Concentrations of polychlorinated dibenzo-*p*-dioxins, polychlorinated dibenzofurans, and dioxin-like polychlorinated biphenyls in blood collected from 195 pregnant women in Sapporo City, Japan

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Abstract

We measured the concentrations of dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), non-*ortho* coplanar polychlorinated biphenyls (non-*ortho* PCBs), and mono-*ortho* coplanar polychlorinated biphenyls (mono-*ortho* PCBs) in blood samples collected between 2002 and 2004 from 195 pregnant women living in Sapporo City of Hokkaido Prefecture, Japan. The arithmetic mean total TEQ concentrations of PCDDs, PCDFs, non-*ortho* PCBs, and mono-*ortho* PCBs of primiparous and multiparous mothers in Sapporo City, Japan were 17.4 (median: 15.7) and 14.0 (median: 13.9) pg TEQ/g lipid, respectively, and the concentrations were in the range of 6.6-43.4 and 3.4-28.2 pg TEQ/g lipid, respectively. In regard to the relationship between the total TEQ concentrations of PCDDs, PCDFs, non-*ortho* PCBs, and mono-*ortho* PCBs in maternal blood and the number of deliveries, the levels of these dioxin-like compounds tended to decrease with increases in the number of deliveries. Furthermore, significant correlations observed between the total TEQ concentrations of these dioxin-like compounds and the age of primiparae and multiparae. The total TEQ concentrations of PCDDs, PCDFs, non-*ortho* PCBs, and mono-*ortho* PCBs measured in 195 pregnant women has decreased compared to past levels in Japan for the last several decades. The results of the present study have indicated that dioxin contamination in the blood for young women in Japan is continuing to decrease.

Introduction

Polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), non-*ortho* coplanar polychlorinated biphenyls (non-*ortho* PCBs), and mono-*ortho* coplanar polychlorinated biphenyls (mono-*ortho* PCBs) are persistent environmental pollutants. When PCDDs, PCDFs, and dioxin-like PCBs are released into the environment, these dioxin-like compounds accumulate in the human body through ingested food[1]. In fact, over 90% of human exposure to PCDDs, PCDFs, and dioxin-like PCBs has been attributed to food intake, particularly from food of animal origins[2]. PCDDs, PCDFs, and dioxin-like PCBs accumulated over a long period in the maternal body is thought to be transferred from the mother to her fetus via the placenta during pregnancy and from mothers to infants via breast milk. Therefore, survey studies of the transplacental and lactational exposures to PCDDs, PCDFs, and dioxin-like PCBs have been conducted in various countries to elucidate the influence of these dioxin-like compounds on the health of fetuses and infants. Human breast milk has been used as a bioindicator for the maternal body burden of PCDDs, PCDFs, and dioxin-like PCBs and as a biomarker to assess the risk of these dioxin-like compounds for breast-fed infants. Consequently, the exposure study of these dioxin-like compounds in breast milk has been chiefly developed in comparison with levels found in blood. In most cases, however, the degree of the human body burden is assessed based on concentrations of PCDDs, PCDFs, non-*ortho* PCBs, and mono-*ortho* PCBs in blood. In particular, concentrations of PCDDs, PCDFs, non-*ortho* PCBs, and mono-*ortho* PCBs in the blood of pregnant women not only offer the levels of these dioxin-like compounds that have accumulated in the maternal body, but also seem to offer clues regarding the amounts of these dioxin-like compounds transferred from the mother to the fetus. However, published data showing the specific concentrations of all dioxin-like compounds in blood collected from pregnant women are limited.

In this study, we carried out the first survey of the concentrations of PCDDs, PCDFs, non-*ortho* PCBs, and mono-*ortho* PCBs in blood samples collected between 2002 and 2004 from 195 pregnant women living in

Sapporo City of Hokkaido Prefecture, Japan. The objectives of our primary study were: (1) to determine the current levels of PCDDs, PCDFs, and dioxin-like PCBs in the blood of pregnant woman in Sapporo City, Japan, and (2) to examine the relationship between concentrations of PCDDs, PCDFs, and dioxin-like PCBs in the blood and the delivery time or age of the mother.

Materials and Methods

Hokkaido Prefecture is located in the northern Japanese archipelago that extends from north to south, and its area accounts for one-fifth of the nation's total land area. Hokkaido Prefecture consists of a total of 212 characteristic municipalities, including its capital, Sapporo City, which has a population of 1.8 million. All the subjects participating in this study were native Japanese and were residents of Sapporo City or the surrounding area. The blood samples were collected between 2002 and 2004 from 195 pregnant women, from whom informed consent was obtained. The blood samples were collected from the maternal peripheral vein after the second trimester during their last pregnancy. Among the 195 pregnant women, 101 mothers were primipara and 94 mothers were multipara. The ages of the primiparous and the multiparous mothers were within 18-40 years (mean: 28.8 years) and 20-47 years (mean: 32.4 years), respectively. After collection, the blood samples were stored at 4°C until analyses for concentrations of PCDDs, PCDFs, and dioxin-like PCBs. The extraction of PCDDs, PCDFs, and dioxin-like PCBs from the blood was performed using a previously reported method[3,4]. Concentrations of the PCDDs, PCDFs and dioxin-like PCBs were measured using high-resolution gas chromatography/high-resolution mass spectrometry equipped with a solvent cut large-volume injection system[3, 4]. To estimate the total toxic equivalents (TEQ) concentration, we introduced ND (less than the detection limit) values to half values of the detection limit and the estimates based on the toxic equivalency factor (TEF) values proposed by the World Health Organization (WHO) in 2005. The statistical analysis was conducted using Mann-Whitney's *U* test and Spearman's rank correlation in the software program from SAS Institute (SAS Inc.). Significant probabilities (*p* values) were calculated for the respective number of samples analyzed.

Results and discussion

The arithmetic mean total TEQ concentrations of PCDDs, PCDFs, non-*ortho* PCBs, and mono-*ortho* PCBs of primiparous and multiparous mothers in Sapporo City, Japan were 17.4 (median: 15.7) and 14.0 (median: 13.9) pg TEQ/g lipid, respectively, and the concentrations were in the range of 6.6-43.4 and 3.4-28.2 pg TEQ/g lipid, respectively (Table 1). The total TEQ levels of PCDDs, PCDFs, and dioxin-like PCBs in blood calculated based on the WHO 2005 TEF are approximately 15% lower than those of WHO 1998 TEF. Among PCDDs, PCDFs, and dioxin-like PCB congeners, 1,2,3,7,8-PeCDD, 1,2,3,6,7,8-HxCDD, 2,3,4,7,8-PeCDF, 3,3',4,4',5-PeCB (#126), and 2,3,3',4,4',5-HxCB (#156) showed particularly high concentrations in the blood of primiparous and multiparous mothers. The total concentrations of these five congeners in both primiparous and multiparous mothers contributed approximately 80% of the total TEQ concentrations.

To better understand the levels of PCDDs, PCDFs, and dioxin-like PCBs in the blood of women in different regions and past levels of Japan, we compared the present data, which were calculated based on the WHO 1998 TEF with those from 50 single women (mean: 20.2 years) who had lived in Fukuoka Prefecture in 1993-1994, which were previously reported by our group, although we did not analyze mono-*ortho* PCBs in our previous study[5]. The concentrations of each congener of PCDDs, PCDFs, and non-*ortho* PCBs in the blood of primiparous mothers (mean: 26.1 years) under 30 years old in the present study were lower than those in the women of Fukuoka Prefecture. The sum of TEQ concentrations of PCDDs, PCDFs, and non-*ortho* PCBs in the blood of 50 single women in Fukuoka Prefecture was 21.3 pg TEQ/g lipid, which was 1.3 times higher than the same sum for women of Sapporo City (16.0 pg TEQ/g lipid). Moreover, the total TEQ concentrations of PCDDs, PCDFs, and dioxin-like PCBs in the present study were slightly lower than those of the subjects in other domestic areas, in which the subject age was similar to that in this study[6]. These results suggest that environmental pollution levels and human exposure to PCDDs, PCDFs, and dioxin-like PCBs in Sapporo City are relatively low.

During the past few decades, extensive research regarding human exposure to PCDDs, PCDFs, and dioxin-like PCBs has been conducted in various countries in order to assess human health risk. The results of various studies have shown that levels of these dioxin-like compounds in the United States and Europe are decreasing, both in the environment and in the population. The results of the present study indicate that dioxin contamination in the blood of young women has decreased compared to past levels in Japan for the last several

Table 1. Concentrations of PCDDs, PCDFs, and dioxin-like PCBs in the blood of 195 pregnant women collected in Sapporo City, Japan

	Concentration(pg/g lipid)										
	Primipara (n=101)					Multipara (n=94)					*p* values
Congeners	Mean	Median	SD	Max.	Min.	Mean	Median	SD	Max.	Min.	
2,3,7,8-TCDD	1.2	1.1	0.7	3.4	0.5	0.9	0.5	0.5	3.4	0.5	<0.001
1,2,3,7,8-PeCDD	4.7	4.5	1.9	10	1.5	3.7	3.6	1.4	7.9	0.5	<0.001
1,2,3,4,7,8-HxCDD	1.9	1.0	1.0	5.1	1.0	1.6	1.0	1.4	14	1.0	0.004
1,2,3,6,7,8-HxCDD	16	14	7.4	39	5.6	13	12	5.6	42	2.4	<0.001
1,2,3,7,8,9-HxCDD	2.5	2.3	1.5	9.0	1.0	2.0	2.0	1.1	5.0	1.0	0.016
1,2,3,4,6,7,8-HpCDD	29	26	13	71	9.2	26	24	9.4	59	13	0.23
OCDD	526	476	244	1492	163	500	476	181	1353	232	0.875
Total PCDDs	574	507	266	1602	191	548	510	189	1419	274	0.972
2,3,7,8-TCDF	0.8	0.5	0.5	3.8	0.5	0.7	0.5	0.4	2.5	0.5	0.759
1,2,3,7,8-PeCDF	ND					ND					
2,3,4,7,8-PeCDF	6.8	6.0	3.1	19.9	0.5	5.4	5.4	2.3	14	1.2	0.002
1,2,3,4,7,8-HxCDF	2.9	2.7	1.4	7.7	1.0	2.4	2.3	1.5	12	1.0	0.002
1,2,3,6,7,8-HxCDF	3.4	2.9	1.7	10.1	1.0	2.6	2.6	1.2	6.8	1.0	0.003
2,3,4,6,7,8-HxCDF	ND					ND					
1,2,3,7,8,9-HxCDF	ND					ND					
1,2,3,4,6,7,8-HpCDF	3.5	2.8	3.1	19.5	1.0	4.7	2.2	18	162	1.0	0.001
1,2,3,4,7,8,9-HpCDF	ND					ND					
OCDF	ND					ND					
Total PCDFs	23	21	8.7	53	11	22	18	21	192	10	0.003
344'5-TCB(#81)	ND					ND					
33'44'-TCB(#77)	18	13	46	475	5.0	12	13	5.3	27	5.0	0.27
33'44'5-PenCB(#126)	45	39	28	157	10	38	36	20	111	5.0	0.075
33'44'55'-HxCB(169)	32	29	15	86	5.0	27	26	12	71	5.0	0.027
Total Non-*ortho* PCBs	99	86	63	554	30	81	78	31	197	27	0.042
2'344'5-PenCB(#123)	141	119	81	427	41	114	101	61	308	5.0	0.043
23'44'5-PenCB(#118)	7294	6182	4086	20284	2443	5991	5533	3014	15627	1325	0.039
2344'5-PenCB(#114)	440	391	259	1695	109	349	321	186	1121	79	0.004
233'44'-PenCB(#105)	1824	1481	1025	5421	506	1475	1429	742	3806	256	0.023
23'44'55'-HexCB(#167)	855	739	468	2365	291	741	717	375	1926	159	0.121
233'44'5-HexCB(#156)	2220	1950	1156	6428	658	1989	1798	1044	6026	441	0.171
233'44'5'-HexCB(#157)	563	502	288	1537	118	494	432	259	1438	88	0.088
233'44'55'-HpCB(#189)	249	219	126	626	5.0	250	213	137	807	70	0.766
Total Mono-*ortho* PCBs	13376	12061	7119	36382	4438	11236	10850	5166	27861	3231	0.06
PCDDs-TEQ	8.5	7.5	3.4	18	3.2	6.6	6.4	2.4	14	1.7	<0.001
PCDFs-TEQ	3.0	2.7	1.3	7.8	0.6	2.5	2.4	0.9	6.5	0.9	0.002
PCDDs/PCDFs-TEQ	11	10	4.6	26	4.6	9.1	8.7	3.1	18	2.6	<0.001
Non-*ortho* PCBs-TEQ	5.5	4.7	3.1	17	1.4	4.6	4.3	2.2	13	0.7	0.062
Mono-*ortho* PCBs-TEQ	0.4	0.4	0.2	1.1	0.2	0.3	0.3	0.2	0.8	0.1	0.037
Coplanar PCBs-TEQ	5.9	5.1	3.2	18	1.6	4.9	4.7	2.4	14	0.8	0.055
Total TEQ	17.4	15.7	7.4	43.4	6.6	14.0	13.9	5.1	28.1	3.4	0.002

ND: less than the determination limit; SD: standrad deviation.

TEQ concentrations were computed by using 2005 WHO toxic equivalency factor (TEF) values

decades. These findings indicate that dioxin contamination in the blood of young women in Japan is continuing to decrease. The total TEQ concentrations of PCDDs, PCDFs, and dioxin-like PCBs of primiparous and multiparous mothers in Sapporo City were 6.6-43.4 (mean: 17.4, median: 15.7) and 3.4-28.1 (mean: 14.0, median: 13.9) pg TEQ/g lipid, respectively, indicating that the total TEQ concentrations of primiparous mothers are significantly higher than those of multiparous mothers (Table 1). The relative contribution ratios of the concentrations of PCDDs, PCDFs, non-*ortho* PCBs, and mono-*ortho* PCBs to the total TEQ concentrations for primiparous and multiparous mothers were 48.6, 17.4, 31.6, and 2.3%, respectively, and 47.3, 17.6, 32.6, and 2.3%, respectively, and the ratios were almost the same. These findings suggested that approximately 20% of PCDDs, PCDFs, and dioxin-like PCBs had accumulated in the maternal body by delivery to be eliminated, and the ratios of the concentrations of PCDDs, PCDFs, and dioxin-like PCBs to the total TEQ concentrations in maternal blood were almost the same as those obtained after delivery. In regard to the relationship between the total TEQ concentrations of PCDDs, PCDFs, and dioxin-like PCBs and the age of primiparous and multiparous mothers, the levels of these dioxin-like compounds significantly increased with increasing maternal age in both groups. Further, a significant correlation was observed between the total TEQ concentrations of PCDDs, PCDFs, and dioxin-like PCBs in blood and maternal age (Table 2).

Table 2. Spearman's rank correlations between the concentartions of PCDD, PCDFs, and dioxin-like PCBs and the age of primiparous and multiparous mothers

	Primipara (n=101)		Multipara (n=94)	
	ρ	p values	ρ	p values
PCDDs	0.449	<0.001	0.336	0.001
PCDFs	0.370	<0.001	0.282	0.006
Non-*ortho* PCBs	0.283	0.004	0.368	<0.001
Mono-*ortho* PCBs	0.457	<0.001	0.405	<0.001
Total TEQ	0.395	<0.001	0.366	<0.001

Conclusions

In this study, we measured the concentrations of PCDDs, PCDFs, non-*ortho* PCBs, and mono-*ortho* PCBs collected from 195 pregnant women in Sapporo City of Hokkaido Prefecture, Japan. The present study was one of the few studies where all dioxin-like compounds were measured in the blood of pregnant women. The results indicate that dioxin contamination in the blood of young women in Japan is continuing to decrease and can be used as baseline data for future temporal trends.

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