Worldwide Trends of Dioxin Levels in Human Breast Milk With Comparison between Toyama Prefecture in Japan and Other Areas

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Worldwide Trends of Dioxin Levels in Human Breast Milk

With Comparison between Toyama Prefecture in Japan and Other Areas

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Abstract - The current exposure condition of dioxins (PCDDs/PCDFs) in Toyama Prefecture was studied, analyzing ordinary mother's breast milk, and compared the concentration level with other domestic and overseas areas. As a result, the concentration pattern of the 17 2,3,7,8-substituted isomers demonstrated the typical one of human background values of dioxins, including high concentration of 1,2,3,7,8-PeCDD. The total TEQ levels for Toyama and other areas suggest that worldwide trends of dioxin levels may correspond to the industrial level in the countries, though local exposures to dioxins are remarkably observed.

I. Introduction

Due to the increase of utility of industrial, farm and life chemicals, a variety of toxic compounds have been released into the environment. Especially dioxins (PCDDs; polychlorinated-dibenzo-p-dioxins, PCDFs; polychlorinated dibenzofurans) and polychlorinated biphenyls (PCBs) have been acknowledged as environmental pollutants that do not decompose readily in the environment, which results in high-level accumulation in human body [1]. Recent great concern over dioxins and PCBs, has been directed towards the hypothesis that exposure to these compounds might be capable of causing a spectrum of adverse effects as a result of endocrine modulation [2,3]. Despite the many advances in our understanding of nutrition and general health, human breast milk is still considered to be the preferred food for the developing and growing neonate[4,5]. Human breast milk, however, can be contaminated with lipophilic organochlorine compounds such as dioxins and PCBs[6,7], and neonatal body burden of these compounds may be created by subsequent breast feeding [8,9,10].

Human breast milk is a convenient medium for monitoring extremely small quantities of dioxins and PCBs, because it is easier to sample from the general population than adipose tissue, and abundant sampling is practicable, compared with blood. For that reason, both nation- and world-wide analyses have been carried out to assess the significance of body burdens of the toxic compounds [11,12,13,14]. In spite of that, nationwide studies in Japan have not much involved Hokuriku District so far, to know the current exposure condition to dioxins in total.

Therefore the studies focusing on the general populations in Toyama Prefecture were carried out to grasp concentration levels of dioxins in this area, while comparing with other domestic and overseas areas.

II. Methods

A. *Subjects and samples*

Target population was the 29 Japanese women (19 primiparas and 10 multiparas) in Toyama Prefecture, and delivered their infants at the Toyama Medical Pharmaceutical Hospital. The age of the subjects ranged from 24 to 38 yr in primiparas, and from 28 to 36 yr in multiparas, with an average age of 30.3 yr. No significantly different characteristics in socioeconomic status, nutrition and health management were observed among them.

20-60ml of breast milk were collected from the subjects at their health check (one month postpartum) in 1999, and stored frozen (-20℃) until analysis.

B. *Analytical methods*

Pretreatment procedure for dioxins was followed [15]; after fat extraction from each sample of 10g, ^{13}C-2,3,7,8-substitued PCDDs and PCDFs as internal standards were added to the fat extract. A series of purification operations consisting of alkali digestion, and chromatography on a multi-layered column of silica gel, and on a single-layered column of activated carbon dispersed on silica gel, were carried out to separate and collect PCDDs and PCDFs. The final extract was concentrated by evaporation to 20 μ l.

C. *Determination*

Quantitation was performed by a high resolution mass spectrometer (HRMS; JEOL MStation-JMS700)equipped with a gas chromatograph (HP-6980). A DB-5ms column with 30m × 0.25mm i.d. of 0.25 μ m film thickness (Agilent Technologies) was used, and measurements were performed by selected ion monitoring (SIM) method. Regarding with the sensitivity of the HRMS, at a signal-noise ratio (S/N)=3, detection limit of 0.3 pg/g fat and absolute measurement limit of 0.08 pg/g fat were achieved. Recoveries of the ^{13}C-2,3,7,8-substitued PCDDs and PCDFs were

70-80%, which agreed with the recovery range regulated by the Japanese Industrial Standard (JIS).

D. *Calculations*

Since many studies of dioxins represent concentration level of each congener in lipid base, all concentrations here were indicated in a lipid base. In addition to respective concentration of 17 2,3,7,8-substituted PCDDs and PCDFs, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TeCDD) toxic equivalents (TEQ) were calculated for each sample, submitting the international Toxicity Equivalent Factor (TEF) of WHO-TEF(1997) [16].

III. Results and Discussion

The levels of 7 2,3,7,8-substituted PCDD and 10 2,3,7,8-substituted PCDF isomers found in the Toyama samples are shown in Table 1 and 2, respectively, with those from Fukuoka [17] and a city in southern Catalonia in Spain [18]. Of the total of 135 PCDDs and 75 PCDFs, only those with four or more chlorines, and 2,3,7,8-substitution have significant biological activity and are observed in human populations from industrialized countries [19].

Of the 17 2,3,7,8-substituted PCDDs and PCDFs, the three high level isomers in the Toyama samples were OCDD (abbreviation is explained in Table 1), 1,2,3,6,7,8-HxCDD and 1,2,3,7,8-PeCDD in turn. This pattern was also recognized by the both Fukuoka and Spain studies. Hence concentration pattern observed in the Toyama samples is thought to be a typical pattern for human background values of PCDDs, showing more variation on chlorination from tetra- to octa- than PCDFs. Relative ratio between 2,3,7,8-TeCDD and 1,2,3,7,8-PeCDD, 1,2,3,6,7,8-HxCDD, and OCDD in the Toyama samples, was roughly 1:10:12:46, while that of the Fukuoka studies was roughly 1:4:15:60. This indicates that the concentration of 1,2,3,7,8-PeCDD in the Toyama samples was high, while the concentration of OCDD and 1,2,3,6,7,8-HxCDD was low. Similarly the relative ratio for the Spain study was 1:4:30:150, in which high concentration of OCDD was remarkable in comparison with those of both Toyama and Fukuoka. WHO-TEF (1998) regards 1,2,3,7,8-PeCDD as the most toxic compound in dioxins like 2,3,7,8-TeCDD, which implies that high concentration of 1,2,3,7,8-PeCDD can contribute to the total TEQ concentrations.

Observed amounts were not remarkable for four PCDFs isomers; 1,2,3,7,8-PeCDF, 1,2,3,7,8,9-HxCDF, 1,2,3,4,7,8,9- HpCDF and OCDF, which was also recognized by the studies of both Fukuoka and Spain, as shown in Table 2. Besides these isomers, significant difference in of each isomer was not seen between Toyama and Fukuoka. However the concentration levels of both Toyama and Fukuoka tend to be higher than that of Spain.

TEQ concentrations were estimated for PCDDs (TEQ- PCDDs), PCDFs (TEQ-PCDFs) and total for the sum of PCDDs and PCDFs (TEQ-TOTAL) (Table 3). The 1,2,3,7,8-PeCDD level (TEF for 1,2,3,7,8-PeCDD = 1) reached 81% of the TEQ-PCDDs, which accounted for 60% of the TOTAL-TEQ. The 1,2,3,7,8-PeCDD level in the Fukuoka study reached 90% of the TEQ-PCDD, and contribution to the TOTAL-TEQ was 50%. Resultingly contribution of the 1,2,3,7,8-PeCDD to the TEQ-PCDDs concentration is very significant in both Toyama and Fukuoka, and the PeCDD level makes up over 50% of the TOTAL-TEQ in both of them. On the other hand, contribution of the 1,2,3,7,8-PeCDD level to the TEQ- PCDDs was 47% for the Spain study, which accounted for just 40% of the TOTAL-TEQ. Accordingly predominant tendency of 1,2,3,7,8-PeCDD in PCDDs-TEQ causes increase of the total TEQ level, which results in high level of the total TEQ. This suggests that the 1,2,3,7,8- PCDD level has the impact on TEQ, and influences the toxic assessment.

Table 4 shows the total TEQ levels from several domestic areas with both Toyama and Fukuoka, which were provided by the Ministry of Health, Labour, and Welfare [20]. Each TEQ level from domestic areas in Table 4 demonstrates the difference of the total TEQ level, depending on location, and high level of the total TEQ for the Toyama samples. Since the concentration level of each 2,3,7,8-subtituded PCDD and PCDF isomer is not mentioned in this report, appropriate assessment can not be performed. Hence, further domestic studies should be carried out to obtain the concentration of each isomer for interpreting 1,2,3,7,8-PeCDD level in the total TEQ.

Table 1. Average concentrations of 2,3,7,8-substituted PCDDs congeners in human milk samples from Toyama Prefecture and other areas
(pg/g lipid)

PCDD isomers	Toyama (SD)	Fukuoka[2]	SPAIN[3]
Number of samples	29	95	15
Lipid content (%)(Mean)	3.64	-[4]	2.63
2,3,7,8-TeCDD[1]	1.47 (0.68)	1.90	1.04
1,2,3,7,8-PeCDD	16.77 (8.44)	7.80	4.02
1,2,3,4,7,8-HxCDD	2.23 (1.70)	2.20	2.84
1,2,3,6,7,8-HxCDD	17.54 (8.51)	29.0	27.88
1,2,3,7,8,9-HxCDD	3.24 (2.16)	7.80	4.55
1,2,3,4,6,7,8-HpCDD	11.17 (6.21)	17.0	38.26
OCDD	71.45 (57.60)	120.0	145.67

[1]Abbreviations: CDD-polychlorinated dibenzo-p-dioxins; Te- tetra; Pe-penta; Hx-hexa; Hp-hepta; O-octa
[2]: [17]; [3]: [18]; [4] -: not referred

Table 2. Average concentrations of 2,3,7,8-substituted PCDFs isomers in Toyama and other areas
(pg/g lipid)

PCFD isomers	Toyama (SD)	Fukuoka	SPAIN
2,3,7,8-TeCDF[1]	1.28 (0.61)	1.10	0.49
1,2,3,7,8-PeCDF	0.70 (0.67)	0.87	0.23
2,3,4,7,8-PeCDF	11.33 (4.74)	12.0	6.95
1,2,3,4,7,8-HxCDF	3.17 (1.21)	4.80	1.59
1,2,3,6,7,8-HxCDF	3.34 (2.91)	3.90	1.31
1,2,3,7,8,9-HxCDF	0.084 (0.12)	0.73	0.05
2,3,4,6,7,8-HxCDF	2.65 (1.58)	4.70	0.67
1,2,3,4,6,7,8-HpCDF	1.90 (0.19)	3.60	2.42
1,2,3,4,7,8,9-HpCDF	0.21 (0.34)	0.06	0.07
OCDD	ND[2]	ND	0.31

[1]Abbreviations: CDF-polychlorinated dibenzofran; [2] ND: not detected

Furthermore, total TEQ levels in overseas areas are shown in Table 4. Since each total TEQ for UK, Germany, Canada and USA, which are classified as industrialized countries, was determined in early 1990s, the level of that is higher than those for the domestic areas in Japan shown in the same table.However contribution of 1,2,3,7,8,9- PeCDD to the total TEQ for these countries ranged from 40% to 70%, which was not so different from that shown in Table 3. Accordingly the high level of 1,2,3,7,8-PeCDD may be commonly observed in mother's breast milk from industrialized countries.

Previous studies mainly strived for interpreting concentration level of 2,3,7,8-TeCDD, which was encouraged by the studies on potential health effects of Agent Orange, the principal phenoxy herbicide mixture sprayed over southern Viet Nam between 1962 and 1971, during the Viet Nam War. In fact, contribution of 2,3,7,8-TCDD to the total TEQ in the breast milk samples from mothers exposing to Orange Agent, can be estimated to reach 75-95% of the total [21, 22]. Given that 2,3,7,8-TeCDD is viewed as one of the most toxic congeners in dioxins, during the late of 1960s and continuing to the present [23, 24], numerous toxic effects in humans have been considered in association with 2,3,7,8-TeCDD exposure. Furthermore, as shown in Table 4, the total TEQ in cotton growing districts in Kazakhstan was extremely high, and the mean concentration of 2,3,7,8-TeCDD was 46.5pg/g lipid, which accounted for 81% of the total-TEQ [27]. On the other hand, Table 4 indicates the total TEQ in the countries involved in the different group from the countries like USA, is comparatively low. This tendency is also seen in the mother's milk from Hanoi in Vet Nam where Orange Agent was never sprayed.

The total TEQ levels shown in Table 4 suggest that condition of exposure to dioxins may correspond to the industrial level in the country, though local exposure patterns are observed. Consequently, in order to know the exposure condition in more detail, it is necessary to compare the total TEQ level with the social background in the target area, while analyzing the correlation between biological modification of each isomer, and exposure sources.

IV. Summary and Conclusions

This study showed the current exposure condition of dioxins (PCDDs/PCDFs) in Toyama Prefecture in Japan, analyzing ordinary mother's breast milk, and compared the concentration level with other domestic and overseas areas. As a result, the concentration pattern of the 17 2,3,7,8-substituted isomers demonstrated the typical one of human background values of dioxins, including high concentration of 1,2,3,7,8-PeCDD.

The total TEQ levels, with comparison between Toyama Prefecture and other areas, suggest that worldwide trends of dioxin levels may correspond to the industrial level in the countries, though local exposures to dioxins are remarkably observed.

Consequently, in order to know the exposure condition in more detail, it is necessary to compare the total TEQ level with the social background in the target area, while analyzing the correlation between biological modification of each isomer, and exposure sources.

Table 3. TEQ levels in human breast milk samples from Toyama Prefecture and other areas
(pgTEQ/g lipid)

	Toyama (SD)	Fukuoka[1]	Spain[2]
TEQ-PCDDs	20.7 (9.62)	8.6	9.0
TEQ-PCDFS	6.8 (2.75)	6.8	1.2
TEQ-TOTAL	27.5 (12.09)	15.4	10.2

[1]: [17]; [2]: Calculated by the authors

Table 4. Comparison of TEQ levels for PCDDs/DFs in human breast milk samples from Toyama Prefecture with those from other areas
(pgTEQ/g lipid)

Domestic Areas[1]	Total-TEQ	Overseas Areas	Total-TEQ
Akita Pref.[2]	9.2	Siberia, Russia[4]	14.2
Miyagi Pref.	11.1	China[5]	3.0
Gunma Pref.	13.7	Hanoi, Vietnam[4]	10.8
Chiba Pref.	13.1	Aluoi Valley, Viet Nam[6]	18.7
Kanagawa Pref.	14.3	Cotton growing districts, Kazakhstan[7]	57.2
Niigata Pref.	10.4	Kyiv, Ukraine[8]	11.1
Shizuoka Pref.	12.7	Dinprozerzhinsk, Ukraine[8]	12.8
Aichi Pref.	13.4	Birmingham, UK[9]	42.4
Osaka Pref.	14.5	Germany[10]	33.7
Shimane Pref.	16.0	Uppsala, Sweden[11]	8.7
Fukuoka Pref.[3]	15.4	Rio de Janeiro, Brazil[12]	9.7
Kumamoto Pref.	11.8	Several locations, Canada[13]	23.3
Okinawa Pref.	6.4	Los Angels, USA[9]	19.3
Toyama Pref.	27.5		

[1]: [20]; [2]Pref. = Prefecture; [3]: [17]; [4]: [26]; [5]: [27]; [6]: [24]; [7]: [28]; [8]: [29]; [9]: [30]; [10]: [31]; [11]: [14]; [12]: [32]; [13]: [19]

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