ESTIMATION OF DIOXIN CONCENTRATIONS IN TISSUES IN JAPANESE BREAST-FED INFANT USING A PHYSIOLOGICAL MODEL

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Introduction

Dioxins such as polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and coplanar polychlorinated biphenyls (Co-PCBs) enter an infant's body through breast feeding, and are considered to accumulate more in infant tissue than in adult tissue. However, dioxin levels in infant tissue and its correlation to health risks are not clear. For evaluation of the possible health risks of dioxins, we estimated the concentrations of dioxins in infant tissue using a physiologically based pharmacokinetic (PBPK) model. The estimated concentrations of dioxins in infant tissue were compared to those in Japanese adult tissue. To investigate the effect of breast milk on dioxin levels in infant, the patterns of dioxin accumulation in formula-fed infant tissue were also estimated by PBPK model.

Materials and Methods

The PBPK model is composed with six compartments, which are liver, kidney, fat, blood, muscle and richly perfused tissues (brain, lung and spleen). The source of exposure to dioxins for infants was assumed to be solely through breast milk, and baby food was not considered as a source. Tissue volume and blood flow rate in each tissue and milk intake volume[1] were changed corresponding to the infant's growth. The levels of dioxin intake through the milk were calculated from data on dioxin concentration in Japanese breast milk. In addition, tissue-blood partition coefficients[2] which determine the distribution of dioxin in tissues, were calculated from data on dioxin concentration in tissue in Japanese [3,4]. For the estimation of the dioxin levels in child tissue, the levels of dioxin intake through food ingestion were calculated using data on dioxin concentration in Japanese foods[5]; the levels of dioxin intake from formula milk were calculated using data on dioxin concentration in cow's milk. Other parameters required for the model were obtained from previous reports [6, 7,8].

Table 1. Daily intake of PCDDs, PCDFs and Co-PCBs for infants and adults.

Total Daily Intake	pg TEQ /kg/day*	pg TEQ/day			
		PCDD	PCDF	Co-PCB	PCDD/F+Co-PCB
Infant**	83.9	246.5	126.0	249.2	621.6
Adult***	2.54	44.0	38.2	70.1	83.9

* Dioxin intake levels per average body weight (kg).
** Average intake level of dioxin from milk during 0 - 48 weeks.
*** Intake level of dioxin from Japanese food[4] for a man of 60 kg body weight.

Results and Discussion

The average levels of daily dioxin intake for infants and adults determined by PBPK model are shown in Table 1. The sum of daily intake of dioxins was 83.9 pg TEQ/day/kg body weight for Japanese infants, about 30 times greater than that for adults. Forty percent of the total dioxin intake was Co-PCBs. The estimated concentrations of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) in the liver, fat and blood of infant are shown in Fig.1. In most dioxin congeners, the concentrations peaked at 18-37 weeks in the liver (Fig.1a), kidney, muscle and richly perfused tissue, and peaked at about 5-6 weeks in blood (Fig.1b). However, dioxin concentrations continuously increased in fat (Fig.1c).

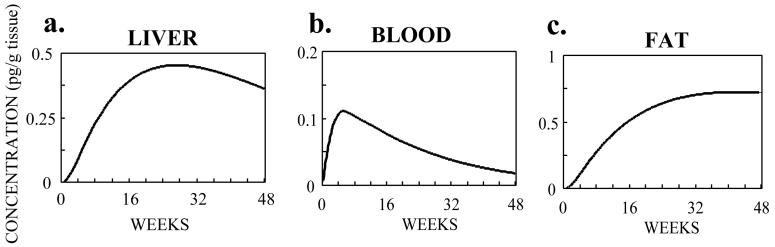

Fig.1. Concentration of 2,3,7,8-TCDD in liver, blood and fat of breast-fed infant.

The 2,3,7,8-TCDD concentration in the infant liver was compared between breast-fed and formula-fed infants (Fig.2a). The dioxin concentration in the liver decreased rapidly after breast feeding was terminated, and the concentraitons maintained a steady level due to low exposure from food. The dioxin levels in breast-fed and formula-fed infants became similar at the age of about 10 (Fig.2a). Dioxins tend to accumulate in the infant liver, since the dioxin level in the liver was more than 20 times higher than that of fat in lipid bases, while the concentrations in the liver and fat were almost the same as in adults (data not shown). The estimated dioxin level in the infant liver was within the range of measured data for the adult liver[3, 4] (0.02 to 1.1 pg/g tissue), and the maximum level was 0.45 pg/g in infant tissue, 3.5 times greater than the average concentration in adults (0.14 pg/g tissue) (Fig.2b).

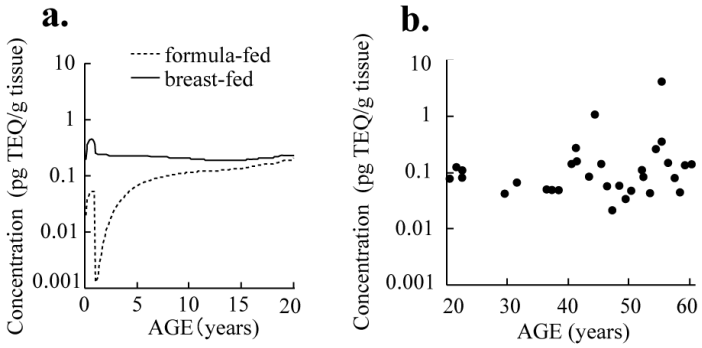

Fig.2. Concentration (pg/g tissue) of 2,3,7,8-TCDD in the child (a) and adult (b) liver.

a) Time course of concentration for 20 years after breast-feeding and formula-feeding.

b) Measured dioxin concentration in the adult liver (circle).

When the dioxin concentration in breast milk was assumed to take different values within the range of the standard deviation of the measured data, the 95 % confidence interval of the concentration in infant liver was 0.22 to 0.51 pg/g tissue at 48 weeks, and these values were still within the range of variation in measured data[3, 4]. These results suggest that the dioxin level in

breast-fed infant liver do not exceed the level in adult liver, and its toxic effect may insignificant since no obvious harmful effect is reported in this contaminated level in adult liver. These method of estimating dioxin levels in human tissue is useful when analyzing the toxicity in reports on experimental animals or in epidemiological data of humans, to assess the health risk of dioxins in environment.

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