced the CD8+ lymphocytes, respectively, in the blood of female infants, but not in the male infants. Dieldrin significantly enhanced the CD4+/CD8+ ratios only in the female infants. PCBs, however, decreased the ratio only in the male infants. HCE and chlordane increased the CD3+ lymphocytes only in the male infants. Dioxins and DDT significantly enhanced the CD20+ lymphocytes only in the male infants and HCE lowered it only in the female infants. As shown in Table 3, DDT significantly decreased the serum levels of T_3 both in the male and female infants. Dioxins and DDT lowered the serum levels of T_4 in the male and female infants, respectively. HCE significantly decreased the serum levels of TSH only in the female infants. DDT also lowered the serum levels of TBG only in the female infants.

Table 3. Effects of perinatal exposure to organochlorine pesticides, PCBs and dioxins on lipid weight basis on the thyroid hormone system in the serum of Japanese male and female infants

	Male		Female	
Compound	Odds Ratio	90%C.I	Odds Ratio	90%C.I.
T_3				
DDT	**0.33**	**0.13 ~ 0.81**	**0.32**	**0.10 ~ 0.92**
T_4				
Dioxins	**0.35**	**0.14 ~ 0.86**	2.06	0.03 ~ 6.12
DDT	0.46	0.19 ~ 1.11	**0.36**	**0.12 ~1.02**
TSH				
HCE	0.71	0.27 ~ 1.80	**0.19**	**0.05 ~ 0.58**
TBG				
DDT	0.81	0.34 ~ 1.94	**0.15**	**0.04 ~ 0.48**

The results mentioned above seem to support the idea of sexual distinction in their effects on the immune response and thyroid hormone systems of Japanese infants. However, this study was done with rather small number of infant-mother pairs. Therefore, further large-scale investigations are required to get more conclusive findings.

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