EFFECTS OF INTAKES OF ORGANOCHLORINE PESTICIDES, PCBs AND DIOXINS FROM BREAST MILK ON IMMUNE RESPONSE AND THYROID HORMONE SYSTEMS IN JAPANESE MALE AND FEMALE INFANTS

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Abstract

Effects of postnatal exposure to the organochlorine compounds such as dioxins (PCDDs, PCDFs and Co-PCBs), PCBs and pesticides on immune response and thyroid hormone systems in the peripheral blood of Japanese male and female infants about 1 year after birth were examined and we observed their different effects by sex in these two biological systems. In immune response system, for example, dioxins, DDT, HCE and chlordane significantly increased the percentage of CD3+ lymphocyte subset in male infants, but not in female infants, and CD4+/CD8+ ratio was significantly decreased by dioxins and PCBs only in male infants and enhanced by deildrin and PCBs only in female infants. Also in thyroid hormone system, serum concentration of T_3 was significantly lowered by dioxins and DDT and that of T_4 by DDT only in male infants, and DDT significantly enhanced the serum concentration of TSH only in female infants. These results may support the idea of sexual distinction in their effects.

Introduction

Our environments including food have been polluted with some organochlorine compounds such as dioxins, polychlorinated biphenyls (PCBs) and pesticides [1, 2]. Japanese people have also been contaminated with these chemicals [3, 4]. Consequently, some pesticides such as hexachlorocyclohexans (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 [5]. Their levels were considered more than 100 to 10,000 times higher than those of polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and coplanar polychlorinated biphenyls (Co-PCBs), which were so-called dioxins, in TEQ value as a whole. 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 the perinatal exposure to these compounds on lymphocyte subsets [6, 7] and thyroid hormone statuses [8, 9] in the peripheral blood of Japanese infants. In this study, in order to clarify the sexual distinction in their effects on the immune response and thyroid hormone systems, we investigated the lymphocyte subsets and thyroid related hormones in the blood of Japanese male and female infants in relation to their intakes from the breast milk.

Materials and Methods

In this study, 93 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 2 to 4 months after childbirth, was used to determine concentrations of organochlorine pesticides and

PCBs by ECD gas chromatographic method [5] and dioxins by HRGC/HRMS method [5]. Intakes of the organochlorine compounds from the breast milk in whole breast-feeding periods were estimated with multiplying their daily intakes (their concentrations on lipid weight basis × 4 g/kg body weight/day) by individual duration of breast-feeding (days).

About 1 year after birth, 5 to 10 ml of peripheral blood samples were 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 and TSH 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 intakes of the organochlorine compounds from the breast milk, the percentages of the lymphocyte subsets, as well as CD4+/CD8+ ratio, and the serum concentrations of thyroid related hormones were categorized into two groups ; namely, the measurements which were less than the mean and equal to or over the mean in each year were 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.

Table 1. Effects of intakes of organochlorine pesticides, PCBs and dioxins on lipid weight basis from the breast milk on the subsets of CD16+, HLA-DR+, CD4+8+, CD3+ and CD20+ lymphocytes in the peripheral blood of Japanese male and female infants

	Male Infants		Female Infants	
Compound	Odds Ratio	*p*-value	Odds Ratio	*p*-value
		< CD16+ >		
Dieldrin	1.38	0.39	1.30	0.48
		< HLA-DR+ >		
Dioxins	**0.39**	**0.08**	1.86	0.27
HCH	1.15	0.51	0.35	0.13
		< CD4+8+ >		
Dioxins	**3.14**	**0.05**	**0.28**	**0.07**
DDT	1.75	0.26	**0.16**	**0.01**
		< CD3+ >		
Dioxins	**2.47**	**0.09**	0.54	0.27
DDT	**3.10**	**0.05**	0.42	0.17
HCE	**3.59**	**0.03**	2.69	0.18
Chlordane	**4.40**	**0.02**	1.02	0.61
		< CD20+ >		
HCE	0.63	0.30	**0.28**	**0.10**

Boldface indicates the statistically significant compound ($p<0.10$)

Results and Discussion

Mean intake in whole breast-feeding periods of HCH or DDT was about 100 times higher than that of dieldrin or HCE. Mean intakes of chlordane and PCBs were 95 and 153 μg/kg body weight, respectively and 3 to 5 times less than those of HCH and DDT. In case of dioxins, their TEQ concentrations were computed by using 1998 WHO toxic equivalency factor (TEF) values [12] and the mean intake was about 27 ng-TEQ/kg body weight, which was about 200 times lower than that of dieldrin or HCE.

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 1 summarizes the effects of lactational exposure to the organochlorine compounds on the subsets of CD16+, HLA-DR+, CD4+8+, CD3+ and CD20+ lymphocytes. Dioxins decreased the HLA-DR+ lymphocyte subset in the blood of male infants (p=0.08), but not in the female infants. Dioxins increased and decreased the CD4+8+ lymphocyte subset in the blood of male infants (p=0.05) and female infants (p=0.07), respectively and DDT decreased it only in the female infants (p=0.01). Dioxins, DDT, HCE and chlordane significantly increased the CD3+ lymphocyte subset only in the male infants. HCE decreased the CD20+ lymphocyte subset only in the female infants.

The effects of intakes of the organochlorine chemicals from the breast milk on the subsets of CD4+ and CD8+ lymphocytes and CD4+/CD8+ ratio are shown in Table 2. PCBs significantly decreased and increased the CD4+ lymphocyte subsets in male and female infants, respectively. In CD8+ lymphocyte, dioxins decreased the subset only in the female infants, and dieldrin and DDT enhanced it only in the male infants. Dioxins significantly decreased the CD4+/CD8+ ratio only in the male infants and dieldrin increased it only in the female infants. PCBs, however, decreased the CD4+/CD8+ ratio in the male infants (p=0.06) and increased it in the female infants (p=0.10).

Table 2. Effects of intakes of organochlorine pesticides, PCBs and dioxins on lipid weight basis from the breast milk on the subsets of CD4+ and CD8+ lymphocytes and CD4+/CD8+ ratio in the peripheral blood of Japanese male and female infants

	Male Infants		Female Infants	
Compound	Odds Ratio	*p*-value	Odds Ratio	*p*-value
		< CD4+ >		
Dioxins	0.55	0.21	1.20	0.52
Dieldrin	0.96	0.58	2.07	0.23
DDT	0.90	0.54	1.00	0.63
HCE	1.47	0.35	2.00	0.29
PCBs	**0.21**	**0.01**	**3.00**	**0.10**
		< CD8+ >		
Dioxins	1.80	0.22	**0.34**	**0.10**
Dieldrin	**2.75**	**0.08**	1.22	0.52
DDT	**2.52**	**0.10**	0.65	0.37
HCE	1.54	0.32	2.69	0.18
PCBs	1.35	0.41	0.85	0.53
		< CD4+/CD8+ >		
Dioxins	**0.25**	**0.01**	1.86	0.27
Dieldrin	0.49	0.17	**3.38**	**0.08**
DDT	0.52	0.20	1.53	0.37
HCE	0.45	0.14	2.00	0.29
PCBs	**0.35**	**0.06**	**3.00**	**0.10**

Boldface shows the statistically significant compound (p<0.10)

Table 3 indicates the effects of these organochlorine compounds on the serum concentrations of T_3, T_4 and TSH. Concentrations of T_3 were significantly lowered by the intakes of dioxins and DDT from the breast milk only in the male infants. DDT also decreased the concentrations of T_4 only in the male infants (p=0.02). Concentration of TSH was significantly enhances by the intake of DDT only in the female infants.

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

Table 3. Effects of intakes of organochlorine pesticides, PCBs and dioxins on lipid weight basis from the breast milk on the serum concentrations of T_3, T_4 and TSH in the peripheral blood of Japanese male and female infants

	Male Infants		Female Infants	
Compound	Odds Ratio	*p*-value	Odds Ratio	*p*-value
		< T_3 >		
Dioxins	**0.35**	**0.05**	0.46	0.19
Dieldrin	0.45	0.13	0.58	0.31
DDT	**0.21**	**0.008**	0.44	0.17
Chlordane	0.76	0.42	0.66	0.37
PCBs	0.53	0.17	1.25	0.50
		< T_4 >		
DDT	**0.25**	**0.02**	0.73	0.43
Chlordane	0.60	0.28	0.49	0.21
		< TSH >		
Dioxins	0.95	0.57	0.70	0.41
DDT	1.95	0.18	**3.43**	**0.06**

Boldface indicates the statistically significant compound (p<0.10)

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