The transfer of hydroxylated PCBs (HO-PCBs) across the human placenta and into maternal milk, and their relationship to thyroid hormones of human newborn period.

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Abstract

The purpose of this study was to determine the concentration levels of HO-PCBs in maternal blood and umbilical cord blood and breast milk, and to evaluate the transfer of these compounds across the human placenta. The total HO-PCB concentrations ranged 9.90-120pg/g wet weight (median 33.0 pg/g wet weight) in maternal blood and 8.70-93.0 pg/g（median 23.0 pg/g）in umbilical cord blood, <0.05-7.80pg/g（median 0.2pg/g）in mother breast milk. The concentration levels of HO-PCBs detected in cord blood were the same levels of maternal blood. It was found that the fetus was exposed to HO-PCBs at the same concentration level of maternal blood. These results indicated that HO-PCBs tend to transfer to fetus from mother through her placenta. Significant correlation was not found in the relation between the HO-PCBs concentration levels in the umbilical cord blood and the concentration levels of FT4 and thyroid stimulating hormone of the newborn period.

Introduction

Those persistent organic pollutants (POPs) such as PCBs and DDTs are the highly accumulated chemical substances taken into living body through the food chain and remain there over a long period of time. They are transmitted to the human fetus through the placenta and suspected of causing the endocrine confusion to the embryo as a toxicity effect. In particular PCBs are metabolized to the hydroxylated PCBs (HO-PCBs) due to the drug-metabolizing enzyme in the body. This HO-PCBs are suspected of causing the confusion of thyroid hormone effect. Since it is pointed out that the thyroid hormone is very important to develop the central nerve in the period of the pre-born child and the infant and at the same time there is concern that the HO-PCBs have a harmful effect to the development of the brain function, its toxicity effect is drawing attention in recent years.[1]
In this study we intend to carry out the maternofetal transmission of the HO-PCBs in the period of the pre-born child and the infant with its exposure assessment, to clarify the concentrations of the HO-PCBs level in the maternal blood and breast milk given by the pregnant women and that in the umbilical cord blood obtained at the delivery and then to weigh them against the PCBs. We report the relationship between the maternofetal transmission of the HO-PCBs and the thyroid hormone level during the newborn period

Materials and Methods

We obtained the maternal blood samples from 58 expectant mothers that include 19 primiparous and 39 parous women and the umbilical cord blood at the time of the birth. When we obtained their umbilical cord blood we paid attention not to contaminate it with the maternal blood collecting it in the blood sample tubes. We collected approximately 5 ml each of the blood sample and put it to every blood sample tube with heparin sodium in it to be frozen at -30℃ for preservation before the analysis. And to analyze the free thyroxine (FT4) and the thyroid-stimulating hormone (TSH) during the newborn period, we collected the blood from newborn babies on the blood collecting filter paper and after drying we put it to the freeze preservation at -30℃ before the analysis. We obtained these samples from mothers who made natural delivery at the Hannan Central Hospital in Osaka Prefecture. Before we collect the samples we obtained the approval from the Ethics Committee of the hospital and got informed consent from the mothers and their families.

Analysis operations

We made the analysis for measurement using HRGC/HRMS [6890GC(Agilent)/JMS-800D (JEOL)] following the privious report[2].

Analysis of FT4 and TSH

For FT4 and TSH analyses, we used the kits for enzyme immunoassay method (ELISA) (FT4: Enzaplate N-FT4, TSH: Enzaplate Neo TSH, both supplied by Bayer Medical K.K.) for quantification that are applied to mass screening of the newborn babies with the congenital hypothyroidism.

Results and Discussion

We show the concentrations of the HO-PCBs and ΣPCBs (4Cl – 7Cl) detected in the maternal blood, umbilical cord blood and breast milk in the Table 1 below. Six kinds of the HO-PCBs isomers for quantification are all detected in the maternal blood and umbilical cord blood. Among them, these three, 4-HO-CB107, 4-HO-CB146 and 4-HO-CB187, are the principal isomers in the maternal blood and umbilical cord blood and they are detected in the following order by concentration; 4-HO-CB187≫4-HO-CB146>4-HO-CB107. In addition the HO-PCBs concentration level in the breast milk shows less than 1/10 compared to that of the blood sample. The concentrations and residual compositions of the HO-PCBs isomers obtained in this study have a resemblance to the reports on the umbilical cord blood of mothers living in the urban district of Quebec in Canada[3]and that in Stockholm in Sweden[4]（Fig.1）.

Table1 Concentrations (median and range, pg/g wet weight) of HO-PCBs and ΣPCBs (4Cl-7Cl) detected in maternal blood, umbilical cord blood and breast milk.

	Maternal blood	**Cord blood**	**Breast milk**
4-HO-2,3,3',4',5-pentaCB (4-HO-CB107)	4.10 (0.69-27.0)	3.00 (0.92-16.0)	0.068 (<0.05-7.6)
3-HO-2,2',4,4',5,5'-hexaCB (3-HO-CB153)	3.20 (0.57-11.0)	2.40 (0.50-13.0)	<0.05 (<0.05-0.079)
4-HO-2,2',3,4',5,5'-hexaCB (4-HO-CB146)	8.60 (2.40-28.0)	5.60 (2.10-19.0)	0.061 (<0.05-0.22)
3'-HO-2,2',3,4,4',5'-hexaCB (3'-HO-CB138)	2.70 (0.32-15.0)	2.50 (0.54-21.0)	<0.05 (<0.05-0.19)
4-HO-2,2',3,4',5,5',6-heptaCB (4-HO-CB187)	13.0 (4.80-40.0)	8.00 (2.80-22.0)	0.089 (<0.05-0.54)
4'-HO-2,2',3,3',4,5,5'-heptaCB (4'-HO-CB172)	1.80 (0.54-6.10)	1.50 (0.49-6.80)	<0.05(<0.05-0.14)
ΣHO-PCBs	33.0 (9.90-120)	23.0 (8.70-93.0)	0.2 (<0.05-7.80)
ΣPCBs(4Cl-7Cl)	320 (93-1300)	64.0 (20.0-260)	1900 (450-4900)

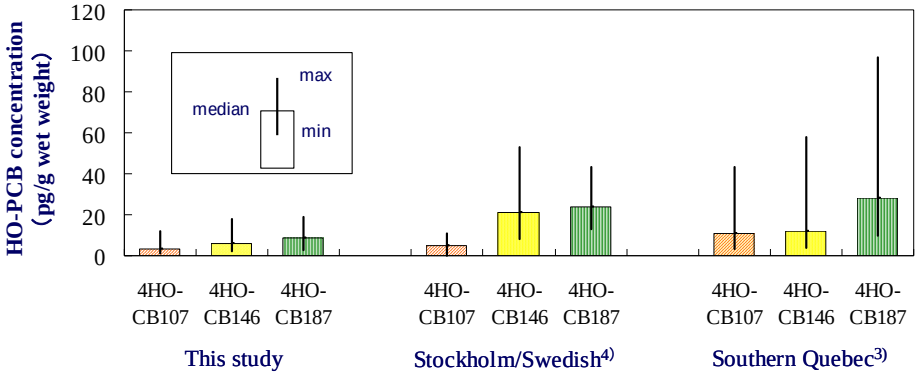

Fig. 1 Major HO-PCB isomers determined in this study and those in previous reports.

To study the PCB and HO-PCBs transmission to the pre-born child should be important to evaluate the exposure amount to the pre-born child. Therefore we reviewed the relationship between the umbilical cord blood concentration and the maternal blood concentration with regard to the PCBs and HO-PCBs（Fig.2）. As a result, we observed that there exists a positive correlation between the umbilical cord blood concentration and the maternal blood concentration for the PCBs and HO-PCBs (PCBs: r=0.87, p<0.01, HO-PCBs: r=0.84, p<0.01). The PCBs concentration (wet weight) in the umbilical cord blood show 1/5 compared to that in the maternal blood. On the other hand, the HO-PCBs concentration (wet weight) in the umbilical cord blood represents 2/3 compared to that in the maternal blood. When we compare every individual sample each other, some shows that the level of the total HO-PCBs concentrations in the umbilical cord blood and that in the maternal blood are nearly identical indicating that the pre-born child is exposed to the HO-PCBs with a similar level of the concentration to the mother during the pre-born period. Accordingly we consider that the placental barrier works to block the PCBs exposure from mother body while it does not work as barrier for the HO-PCBs that seem to readily transit from mother body to pre-born child. We therefore consider that the HO-PCBs maternofetal transmission should be more significant during the period of pre-born child in a mother body rather than intake through breast milk after birth.

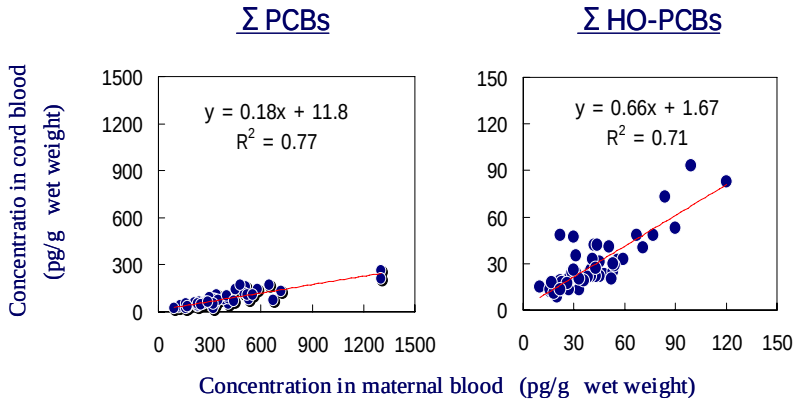

Fig. 2 Comparison of ΣHO-PCBs and ΣPCBs concentrations between in maternal blood and in cord blood.

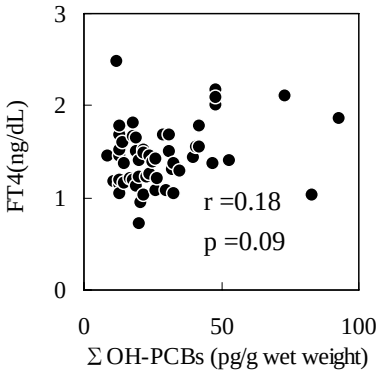

Fig.3 Relationship between FT4 and ΣHO-PCBs concentrations (Spearman's rank correlation)

We observed that the FT4 and TSH hormone level of newborn infant we analyzed remains in the normal range.

With regard to the HO-PCBs dosing experiment to rats it is reported that the T4 concentration level is lowered. As to the relationship between the PCB/HO-PCB concentration levels in the human umbilical cord blood and the FT4/TSH levels of newborn infant, we could not confirm any significant correlation exists between PCBs/HO-PCBs and FT4, and between PCBs/HO-PCBs and TSH respectively（Fig.3）. This is because, we consider, release of the thyroid hormone begins during the newborn period and it is controlled to keep the hormone level constant. The HO-PCBs are considered to affect the site where thyroid hormone works, for instance to develop the central nerve, instead of fooling the thyroid hormone level. It is not known how the HO-PCBs concentration level we cleared in this study gives such a toxicity effect to child as fooling the thyroid hormone. We need to investigate more detail of the HO-PCBs contamination level to the mothers who were heavily exposed to PCBs and to evaluate its influence to the children.

References

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