FOLLOW-UP SURVEY OF DIOXINS AND RELATED CHEMICALS IN THE BLOOD OF YUSHO PATIENTS IN 2003

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Introduction

In 1968, a case of mass poisoning, the so-called Yusho incident[1] , occurred in western Japan due to the contamination of cooking oil by heat-degraded polychlorinated biphenyls (PCBs). As a result of a survey, the cause of Yusho disease is thought to be ingested toxic substances, including not only PCBs, but also polychlorinated dibenzo-*p*-dioxin (PCDDs) and polychlorinated dibenzofuran (PCDFs) in Kanemi rice oil. The medical aspects of this poisoning have been demonstrated by many researchers. Since 1995, extensive studies have been performed by the Yusho study group involving follow-up surveys of the human tissues and/or blood concentrations of the casual compounds in Yusho patients as well as clinical trials for accelerating the excretion of these compounds in Yusho patients.

We have reported that high levels of toxic substances such as PCDFs have persisted in Yusho patients even up through 1995, more than 27 years after the original incident[2]. The data obtained in the latest follow-up survey was reported in Dioxin 2004[3].

In the present study, we determined the blood concentration of dioxin-like isomers collected in the fiscal year 2003 from Yusho patients and from Yusho-suspected persons as well as normal controls that live in Japan, and compared the concentrations with the levels of Yusho isomers measured between 1995 and 2003.

Materials and Methods

The blood samples were collected from a total of 343 people who had given their informed consent at their medical checkups in the 2003 fiscal year. The details of the subjects are as follows: 269 Yusho patients (authorized by the Yusho medical team) and 74 Yusho-suspected persons (those suspected to have ingested Kanemi rice oil, though unauthorized by the medical team according to the diagnostic criteria for Yusho disease). The blood samples from a total of 128 normal controls were also collected in Fukuoka prefecture. The ages of the controls were from 60-86 years old, which matches the age of the Yusho patients. 10 mL of blood samples were collected using a vacuum blood collecting pipe containing heparin and stored at 4°C for later analysis. The details of the method for blood lipid extraction, purification and mass-spectrometric measurements have been described elsewhere[4].

Results and Discussion

Table 1 shows the concentrations of PCDDs, PCDFs, and non-ortho-coplanar-PCBs in the blood of Yusho patients, of Yusho-suspected persons, and of normal controls. In Yusho patients, the mean TEQ concentrations of PCDDs, PCDFs, and non-ortho-coplanar-PCBs in the blood collected in 2003 were 18, 96, and 12 pg-TEQ/g lipid, respectively. In the case of the Yusho-suspected persons, the mean TEQ concentrations in the blood were 12, 17, and 8.3 pg-TEQ/g lipid, respectively. However, the levels found in the normal controls were 12, 10, and 15 pg-TEQ/g lipid, respectively. The levels of PCDDs and non-ortho-coplanar-PCBs were similar in the three groups; however, the levels of PCDFs in the Yusho patients were 5.6 and 9.6 times higher than those of the Yusho-suspected individuals and normal controls, respectively. The mean total-TEQ concentration of the blood of Yusho patients was about 3.4 times higher than that of normal controls, and even after the passage of 35 years, the levels of this substance

remains high in victims of this accident.

Table 1 Concentrations of dioxins in the blood of Yusho, Yusho-suspected and normal controls

Congeners	Yusho patients (N=269)		Yusho-suspected group (N=74)		Normal controls (N=128)	
	Mean	Range	Mean	Range	Mean	Range
2,3,7,8-TCDD	1.7	ND-5.6	1.5	ND-3.2	1.9	ND-4.3
1,2,3,7,8-PeCDD	10	ND-45	6.6	ND-16	9.0	3.2-20
1,2,3,4,7,8-HxCDD	2.6	ND-8.5	2.4	ND-6.1	3.6	ND-13
1,2,3,6,7,8-HxCDD	50	3.8-444	26	2.9-93	28	7.3-70
1,2,3,7,8,9-HxCDD	3.9	ND-18	3.6	ND-14	4.5	ND-16
1,2,3,4,6,7,8-HpCDD	39	8.5-167	40	12-153	78	18-470
OCDD	763	148-3716	796	200-3835	1217	181-7614
2,3,7,8-TCDF	1.2	ND-4.9	1.0	ND-3.5	1.0	ND-4.5
1,2,3,7,8-PeCDF	0.85	ND-5.6	0.70	ND-4.8	0.67	ND-4.6
2,3,4,7,8-PeCDF	176	26-1945	30	1.2-272	17	6.0-63
1,2,3,4,7,8-HxCDF	52	ND-738	8.3	ND-104	5.0	ND-20
1,2,3,6,7,8-HxCDF	20	ND-232	6.3	ND-39	5.7	ND-16
2,3,4,6,7,8-HxCDF	1.3	ND-5.3	1.4	ND-7.0	1.2	ND-5.2
1,2,3,7,8,9-HxCDF	ND	-	ND	-	ND	-
1,2,3,4,6,7,8-HpCDF	2.8	ND-232	3.6	ND-23	2.2	ND-14
1,2,3,4,7,8,9-HpCDF	ND	-	ND	-	ND	-
OCDF	ND	-	ND	-	2.1	ND-18
3,4,4',5-TCB(#81)	5.3	ND-22	5.2	ND-11	6	ND-24
3,3',4,4'-TCB(#77)	8.6	ND-72	7.8	ND-21	8.4	ND-31
3,3',4,4',5-PenCB(#126)	98	11-532	76	ND-265	113	17-519
3,3',4,4',5,5'-HxCB(#169)	184	13-1116	74	ND-264	64	16-192
Total PCDDs-TEQ	18	2.2-82	12	1.8-26	15	5.0-34
Total PCDFs-TEQ	96	1.8-1074	17	1.1-151	10	3.5-33
Total PCDDs/PCDFs-TEQ	113	3.9-1157	29	3.3-174	26	8.5-54
Total Non-ortho-coplanar PCBs-TEQ	12	1.4-56	8.3	0.55-29	12	2.1-54
Total TEQ	125	5.5-1177	37	3.9-189	37	12-100
Age	66	32-89	52	6-82	68	60-86

The levels of Yusho-specific isomers which were contained in both causal Yusho oil and patients were compared. Figure 1 shows the levels of these compounds in the three groups. Among these compounds, the predominant toxic substance present in Yusho patients was 2,3,4,7,8-PeCDF. Figure 2 also suggests that there is a difference of the concentration ratio of 1,2,3,4,7,8-HxCDF and 1,2,3,6,7,8-HxCDF among the three groups. To elucidate the nature of this difference, we estimated the relationship between TEQ and the ratio of 1,2,3,4,7,8-HxCDF and 1,2,3,6,7,8-HxCDF among the three groups.

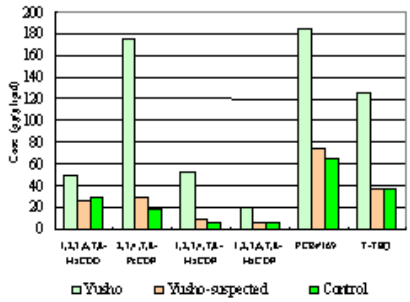

Figure 1 Mean concentrations of Yusho-related isomers in the blood of the three groups

The mean concentration ratio of 1,2,3,4,7,8-HxCDF and 1,2,3,6,7,8-HxCDF were 3.2, 1.5 and 1.0 for Yusho patients, Yusho-suspected persons and normal controls, respectively. A significant difference was observed among these three groups.

Figure 2 shows the toxic contribution of each congener to the total TEQ. The toxic contributions of PCDDs, PCDFs, and non-ortho-coplanar-PCBs in the Yusho patients, in the Yusho-suspected persons, and in the normal controls were 14, 77, and 9%, 33, 44, and 23%, and 44, 24, and 32% of the total TEQ value, respectively.

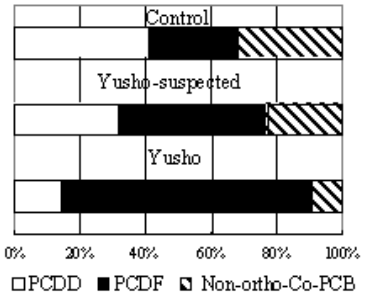

Figure 2 Percent distributions of PCDD, PCDF and Non-ortho-Co-PCB to the total TEQ

The order of the toxic contribution rate of PCDFs-TEQ, which was thought to be the primary cause of Yusho disease, was the Yusho patient group, the Yusho-suspected persons, and the normal controls.

In the Yusho-suspected persons, however, the toxic contribution rate was intermediate between typical Yusho patients and normal controls. However, some individuals in the Yusho-suspected persons showed a high toxic contribution rate of PCDFs -TEQ in relation to the total TEQ, due perhaps to exposure to contaminated Yusho oil at the onset of the contamination period in 1968.

Figure 3 shows the relationship between TEQ and the concentration ratio of

1,2,3,4,7,8-HxCDF and 1,2,3,6,7,8-HxCDF in the three groups. A significant relationship between TEQ and the ratio of 1,2,3,4,7,8-HxCDF and 1,2,3,6,7,8-HxCDF was observed in the Yusho patients and Yusho-suspected persons, but no significant relationship was observed in the normal controls .

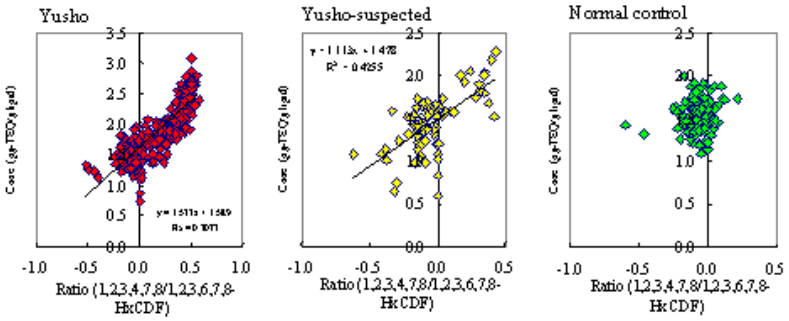

Figure 3 Relationship between TEQ and ratio of 1,2,3,4,7,8-HxCDF, and 1,2,3,6,7,8-HxCDF in the blood of three different groups

We reported that the ratio of 1,2,3,4,7,8-HxCDF and 1,2,3,6,7,8-HxCDF in Yusho oil and in the blood of Yusho patients was quite similar. It is suggested that the ratio and the levels of 2,3,4,7,8-PeCDF are an effective indicator of exposure to Yusho oil.

It is necessary to continue these follow-up investigations in the future because of their importance when evaluating the health status of Yusho patients and for their possible treatment.

References

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