Effects of Perinatal Exposure to Dieldrin and Heptachlor Epoxide on Thyroid Hormone Status in Japanese Infants

Junya Nagayama ^a, Ken Okamura ^b, Reiko Nakagawa ^c, Takao Iida ^c, Takashi Yanagawa ^d,
Hisaji Igarashi ^e, Jun'ichiro Fukushige ^e and Tadayoshi Watanabe ^f

a) Laboratory of Environmental Health Sciences, School of Health Sciences, Kyushu University, Fukuoka 812-8582, Japan; b) Laboratory of Clinical Chemistry, School of Health Sciences, Kyushu University, Fukuoka 812-8582, Japan; c) Department of Environmental Sciences, Fukuoka Institute of Health and Environmental Sciences, Fukuoka 818-0135, Japan;
d) Department of Mathematical Statistics, Faculty of Science, Kyushu University, Fukuoka 812-8581, Japan; e) Department of Pediatrics, Faculty of Medicine, Kyushu University, Fukuoka 812-8582, Japan; f) Watanabe O.B.G.Y.
Clinic, Fukuoka 813-0044, Japan

Introduction

Foods in Japan have been contaminated with some organochlorine pesticides ¹⁾ and Japanese people have also been contaminated with these pesticides ²⁾. Consequently, some pesticides such as hexachlorocyclohexanes (HCHs), 1,1,1-trichloro-2,2'-bis-(4-chlorophenyl)-ethane (DDT), dieldrin and heptachlor epoxide (HCE) have been determined in Japanese breast milk and their mean concentrations on fat weight basis were about 1,300, 950, 20 and 9 ppb, respectively ³⁾. More recently, their levels were decreased and the respective levels in the breast milk were 420, 345, 3 and 4 ppb ⁴⁾. However, their levels were still much higher than those of polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and coplanar polychlorinated biphenyls (Co-PCBs) in the breast milk of Japan ⁴⁾. Therefore, we should give due attention to possible health consequences of these organochlorine pesticides in Japanese infants.

We have already reported effects of β -HCH, DDT and chlordane on the thyroid hormone status in the peripheral blood of Japanese infants ⁵⁾, so in this study, effects of dieldrin and HCE on it were investigated 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 the childbirth, was used to determine the concentrations of dieldrin, and HCE by ECD gas chromatography method ¹⁾.

About 1 year after birth, 5 to 10 ml of peripheral blood samples were individually obtained from 101 breast-fed infants. These blood samples were used to determine serum concentrations of triiodothyronine (T₃), thyroxine (T₄), thyroid stimulating hormone (TSH) and thyroxine binding globulin (TBG) by radioimmunoassay methods using commercially available kits ⁶).

It was found that the concentrations of dieldrin and HCE in the breast milk were truncated at the lower detection limit and also censored. So in order to conduct more reliable statistical analysis, those data were categorized into three classes according to the concentrations of the pesticide, denoted by 0 (low level), 1 (medium level) and 2 (high level). More specifically, the ranges of categories for dieldrin are 0 (~2.0 ng/g), 1 (2.0~3.0 ng/g) and 2 (3.0 ng/g~) and for HCE 0 (~2.0 ng/g), 1 (2.0~6.0 ng/g) and 2 (6.0 ng/g~).

Statistical significance was evaluated by the analysis of variance or Wilcoxon/Kruskal-Wallis test.

Results

1) Concentrations of the organochlorine pesticides in the breast milk

Distributions in concentrations on fat weight basis of dieldrin and HCE in the breast milk of 124 mothers are shown elsewhere ⁷⁾ and about 61 and 37% of the samples in dieldrin and HCE, respectively, were less than the detection limit. So, analytical results on whole weight basis of the pesticides in 124 breast milk samples are indicated in Fig.1.

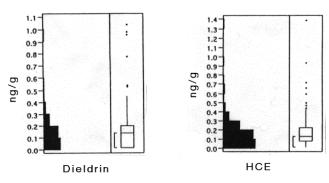


Fig.1. Distributions in concentrations of dieldrin and HCE on the whole weight basis (ng/g) in the Japanese breast milk of 124 mothers

Median and maximum levels on whole weight basis for dieldrin were 0.14 and 1.04 ng/g, and those for HCE 0.13 and 1.39 ng/g.

2) Thyroid function tests in the peripheral blood of Japanese infants

Results of the examination in thyroid function in the serum of 101 infants have already been published elsewhere ⁸⁾, so the main results are summarized in Table 1.

Table 1. Thyroid hormone status in the peripheral blood of 101 Japanese 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)

2) Relationship between levels of the organochlorine pesticides and concentrations of thyroid hormones and related chemicals in Japanese infants

We could not find any significant correlation between the levels of dieldrin in the breast milk and those of thyroid hormones and related chemicals listed in Table 1. HCE did not affect the serum levels of T_3 , T_4 and TBG. However, the mean level of TSH in the serum of the infants was the lowest in the group of the high level of HCE, compared with those of its low and medium levels, as shown in Fig.2.

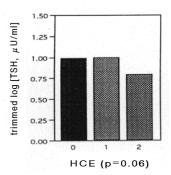


Fig.2. Relationship between the serum concentrations of TSH and the levels of HCE in the breast milk

Discussion

Effects of β -HCH, DDT and chlordane in the breast milk on the thyroid hormone status in the same infants have already been published and DDT significantly decreased the serum levels of T_4 and increased those of TSH $^{5)}$. Contrary to our expectation, HCE seemed to lower the level of TSH. Therefore, these two pesticides were considered to neutralize the effect on the TSH levels each other.

Based on the results of our several investigations ^{5) 7)} including this study, dieldrin and HCE seemed to affect more strongly on the immune system than on the thyroid hormone system. DDT, however, was considered to evoke more effects on the thyroid hormone status than on the lymphocyte subpopulations ^{5) 9)}.

References

- 1) Nakagawa R, Hirakawa H and Hori T; J. AOAC Int. 1995, 78, 921-929.
- 2) Kashimoto T, Takayama K, Mimura M, Miyata H, Murakami Y and Matsumoto H; *Chemosphere* **1989**, <u>19</u>, 921-926.
- 3) Hirakawa H, Iida T, Matsueda T, Nakagawa R, Hori T and Nagayama J; *Organohal. Comp.* 1995, 26, 197-200.
- 4) Nakagawa R, Hirakawa H, Iida T, Matsueda T and Nagayama J; J. AOAC Int. 1999, in press.
- 5) Nagayama J, Okamura K, Nakagawa R, Iida T, Tsuji H, Hasegawa M, Sato K, Tomita A, Yanagawa T, Igarashi H, Fukushige J and Watanabe T; *Organohal. Comp.* **1998**, <u>37</u>, 235-239.
- 6) Okamura K, Sato K and Ikenoue H; J. Clin. Endocrinol. Metab. 1988, 67, 720-726.
- 7) Nagayama J, Tsuji H, Nakagawa R, Iida T, Yanagawa T, Igarashi H, Fukushige J and Watanabe T; *Organohal. Comp.* **1999**, in press.
- 8) Nagayama J, Okamura K, Iida T, Hirakawa H, Matsueda T, Tsuji H, Hasegawa M, Sato K, Tomita A, Yanagawa T, Igarashi H, Fukushige J and Watanabe T; *Organohal. Comp.* **1998**, <u>37</u>, 313-316.
- 9) Nagayama J, Tsuji H, Nakagawa R, Iida T, Okamura K, Hasegawa M, Sato K, Tomita A, Yanagawa T, Igarashi H, Fukushige J and Watanabe T; *Organohal. Comp.* **1998**, <u>37</u>, 157-161.