

Perinatal Exposure to Chlorinated Dioxins and Related Chemicals on Thyroid Hormone Status in Japanese Breast-Fed Infants

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Introduction

Human beings have been contaminated with extremely toxic PCDDs, PCDFs and Co-PCBs^{1) 2)}. Consequently, these chemicals have been also determined in the human breast milk and their mean total concentrations were about 1.2 to 1.4ppt in 2,3,7,8-TCDD TEQ values on whole weight basis^{3) 4) 5)}. According to their mean levels in the breast milk, breast-fed infants in Japan are considered to have relatively large amounts of these chemicals, namely, about 100 to 200 pg/kg body weight/day in 2,3,7,8-TCDD TEQ value^{3) 4) 5)}. Babies seem more sensitive to the toxic chemicals, so we should give due attention to their possible health consequences in breast-fed infants.

In order to clarify the effects of perinatal exposure to PCDDs, PCDFs and Co-PCBs on thyroid

function, we investigated the levels of the thyroid hormones, thyroid stimulating hormone (TSH) and thyroxine binding globulin (TBG) in the peripheral blood of 101 breast-fed infants in relation to their total TEQ levels in the breast milk.

Material and Methods

One hundred and twenty four mothers volunteered to participate 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 (50~100mℓ), sampled 2 to 4 months after the childbirth, was used to determine the concentrations of PCDDs, PCDFs and Co-PCBs by high resolution GC/MS method⁴⁾. The international toxic equivalency factor approach of NATO/CCMS was employed for PCDDs and PCDFs⁶⁾ and WHO-ECEH and IPCS approach for Co-PCBs⁷⁾. By multiplying the concentration (pg/g) and the toxic equivalency factor value, the concentration in 2,3,7,8-TCDD TEQ value of each congener was calculated (TEQ pg/g). The TEQ-sum of all congeners of PCDDs, PCDFs and Co-PCBs detected in the breast milk was summarized as the total TEQ concentration or level.

About 1 year after birth, 5 to 10mℓ of peripheral blood samples were individually obtained from 101 breast-fed infants. These blood samples were used to determine serum concentrations of triiodothyronine (T_3), thyroxine (T_4), TSH and TBG by radioimmunoassay methods using commercially available kits⁸⁾.

In order to get more reliable results, the Spearman rank correlation coefficients were computed instead of the Pearson correlation and their statistical significances were evaluated. Each variable was transformed by natural logarithm and their scatter plots were given.

Results

1) Concentrations of PCDDs, PCDFs and Co-PCBs in the breast milk

Respective median total concentrations of PCDDs, PCDFs and Co-PCBs in 2,3,7,8-TCDD TEQ values on the whole and fat weight bases were 0.94 and 22.6ppt in the breast milk of 124 mothers. Ranges of the total concentrations on the whole and fat weight bases were 0.15 to 2.92ppt and 3.4 to 48.5ppt, respectively.

2) Thyroid function tests in breast-fed infants

Results of the examination in thyroid function in the serum of 101 breast-fed infants are summarized in Table 1.

3) Correlation between the concentrations of PCDDs, PCDFs and Co-PCBs in the breast milk and thyroid hormone status in breast-fed infants

Significant correlations were not observed between the total TEQ concentrations of PCDDs, PCDFs and Co-PCBs and levels of T_3 or T_4 in the serum of the infants. As indicated in Fig. 1, only the levels of TSH in the serum of the breast-fed infants positively correlated with the total TEQ concentrations ($p=0.05$).

Table 1. Results of thyroid function tests in the serum of 101 breast-fed infants

	Median (min. ~ max.)
Triiodothyronine (T_3 , ng/ml)	1.99 (1.00 ~ 2.50)
Thyroxine (T_4 , μ g/dl)	11.3 (7.7 ~ 16.7)
Thyroid stimulating hormone (TSH, μ U/ml)	2.58 (0.56 ~ 8.51)
Thyroxine binding globulin (TBG, μ g/ml)	25.3 (17.2 ~ 39.6)
T_4 /TBG	0.45 (0.29 ~ 0.61)

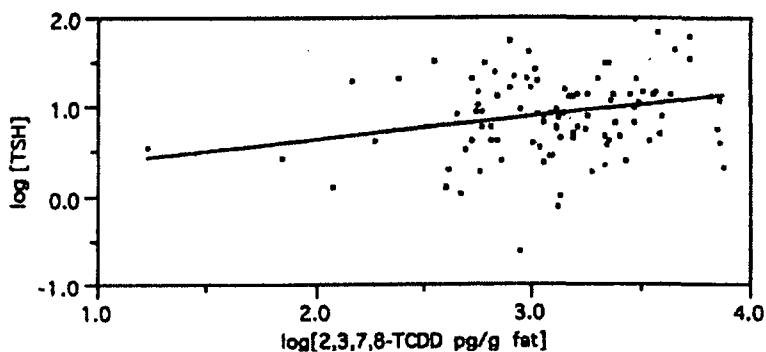


Fig. 1. Positive correlation between the total TEQ concentrations in the breast milk and the levels of TSH in the serum of breast-fed infants ($p=0.05$)

Discussion

The presence of PCDDs, PCDFs and Co-PCBs in the breast milk results in daily intakes of about 18 to 350 TEQ pg/kg body weight with the median figure of 113 TEQ pg/kg body weight. In

our former paper⁹⁾, negatively significant correlation between T_4 levels in the serum of breast-fed infants and the total TEQ concentrations was reported. In that paper, the Pearson correlation coefficient was employed for the statistical evaluation, so extremely large or small values of data may cause such a kind of significant correlation and in order to avoid such fallible effects, the Spearman rank correlation method was used in this study. Therefore, the results of this study were considered to be more reliable. Even in this method, as shown in Fig. 1 which was drawn by log-log scale, the levels of TSH in the serum proportionally increased with the total TEQ concentrations in the breast milk. In other investigation, T_4 and the ratio of T_4 /TBG were significantly higher in high-exposed babies than in low-exposed ones at 7 days and 11 weeks of age¹⁰⁾. Anyhow, exposure to background levels of PCDDs, PCDFs and Co-PCBs via the placenta or breast milk may have some effects on thyroid hormone status in breast-fed infants.

The results of more thorough analysis using trimmed log transformed data will be given in a follow-up paper.

References

- 1) Hirakawa H, Iida T, Matsueda T, Tokiwa H, Nagata T and Nagayama J ; *Organohalo. Comp.* **1992**, 10, 93-96.
- 2) Hirakawa H, Matsueda T, Iida T, Nakamura M, Nagata T and Nagayama J ; *Organohalo. Comp.* **1994**, 21, 419-422.
- 3) Matsueda T, Iida T, Hirakawa H, Fukamachi K, Tokiwa H and Nagayama J ; *Organohalo. Comp.* **1992**, 9, 143-146.
- 4) Matsueda T, Iida T, Hirakawa H, Fukamachi K, Tokiwa H and Nagayama J ; *Chemosphere* **1993**, 27, 187-194.
- 5) Hirakawa H, Iida T, Matsueda T, Nakagawa R, Hori H and Nagayama J ; *Organohalo. Comp.* **1995**, 26, 197-200.
- 6) North Atlantic Treaty Organization/Committee on the Challenges of Modern Society ; Report No. 176, **1988**.
- 7) Ahlborg US, Bedring GC and Birnbaum LS ; *Chemosphere* **1994**, 28, 1049-1067.
- 8) Okamura K, Sato K, Ikenoue H ; *J. Clin. Endocrinol. Metab.* **1988**, 67, 720-726.
- 9) Nagayama J, Iida T, Hirakawa H, Matsueda T, Tsuji H, Okamura K, Hasegawa M, Sato K, Kitahara E, Ma HY, Yanagawa T, Igarashi H, Fukushige J and Watanabe T ; *Organohalo. Comp.* **1996**, 30, 228-233.
- 10) Pluim HJ, Koppe JG and Olie K ; *Chemosphere* **1993**, 27, 391-394.