TIME TREND OF CONCENTRATIONS OF DIOXIN LIKE PCBs, PCDFs, AND PCDDs IN BLOOD OF YUSHO PATIENTS.

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Abstract

We determined the dioxin-like isomers concentration in the blood of Yusho patients collected in the fiscal years 2002 to 2005 and in those of normal controls living in Fukuoka Prefecture. The blood samples of 103 Yusho patients were collected in each of these 4 years, their ages being over 60 years old in fiscal year 2004. Blood samples from a total of 127 normal controls were also collected in Fukuoka prefecture in 2004. We compared these concentrations with the levels of dioxin-like isomers for each group. The mean concentration of 2,3,4,7,8-PeCDF in the blood of Yusho patients did not show significant change, while the mean concentration of 1,2,3,4,7,8-HxCDF was gradually decreased from 70 to 59 pg/ g lipid. Then, we divided the 103 Yusho patients into three groups based on 2,3,4,7,8-PeCDF concentration according to the diagnostic criteria for Yusho. The 2,3,4,7,8-PeCDF concentrations of low and middle level groups which were similar to those of the normal controls showed no change. However, the high concentration group was still decreased.

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 the results of a survey, the cause of Yusho disease is thought to be ingested toxic substances, including not only PCBs but also polychlorinated dibenzofuran (PCDFs) , polychlorinated quarterphenyls (PCQs), and polychlorinated terphenyls (PCTs) 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 regarding the acceleration of 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 2006[3].

In the present study, we determined the dioxin-like isomers concentration in the blood of Yusho patients collected in the fiscal years 2002 to 2005 and in normal controls living in Fukuoka Prefecture, and compared these concentrations with the levels of dioxin-like isomers. We also studied the time trend of dioxin-like isomer concentrations in the blood of Yusho patients for 38 years after the incident.

Materials and Methods

Blood samples were collected from a total of 1,381 people who had given their informed consent at their medical checkups through the fiscal years 2002 to 2005 years. The blood samples of 103 Yusho patients were collected in each of these 4 years, their ages being over 60 years old in fiscal year 2004. Blood samples from a total of 127

normal controls were also collected in Fukuoka prefecture in 2004. The ages of the controls ranged from 60-86 years old, which matches the age of the Yusho patients. Ten 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 of 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- PCBs in the blood of Yusho patients and of normal controls. In 103 Yusho patients, the mean TEQ concentrations of PCDDs, PCDFs, and non-ortho- PCBs in the blood were 19-21, 110-130 and 11-13 pg-TEQ/g lipid, respectively. However, the levels found in the normal controls were 15, 10, and 12 pg-TEQ/g lipid, respectively. The levels of PCDDs and non-ortho-PCBs were similar in these groups; however, the levels of PCDFs in the Yusho patients were 11-13 times higher than that of normal controls, respectively. The concentrations of the dominant Yusho isomers (2,3,4,7,8-PeCDF and 1,2,3,4,7,8-HxCDF) in Yusho patients were compared with those in normal controls. The mean concentrations of 2,3,4,7,8-PeCDF and 1,2,3,4,7,8-HxCDF in the blood of Yusho patients were, respectively about 11.6-13.3 and 11.6-14.0 times higher than those of normal controls, and even after the passage of 34-37 years, the levels of these substances remain high in victims of this accident. In this term, the mean concentration of 2,3,4,7,8-PeCDF did not show significant change, while the mean concentration of 1,2,3,4,7,8-HxCDF gradually decreased from 70 to 59 pg/ g lipid. Masuda et al.[5] reported that the half-lives of these compounds were 11.7 years in the case of

Table 1 Concentrations of PCDDs, PCDFs, and non-ortho -PCBs in the blood of Yusho patients and normal controls

(pg / g lipid)

	Yusho patients(N=103)												Normal controls (N = 127)		
	2002			2003			2004			2005			2004		
	Mean	Range	Med	Mean	Range	Med	Mean	Range	Med	Mean	Range	Med	Mean	Range	Med
2,3,7,8-TCDD	1.7	ND-3.9	1.7	1.7	ND-4.9	1.6	1.4	ND-4.4	1.3	1.8	ND-17	1.6	1.9	ND-4.3	1.8
1,2,3,7,8-PeCDD	12	3.6-47	10.3	10	2.2-45	4.0	10	2.2-39	8.7	12	2.4-40	9.7	9.0	3.2-20	8.7
1,2,3,4,7,8-HxCDD	3.2	ND-9.8	2.8	2.6	ND-8.3	2.4	2.7	ND-8.5	2.5	3.1	ND-10	2.8	3.6	ND-13	3.2
1,2,3,6,7,8-HxCDD	58	6.0-290	45	56	3.8-350	41	54	6.4-260	43	56	4.0-270	43	28	7.3-70	25
1,2,3,7,8,9-HxCDD	5.5	ND-15	4.8	4.0	ND-12	3.4	4.3	ND-19	3.8	4.9	ND-20	4.3	4.5	ND-16	3.8
1,2,3,4,6,7,8-HpCDD	75	11-560	59	39	12-170	33	52	14-200	45	47	17-210	39	79	18-470	62
OCDD	960	170-9200	700	790	190-2600	660	760	210-2300	640	790	260-3300	650	1200	180-7600	930
2,3,7,8-TCDF	1.5	ND-5.2	1.4	1.3	ND-3.3	1.3	1.6	ND-7.2	1.4	3.5	ND-25	1.9	1.0	ND-4.5	ND
1,2,3,7,8-PeCDF	1.1	ND-6.3	0.5	0.9	ND-5.6	ND	0.9	ND-4.1	0.5	1.5	ND-9.9	ND	0.70	ND-4.6	ND
2,3,4,7,8-PeCDF	240	6.1-1900	120	210	6.4-2000	110	210	5.1-1600	100	210	6.0-1700	120	18	6.0-37	16
1,2,3,4,7,8-HxCDF	70	ND-670	22	66	ND-740	20	58	ND-600	18	59	ND-550	19	5.0	ND-20	4.4
1,2,3,6,7,8-HxCDF	25	2.1-170	12	24	ND-230	12	21	ND-160	10	22	ND-160	11	5.7	ND-16	5.2
2,3,4,6,7,8-HxCDF	1.5	ND-6.6	ND	1.3	ND-5.3	ND	1.2	ND-5.5	ND	1.2	ND-4.4	ND	1.2	ND-5.2	ND
1,2,3,7,8,9-HxCDF	1.0	ND-2.3	ND	ND	-	ND	ND	-	ND	ND	-	ND	ND	-	ND
1,2,3,4,6,7,8-HpCDF	3.1	ND-40	2.5	3.0	ND-23	2.5	2.7	ND-24	2.2	2.8	ND-17	2.2	2.2	ND-14	ND
1,2,3,4,7,8,9-HpCDF	1.0	ND-2.6	ND	ND	-	ND	1.0	ND-3.4	ND	ND	-	ND	ND	-	ND
OCDF	ND	-	ND	ND	-	ND	2.1	ND-10	ND	ND	-	ND	2.1	ND-18	ND
3,4,4',5-TCB(#.81)	5.9	ND-25	ND	5.5	ND-19	ND	5.5	ND-24	ND	5.5	ND-25	ND	5.6	ND-24	ND
3,3',4,4'-TCB(#77)	12	ND-46	11	8.6	ND-32	ND	11	ND-70	10	9.5	ND-140	ND	8.4	ND-31	ND
3,3',4,4',5-PeCB(#126)	110	22-420	94	100	22-290	86	96	14-350	83	100	ND-310	87	110	17-520	89
3,3',4,4',5,5'-HxCB(#169)	230	34-1100	190	210	36-1100	170	160	24-770	130	170	25-860	140	64	16-190	58
Total PCDD	1100	240-9800	890	900	230-2800	820	890	270-2500	760	920	310-3600	790	1300	210-8100	1000
Total PCDF	340	18-2700	170	320	15-2900	150	300	14-2400	140	300	15-2400	150	37	15-86	35
Total non-ortho PCBs	360	76-1200	310	320	93-1200	280	270	56-870	230	290	57-1000	250	190	59-740	160
Total	1800	410-10000	1500	1500	390-4900	1400	1500	350-4000	1300	1500	470-4200	1400	1600	290-8500	1300
T PCDDs-TEQ	21	5.1-79	18	19	3.5-83	16	18	4.1-67	16	20	3.8-72	18	15	5.0-35	15
T PCDFs-TEQ	130	3.9-1000	64	120	3.7-1100	58	112	3.1-900	55	110	3.5-910	61	10	3.5-34	9.6
T non-ortho PCBs-TEQ	13	2.7-45	12	12	3.1-32	11	11	1.7-38	9.8	12	1.4-34	9.9	12	2.0-54	9.4
Total TEQ	163	12-1100	99	150	12-1200	83	142	8.9-980	80	150	12-1000	88	37	12-100	35
lipid (%)	0.34	0.24-0.56	0.33	0.36	0.27-0.53	0.35	0.35	0.26-0.51	0.35	0.34	0.28-0.46	0.34	0.33	0.22-0.49	0.32
Age(years)	69.7	58-88	70	70.7	59-89	71	71.7	60-90	72	72.7	61-91	73	68.1	60-86	67

ND:less than the determination limit, Med.:Median, TEQ:toxic equivalent quality (WHO 1998)

the Yusho patients. In 2002, we divided the 103 Yusho patients into three groups based on 2,3,4,7,8-PeCDF concentration according to the diagnostic criteria for Yusho: group Pe-L: n=22, <30 pg/g lipid, group Pe-M: n=13, 30-50 pg/g lipid, and group Pe-H: n=68, >50 pg/g lipid.

Figure 1 shows the time trend of 2,3,4,7,8-PeCDF mean concentration for each group. The Pe-H group's mean concentration of 2,3,4,7,8-PeCDF gradually decreased and the Pe-M and Pe-L group's mean concentrations of 2,3,4,7,8-PeCDF were not changed. The Pe-H, Pe-M, and Pe-L group's mean concentrations of 2,3,4,7,8-PeCDF were 340-300, 40-35 and 18-16 pg /g lipid, respectively. However, the level found in the normal controls was 18 pg /g lipid. The levels of the Pe-L and Pe-M groups were similar to those of the normal controls; however, the level of the Pe-H group was 17-19 times higher than that of the normal controls, respectively.

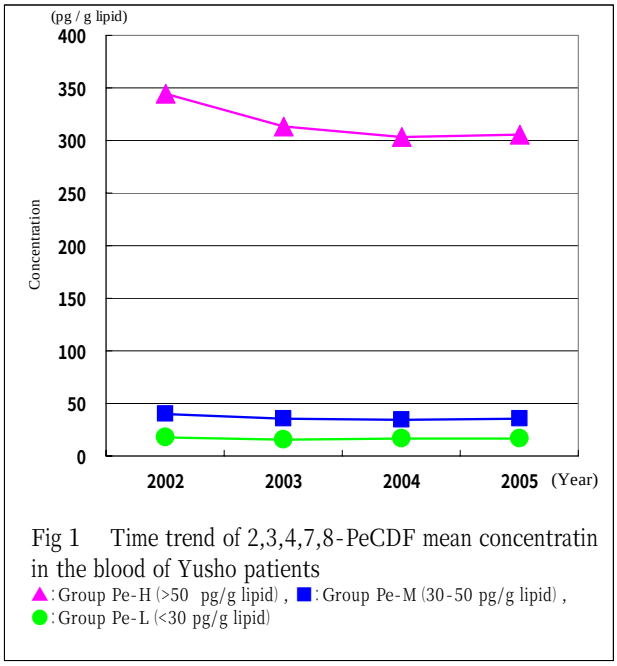

Fig 1 Time trend of 2,3,4,7,8-PeCDF mean concentratin in the blood of Yusho patients
▲: Group Pe-H (>50 pg/g lipid), ■: Group Pe-M (30-50 pg/g lipid), ●: Group Pe-L (<30 pg/g lipid)

The concentrations of the dominant Yusho isomers (2,3,4,7,8-PeCDF and 1,2,3,4,7,8-HxCDF) in Yusho patients gradually decreased over 34-37 years, while the concentrations of 2,3,4,7,8-PeCDF of the Pe-L and Pe-M groups which were similar to those of the normal controls showed no change. However, the high concentration Pe-H group showed a further decrease.

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