Comparison of Frequency of Sister Chromatid Exchanges and Contamination Level of Dioxins and Related Chemicals in Healthy Japanese and "Yusho" Patients

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Introduction

In 1968, Yusho, a mass food poisoning, occurred in western Japan by ingestion of rice oil that has been contaminated with polychlorinated biphenyls (PCBs), polychlorinated quaterphenyls (dimers of PCBs), polychlorinated dibenzofurans (PCDFs), polychlorinated dibenzo-*p*-dioxins (PCDDs) and so forth. The major causal agent of Yusho has been considered PCDFs [1) 2)].

In 1996 and 1997, almost 30 years after the food poisoning, the concentrations of PCDDs, PCDFs and coplanar PCBs (Co-PCBs) were determined in the blood and sebum of 16 Yusho patients. At that time, to evaluate the chronic effects of these etiological chemicals, we examined the frequency of sister chromatid exchanges (SCEs) of the lymphocytes, lymphocyte subsets and thyroid hormone status in the blood of the patients and compared these data with those of healthy Japanese people.

Materials and Methods

In July, 1996 to January, 1997, 60 to 80 ml of the peripheral blood and sebum of the face were individually obtained from 16 Yusho patients (3 males and 13 females, mean age: 55.0 years old and the range: 28~72 years old). In September, 1994 to October, 1995, the same volume of the peripheral blood and sebum of the face were also acquired from 39 healthy volunteers (25 males 14 females, mean age: 44.3 years old and the range: 20~64 years old). The concentrations of PCDDs, PCDFs and Co-PCBs were determined in these samples by the method previously mentioned [3) 4)]. Frequencies of SCEs in the lymphocytes of individual whole-blood cultures were counted and analyzed as described before [5) 6)]. These blood samples were also used to measure the

lymphocyte subsets by indirect immunofluorescence methods to calculate their relative population densities [7], and to determine serum concentrations of thyroid hormones and related chemicals by radioimmunoassay methods [8].

Pearson correlation coefficients between two variables interested were computed and the statistical significance was evaluated by Fisher's test. Significant difference was statistically analyzed in the means of respective two groups by student's *t*-test or Mann-Whitney's test.

Results

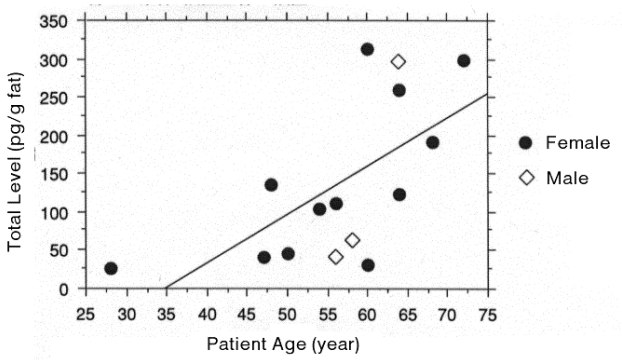
1) Concentrations of PCDDs, PCDFs and Co-PCBs in the blood and sebum of the patients with Yusho

Respective mean concentrations of PCDDs, PCDFs and Co-PCBs in 2,3,7,8-tetrachlorodibe-nzo-*p*-dioxin toxic equivalent (2,3,7,8-TCDD TEQ) value on the fat weight basis were 274.2 and 139.0 pg/g in the blood and sebum of 16 Yusho patients. The mean level in the sebum was apparently lower than that in the blood. Ranges of their total concentrations in the blood and sebum were 25~1,032 pg/g and 26~313 pg/g, respectively.

Statistically significant positive correlation was observed between age of the patients and their total levels in the blood (r=0.58, p=0.017) or sebum (r=0.64, p=0.009). Fig.1 indicates the relation-ship between their total levels in the sebum and the patient age.

In healthy Japanese people, their contamination levels were also increased with age [9].Therefore, we compared their total levels as 2,3,7,8-TCDD TEQ value in the patients with Yusho with those

Fig.1. Positive correlation between the total concentrations of PCDDs, PCDFs and Co-PCBs as 2,3,7,8-TCDD TEQ value on the fat weight basis in the sebum and age of the patients with Yusho (r=0.64, p=0.009)



in healthy Japanese people at the age of over 45 years old and Fig.2 shows the result obtained from the sebum levels. The mean contamination level (147.1 pg/g) of Yusho patients was about 4 times higher than that (39.2 pg/g) of the healthy people in the sebum and in the blood, their mean total level in the patients was about 7 times more than that in the healthy people.

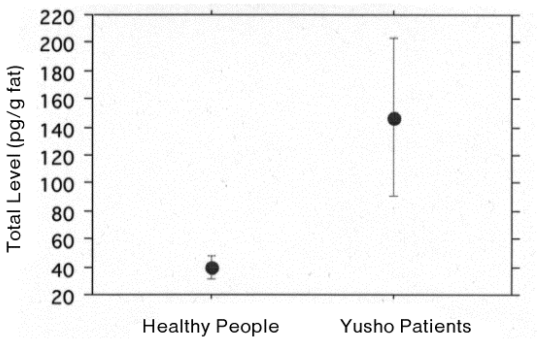


Fig.2. Total concentrations of PCDDs, PCDFs and Co-PCBs as 2,3,7,8-TCDD TEQ value on the fat weight basis in the sebum of healthy Japanese people and the patients with Yusho (p=0.0002)
● : Mean, I : 95% Confidence interval

2) Frequencies of SCE in the control and 7,8-benzoflavone treated cultures in the patients with Yusho

Respective mean ±SD frequencies of SCE in the control (solvent, DMSO, treated) and 7,8-benzoflavone (ANF) treated cultures were 11.1±1.1/cell and 14.9±1.2/cell, and the SCE rate in ANF treated culture was manifestly higher than that in the control one. Age-related increase of SCE frequency in healthy Japanese people was observed in both the control and ANF-treated cultures [9]. In the Yusho patients, however, we could not find such kinds of correlation between them. The mean SCE rates of the Yusho patients did not significantly different from those of Japanese healthy people in the age of over 45 years old in either the control culture, as indicated in Fig.3, or the ANF treated culture.

3) Relationship between levels of PCDDs, PCDFs and Co-PCBs and peripheral lymphocyte subsets or thyroid hormone status in the patients with Yusho

Percentages of all the peripheral lymphocyte subsets examined of the Yusho patients were almost within the normal ranges in healthy Japanese people and we could not find any significant

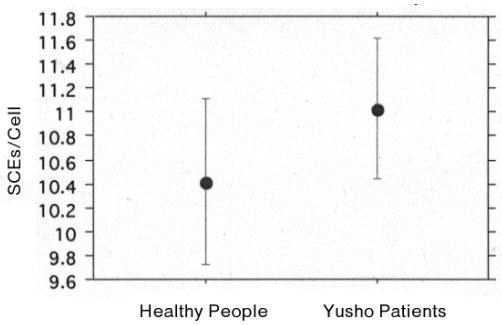


Fig.3. Comparison in the SCE frequencies of lymphocyte in the control culture between the patients with Yusho and the healthy Japanese at the age of over 45 years old (p=0.22)
● : Mean, I : 95% Confidence interval

correlation between the total concentrations of PCDDs, PCDFs and Co-PCBs as 2,3,7,8-TCDD TEQ value in the blood or sebum and any of the lymphocyte subsets.

It is also the same with the case of thyroid hormone status as with that of the lymphocyte subsets and their significant correlations with the total levels of PCDDs and the related chemicals were not found.

Discussion

Almost 30 years have passed since the outbreak of Yusho, when we reexamined the Yusho patients. The mean levels of causal agents such as PCDFs, Co-PCBs and PCDDs, however, in the blood and sebum of the patients with Yusho were still 4 to 7 times greater than those in the healthy Japanese people at the age of over 45 years old. Therefore, at the beginning of Yusho accident, their levels in the blood of some patients with Yusho were expected to be more than 10,000 pg/g on the fat weight basis in 2,3,7,8-TCDD TEQ value [10].

At the present time, even at rather high levels of the toxic chemicals, they did not seem to show any significant effects on the SCE frequency, lymphocyte subsets and thyroid hormone status in the blood of the Yusho patients. One of the reasons which may explain these results is considered that the patients acclimatize themselves to such severe circumstances or that these toxic chemicals truly have no effect on such biological and/or biochemical systems at the levels determined in this study.

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