FREQUENCY OF SISTER CHROMATID EXCHANGES IN JAPANESE INFANTS LACTATIONALLY EXPOSED TO ORGANOCHLORINE PESTICIDES AND DIOXINS

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Introduction

Foods in Japan have been polluted with some organochlorine compounds such as pesticides, polychlorinated biphenyls (PCBs) and dioxins which are polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and coplanar polychlorinated biphenyls (Co-PCBs) [1]. So, 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 that of dioxins in 2,3,7,8-tetrachloro- dibenzo-*p*-dioxin (2,3,7,8-TCDD) toxic equivalent (TEQ) value as a whole [5]. Therefore, we should give due attention to possible health consequences of these organochlorine pesticides and PCBs as well as dioxins in Japanese infants.

Formation and induction of sister chromatid exchanges (SCEs) have been considered as a good index to the synthetic and sharp genotoxicity for several mutagenic and carcinogenic chemicals [7, 8].

In this study, the relationship between the SCE frequency of the infant lymphocytes around postnatal of 1 year and the lactational exposure to the organochlorine pesticides or dioxins was statistically investigated in order to evaluate their genotoxicity to one of the most sensitive stages of human life, namely, sucklings.

Materials and Methods

One hundred and twenty four mothers volunteered to participate in all in our studies. Pregnancy and delivery were completed without overt signs of serious illness or complications. Only infants 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 by ECD gas chromatographic method [5, 9] and dioxins by high resolution GC/MS method [5, 10].

TEQ concentrations of dioxins were calculated by using 1998 WHO toxic equivalent factor (TEF) values [11]. The TEQ-sum of all congeners of dioxins determined in every breast milk sample was summarized as the total 2,3,7,8-TCDD TEQ concentration.

Lactational exposure to the organochlorine pesticides and dioxins was estimated as a product of their respective daily intake, which was calculated with their respective level in the milk times an expected intake of breast milk in Japanese infants, that is, 120 g/kg body weight, multiplied by individual duration (days) of breast feeding.

About 1 year after birth, 5 to 10 ml of the peripheral blood of 105 infants born of these mothers were individually obtained by venipuncture. Among them, SCE frequency of the lymphocytes was measured in 66 infants. Lymphocytes in the whole blood were stimulated with phytohemagglutinin and cultured for two replicative cycles in the presence of bromodeoxyuridine (100mM) as dedailed elsewhere [12, 13]. Differential staining of sister chromatids was obtained by a fluorochrome plus Giemsa technique and the frequency of SCEs was evaluated.

Relationship between control, solvent (DMSO) treated SCE frequency (SCEcontrol), 7,8-benzoflavone (ANF) treated SCE frequency (SCEANF) or DSCEs (SCEANF - SCEcontrol) and lactational exposure to the organochlorine pesticides or dioxins was statistically examined by Spearman rank correlation analysis.

Results and Discussion

Intakes (median, min.~max.) of the organochlorine pesticides and dioxins through breast milk, namely, the lactational exposures in 66 infants were as follows : ß-HCH (369 µg/kg, 41.8~1706 µg/kg), dieldrin (3.48 µg/kg, 0.39~31.3 µg/kg), DDT, sum of *p, p'*-DDE and *p, p'*-DDT (324 µg/kg, 33.5~2261 µg/kg), HCE (3.87 µg/kg, 0.65~26.7 µg/kg), chlordane, sum of oxychlordane, *trans*-nonachlor and *cis*-nonachlor (73.0 µg/kg, 12.9~527 µg/kg) and dioxins (25.0 TEQ-ng/kg, 3.97~70.7 TEQ-ng/kg). Intakes of the organochlorine pesticides were two to four orders of magnitude higher than that of dioxins. In order to get normal distribution, intakes of the organochlorine compounds were transformed by a natural logarithm.

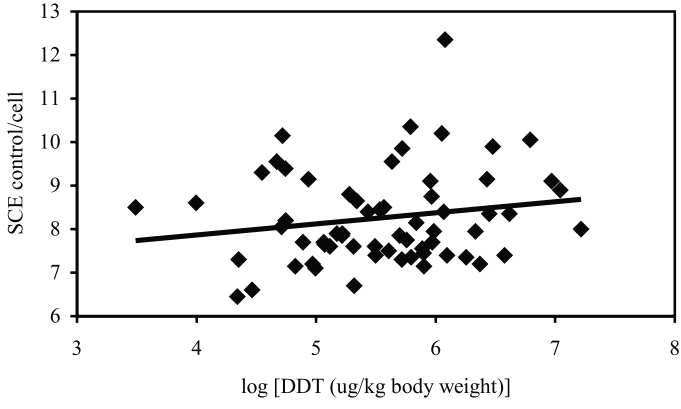

Figure 1. Correlation of frequencies of SCEcontrol in the lymphocytes with intakes of DDT through the breast milk in 63 Japanese infants (rank correlation coefficient = 0.109, p = 0.405)

Frequencies (median, min.~max.) of SCEcontrol, SCEANF and DSCEs were 7.89/cell, 6.45~12.4/cell, 11.9/cell, 9.05~15.6/cell and 3.88/cell, 0.15~7.20/cell, respectively.

Significant correlations were observed between the frequency of DSCEs and the intakes of ß-HCH, DDT or dioxins. Figs 1, 2 and 3 show relationships between lactational exposure to DDT and

frequencies of SCEcontrol, SCEANF or DSCEs. Frequencies of SCEcontrol and SCEANF showed increasing and decreasing tendencies, respectively, with intakes of DDT through the breast milk. Same kinds of tendencies were also seen in case of dioxins.

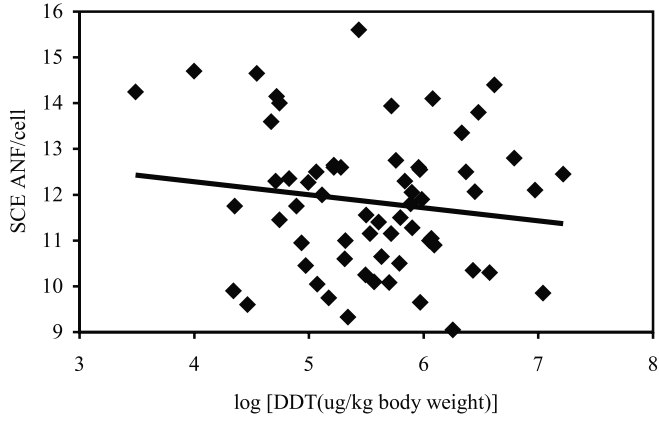

Figure 2. Correlation of frequencies of SCEANF in the lymphocytes with intakes of DDT through the breast milk in 63 Japanese infants (rank correlation coefficient = - 0.029, p = 0.824)

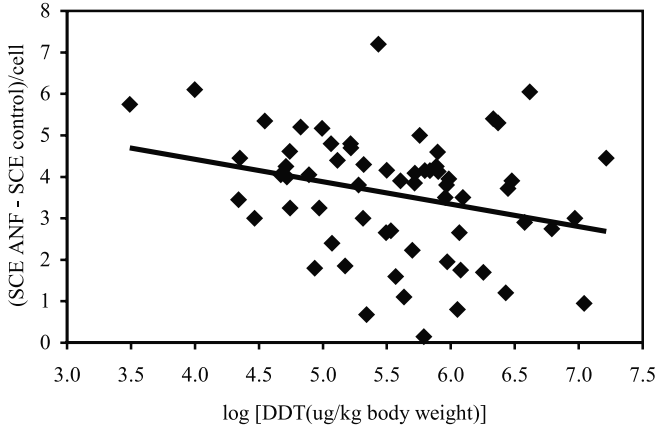

Figure 3. Correlation of frequencies of DSCEs in the lymphocytes with intakes of DDT through the breast milk in 63 Japanese infants (rank correlation coefficient = - 0.247, p = 0.050)

Frequency of DSCEs was considered more sensitive biomarker than those of SCEcontrol and SCEANF in the evaluation of genotoxic compounds [14, 15]. Accordingly, the organochlorine compounds such as ß-HCH, DDT and dioxins seem to elicit some genotoxic effects in Japanese breast-fed infants.

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