EVALUATION ON TOXIC CONTRIBUTION OF PCDDs, PCDFs AND DIOXIN-LIKE PCBs DETERMINED IN THE PRESERVED UMBILICAL CORD OF YUSHO PATIENTS

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Introduction

A mass food poisoning, so-called Yusho, because it was caused by the ingestion of rice bran oil, which was early on contaminated with Kanechlor-400, a commercial brand of Japanese polychlorinated biphenyls (PCBs), occurred in western Japan in 1968 [1)] and more than 1900 patients have been diagnosed and identified as Yusho patients by the study groups of Kyushu and Nagasaki Universities. It was later on found that the rice bran oil had been also contaminated with polychlorinated dibenzofurans (PCDFs) [2) 3)] and polychlorinated quaterphenyls (PCQs) and others [4) 5)]. The concentrations, however, of PCBs and PCQs in the rice bran oil were several hundred times higher than that of PCDFs, PCDFs have been considered the primarycausative agents of Yusho [2) 3) 6) ~ 10)] as well as of Yu-Cheng incident, which occurred in central Taiwan in 1979 [11)].

In this study, the concentrations of PCDFs, polychlorinated dibenzo-*p*-dioxins (PCDDs), dioxin-like PCBs and PCBs in the preserved umbilical cord of Yusho patients and healthy Japanese during 32 to 38 years were determined and their toxic contributions to the fetuses of Yusho patients were evaluated.

Materials and Methods

We were able to get the preserved umbilical cords during 32 to 38 years from seven Yusho patients except one, who was not identified as Yusho patient, but were born from Yusho patient 32 years ago, and two healthy Japanese. Among six preserved umbilical cords of Yusho patients, two of them were obtained from so-called black babies showed a diffuse darkish brown skin color due to the presence of abundant melanin pigment. The nine preserved umbilical cords were ground to powder and then employed to determine the concentrations of PCBs by ECD gas chromatographic method [12) 13)] and PCDDs, PCDFs and dioxin-like PCBs by high resolution GC/MS method [12)]. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD) toxic equivalent (TEQ) concentrations of PCDDs, PCDFs and dioxin-like PCBs were calculated by using 2005 WHO toxic equivalent factor (TEF) values [14)]. Statistical significance of the concentrations of PCDDs and PCBs between Yusho patients and healthy Japanese was evaluated by student's t-test.

Results and Discussion

Table 1 shows the concentrations of PCDD congeners in the preserved umbilical cord. 2,3,7,8-TCDD, 1,2,3,7,8-pentachlorodibenzo-*p*-dioxin (PenCDD) and 1,2,3,4,7,8-hexachlorodibenzo-*p*-dioxin (HxCDD) were not detected in both healthy Japanese and Yusho patients. 1,2,3,6,7,8- and 1,2,3,7,8,9-HxCDDs were determined only in Yusho patients at the mean concentrations of 9.5 and 1.9 pg/g dry weight, respectively. Concentrations of 1,2,3,4,6,7,8-heptachlorodibenzo-*p*-dioxin (HpCDD) were almost the same in both groups. However, concentration of octachlorodibenzo-*p*-dioxin (OCDD) was about two times higher in healthy Japanese than in Yusho patients. As also

indicated in Table 1, mean TEQ concentration of Yusho patienta was 1.3. pg/g dry weight and 6.5 times greater than that of healthy Japanese.

Table 2 shows the concentrations of PCDFs congeners, together with TEQ concentrations. In healthy Japanese, none of the PCDF congeners were detected. However, in Yusho patients several PCDF congeners were determined, and 2,3,4,7,8-pentachlorodibenzofuran (PenCDF) and 1,2,3,4,7,8-hexachlorodibenzofuran (HxCDF) showed the highest concentrations. Mean TEQ concentration of Yusho patients was 11.0 pg/g dry weight.

Concentrations of dioxin-like PCBs, 2,2',4,4',5,5'-hexachlorobiphenyl (HxCB), total PCBs and TEQ are indicated in Table 3. Among dioxin-like PCB, concentrations of 2,3,3',4,4',5-, 2,3,3',4,4',5'- and 2,3',4,4',5,5'-HxCB and 2,3,3',4,4',5,5'-heptachlorobiphenyl (HpCB) were much higher in Yusho patients than in healthy Japanese. Concentrations of 2,2',4,4',5,5'-HxCB were significantly and 3.6 times greater in Yusho patients than in healthy Japanese. However, mean TEQ concentrations of both groups were same and 0.2 pg/g dry weight.

As shown in Table 4, total mean TEQ concentrations of PCDDs, PCDFs and dioxin-like PCBs of healthy Japanese and Yusho patients were 0.4 and 12.5 pg/g dry weight, respectively. So, net mean TEQ concentration of Yusho patients was 12.1 pg/g dry weight and the respective contribution of PCDDs, PCDFs and dioxin-like PCBs to the net TEQ concentration was calculated to be 9, 91 and 0 %. Therefore, this study also demonstrated that in toxic effects of PCDFs, PCDDs and dioxin-like PCBs on the fetuses of Yusho patients, PCDFs exerted the highest contribution on them.

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Table 1. Concentrations of PCDD congeners in the preserved umbilical cord during 32 to 38 years of healthy Japanese and Yusho patients

	Concentration, pg/g dry weight	
PCDD Congener	Healthy Japanese (n=2)	Yusho Patients (n=7)
2,3,7,8- [a]	N.D.	N.D.
1,2,3,7,8- [a]	N.D.	N.D.
1,2,3,4,7,8- [b]	N.D.	N.D.
1,2,3,6,7,8- [b]	N.D.	9.5 ± 7.6
1,2,3,7,8,9- [b]	N.D.	1.9 ± 3.6
1,2,3,4,6,7,8- [b]	13.5 ± 10.1	15.0 ± 11.9
OCDD [c]	179 ± 179	86.4 ± 79.6
TEQ [d]	0.2 ± 0.2	1.3 ± 1.1

a : Detection limit, 0.003 pg/g dry weight
b : Detection limit, 0.006 pg/g dry weight
c : Detection limit, 0.01 pg/g dry weight
d : pg-TEQ/g dry weight

Table 2. Concentrations of PCDF congeners in the preserved umbilical cord during 32 to 38 years of healthy Japanese and Yusho patients

	Concentration, pg/g dry weight	
PCDF Congener	Healthy Japanese (n=2)	Yusho Patients (n=7)
2,3,7,8- [a]	N.D.	6.2 ± 9.4
1,2,3,7,8- [a]	N.D.	N.D.
2,3,4,7,8- [a]	N.D.	24.9 ± 12.8
1,2,3,4,7,8- [b]	N.D.	26.5 ± 14.2
1,2,3,6,7,8- [b]	N.D.	1.9 ± 3.4
2,3,4,6,7,8- [b]	N.D.	N.D.
1,2,3,7,8,9- [b]	N.D.	N.D.
1,2,3,4,6,7,8- [b]	N.D.	5.4 ± 7.0
1,2,3,4,7,8,9- [b]	N.D.	N.D.
OCDF [c]	N.D.	N.D.
TEQ [d]	0.0 ± 0.0	11.0 ± 5.3

a : Detection limit, 0.003 pg/g dry weight
b : Detection limit, 0.005 pg/g dry weight
c : Detection limit, 0.01 pg/g dry weight
d : pg-TEQ/g dry weight

Table 3. Concentrations of PCB congeners and total PCBs in the preserved umbilical cord during 32 to 38 years of healthy Japanese and Yusho patients

PCB Congener and Total PCBs	Concentration, pg/g dry weight	
	Healthy Japanese (n=2)	Yusho Patients (n=7)
Nonortho		
3,4,4',5-	21.8 ± 30.8	27.7 ± 35.5
3,3',4,4'-	345 ± 387	434 ± 480
3,3',4,4',5 -	N.D.	N.D.
3,3',4,4',5,5' -	N.D.	N.D.
Monoortho		
2,3,3',4,4' -	627 ± 494	953 ± 779
2,3,4,4',5 -	52.4 ± 34.4	143 ± 80.9
2,3',4,4',5 -	1141 ± 643	1707 ± 1231
2',3,4,4',5 -	33.8 ± 25.0	36.6 ± 30.9
2,3,3',4,4',5 -	91.9 ± 65.9	582 ± 318 *
2,3,3',4,4',5' -	20.2 ± 14.2	305 ± 418
2,3',4,4',5,5' -	28.3 ± 11.8	91.6 ± 50.6
2,3,3',4,4',5,5' -	N.D.	54.8 ± 32.9
TEQ [a]	0.2 ± 0.2	0.2 ± 0.2
2,2',4,4',5,5' -	742 ± 19.1	2666 ± 1600 **
Total PCBs	60675 ± 45334	88850 ± 54534

Detection limit : 0.03 pg/g dry weight
a : pg-TEQ/g dry weight
* : p=0.08
** : p<0.02

Table 4. Toxic contribution of PCDDs, PCDFs and dioxin-like PCBs to the fetuses of Yusho patients 2 to 8 years after the outbreak of Yusho

Congener	TEQ Concentration, pg-TEQ/g dry weight			
	Healthy Japanese (A)	Yusho Patients (B)	B - A	
PCDDs	0.2	1.3	1.1	(9)
PCDFs	0.0	11.0	11.0	(91)
Dioxin-like PCBs	0.2	0.2	0	(0)
Total	0.4	12.5	12.1	(100)

Figure in parenthesis indicates the percent to total TEQ concentration