DO PCBS, OCPS, AND DIOXIN-LIKE COMPOUNDS WITH HIGH MOLECULAR WEIGHT DECREASE HUMAN MATERNAL-FETAL PLACENTAL TRANSFER RATES?

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Introduction

Although the use of polychlorinated biphenyl (PCB), organochlorine pesticides (OCPs), and dioxin-like compounds is restricted or banned in Japan, they have been detected in human fetuses and human milk (Fukata et al., 2005[1]; Mori, 2003[2]; Mimura et al., 1999[3]). Because of the highly lipophilic and stable properties of these compounds, they have a long half-life in human tissue. Moreover, because these compounds can be accumulated in human adipose tissue, the fetus might be exposed to PCBs, OCPs, and dioxin-like compounds through the blood stream. Thus, measurement of PCBs, OCPs, and dioxin-like compounds in maternal blood (MB) and umbilical cord blood (CB) provides an important means to assess fetal exposure to these chemicals. We previously reported the relationship between concentration of these compounds and the molecular weights. (Mori et al., 2014[4])

The aim of this study was to quantify the levels of PCBs, OCPs, dioxin-like compounds, and their congeners/isomers in human CB and MB. The concentrations of PCBs, OCPs, and dioxin-like compounds, normalized to wet and lipid weights, were compared in sample sets. The data were then used to determine the placental transfer rates of PCBs, OCPs, dioxin-like compounds, and their congeners/isomers and to determine whether the transfer rates correlated with the molecular weights of these compounds using generalized linear regression models (GLMs).

Materials and methods

MB and CB sample sets (n = 70) were collected at deliveries in Chiba University Hospital and various other obstetrics units in Japan. The samples were stored at -20°C until use. The study was approved by the "Congress of Medical Bioethics" of Chiba University, and all the samples were obtained after receipt of written informed consent. The concentrations of PCBs and OCPs (TriCB, TetraCB, PentaCB, HexaCB, HeptaCB, OctaCB, NonaCB, DecaCB, *p, p'*-DDE, trans-nonachlor, hexachlorocyclohexane (HCH), hexachlorobenzene (HCB), and heptachlor epoxide) were analyzed in 29 sample sets using an Agilent 6890 Plus gas chromatography (Agilent Technologies, Palo Alto, CA, USA) and an AutoSpec Ultima NT mass spectrometer (Micromass Ltd., Manchester, UK) equipped with a programmed temperature vaporization (PTV) injection system (Agilent Technologies) (Jotaki et al., 2011[5]). The analytical method used to measure dioxin-like compounds (polychorinated dibenzo-p-dioxin (PCDD), polychlorinated dibenzofuran (PCDF), and dioxin-like polychlorinated biphenyl (DL-PCB)) in 41 sample sets was described by Sakurai et al., (2004). These compounds were analyzed using high resolution gas chromatography/high resolution mass spectrometry (HRGC-HRMS). The lipid weights in MB and CB were measured using a technique previously described by Patterson et al., (1989[6]).

Statistical analysis was performed using R Ver. 3.1.0 (The R Foundation for Statistical Computing). We used GLMs to assess the association between concentrations of contaminants in MB and CB, and to determine the placental transfer rates of PCBs, OCPs, and dioxin-like compounds. We set CB as the response variable in this study. GLMs were also used to assess the association between the transfer rates of PCBs, OCPs, and dioxin-like compounds and the molecular weights of contaminants. The concentrations of PCBs, OCPs, and dioxin-like compounds were not normally distributed and the data were therefore analyzed by GLMs with a gamma distribution of the response variable and an identity-link function. This analysis included only the contaminants

that were detected in at least 80% of the samples. A *p*-value of < 0.05 was considered to be statistically significant. Results below the LOQ were given a value of 0.5 LOQ.

Results and discussion

Residue levels of PCBs, OCPs, and dioxin-like compounds in maternal and cord blood

The levels of total PCBs were significantly higher ($p < 0.05$) in MB (mean ± SD: 1134 ± 1060 pg g^{-1} wet wt.) than in CB (mean ± SD: 186 ± 142 pg g^{-1} wet wt.). The same pattern was observed for total dioxin-like compounds and OCPs (mean ± SD in MB and CB: p, p'-DDE: 466 ± 380, 242 ± 268 pg g^{-1} wet wt., trans-nonachlor: 116 ± 87, 25 ± 21 pg g^{-1} wet wt., HCH: 640 ± 943, 110 ± 139 pg g^{-1} wet wt., HCB: 157 ± 75, 40 ± 14 pg g^{-1} wet wt., heptachlor epoxide: 37 ± 24, 5.9 ± 3.1 pg g^{-1} wet wt, and total dioxin-like compounds (PCDDs + PCDFs + DL-PCBs): 66 ± 16, 13 ± 22 pg g^{-1} wet wt., respectively).

Correlation of PCBs, OCPs, and dioxin-like compounds between maternal and cord blood

Tables 1 and 2 show the slopes (placental transfer rates), standard error of the slopes and *p*-values of GLMs for the concentrations of contaminants from MB and CB. The slopes for the PCB congeners and OCPs (normalized to wet weight) were 0.121 ± 0.015 to 0.176 ± 0.019 ($p < 0.01$) and 0.118 ± 0.019 to 0.498 ± 0.050 ($p < 0.01$), respectively (Table 1). For coplanar PCBs, PCDDs, and, PCDFs, the corresponding values were 0.114 ± 0.010 to 0.167 ± 0.014 ($p < 0.01$), 0.079 ± 0.0086 to 0.182 ± 0.013 ($p < 0.01$), and, 0.130 ± 0.019 to 0.209 ± 0.024 ($p < 0.01$), respectively (Table 2). This negative correlation between the transfer rate and molecular weight was also present in the data normalized to lipid weight (Tables 1 and 2).

These results clearly indicate that the fetus was exposed to PCBs, OCPs, and dioxin-like compounds in the maternal body and the transfer rates of PCB and coplanar PCB congeners (wet weight) decreased as molecular weight increased (Tables 1 and 2).

Correlation of transfer rates and molecular weights

These results indicated that the molecular weight was significantly negatively correlated with the transfer rates of PCBs (slope and *p*-value, fat and wet wt. base: -468 ± 81, $p < 0.05$, and -2260 ± 312, $p < 0.01$) and coplanar PCBs (slope and *p*-value, fat and wet wt. base: -215 ± 39, $p < 0.01$, and -1150 ± 237, $p < 0.05$), suggesting that high molecular weight PCB congeners did not transfer easily from mother to fetus. The correlation between transfer rates and molecular weight of PCDDs was not significant (slope and *p*-value, fat and wet wt. base: -495 ± 120, $p = 0.054$, and -1160 ± 484, $p = 0.14$); however, a weak negative tendency was observed and the slope values were close to those of coplanar PCBs, indicating that PCDDs might also transfer from mother to fetus. This is similar result to that found for PBDEs in our previous study (Kawashiro et al., 2008[7]).

However, no significant associations were found between transfer rates and molecular weight in OCPs (slope and *p*-value, fat and wet wt. base: -25 ± 66, $p = 0.73$, and -70 ± 242, $p = 0.79$), and, PCDFs (slope and *p*-value, fat and wet wt. base: 325 ± 213, $p = 0.37$, and 345 ± 770, $p = 0.73$). OCPs have various chemical structures and physico-chemical qualities and therefore the association between transfer rates and molecular weight might be difficult to clarify. The lower concentrations and detection frequency of PCDFs might reflect the lack of correlation. Further studies are required to provide more accurate measurements of PCDFs.

Finally, we determined the correlation between transfer rates and the molecular weight of all compounds. The correlation between transfer rates and molecular weight of PCDDs was not significant (slope and *p*-value, fat and wet wt. base: -47 ± 27, $p = 0.098$, and -194 ± 122, $p = 0.13$); however, significantly negative associations were found when OCPs were removed from the variables (slope and *p*-value, fat and wet wt. base: -178 ± 62, $p < 0.05$, and -1310 ± 384, $p < 0.01$). Overall, the data indicated that human fetal exposure to the higher chlorinated congeners of PCBs or dioxins with larger molecular weights might be lower than the exposure to lower molecular weight molecules.

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Table 1. Coefficients of generalized linear regression of PCB and OCP levels in maternal and cord blood.*

	Lipid wt. base			Wet wt. base		
Compounds	Slope	Standard Error	*p* -value	Slope	Standard Error	*p* -value
TetraCB	0.753	0.059	5.97E-13	0.176	0.019	1.08E-09
PentaCB	0.755	0.049	5.55E-15	0.173	0.019	1.29E-09
HexaCB	0.668	0.045	2.01E-14	0.146	0.018	9.28E-09
HeptaCB	0.581	0.042	7.35E-14	0.136	0.016	4.14E-09
OctaCB	0.489	0.038	3.85E-13	0.121	0.015	9.45E-09
DDE	1.91	0.175	2.15E-11	0.498	0.050	1.39E-10
HCB	0.718	0.222	3.23E-03	0.139	0.037	8.34E-04
HCH	0.692	0.050	7.43E-14	0.177	0.017	4.84E-11
Heptachlor epoxide	0.501	0.074	2.75E-07	0.118	0.019	9.54E-07
Trans-nonachlor	0.818	0.104	1.97E-08	0.204	0.027	4.75E-08

*Levels in CB as response variable

Table 2. Coefficients of generalized linear regression of dioxin-like compounds levels in maternal and cord blood.*

	Lipid wt. base			Wet wt. base		
Compounds	Slope	Standard Error	*p* -value	Slope	Standard Error	*p* -value
CB77	0.689	0.085	7.29E-10	NA		
CB126	0.397	0.032	5.16E-15	NA		
CB169	0.311	0.023	9.28E-09	0.126	0.010	1.27E-15
CB105	0.440	0.037	3.06E-16	NA	0.038	
CB114	0.430	0.029	1.07E-14	NA		
CB118	0.450	0.040	2.00E-16	0.17	0.014	1.78E-14
CB123	0.498	0.037	6.09E-14	NA		
CB156	0.339	0.027	3.55E-16	0.136	0.011	1.62E-15
CB157	0.410	0.031	5.58E-16	NA		
CB167	0.397	0.032	2.57E-15	NA		
CB189	0.288	0.022	1.43E-15	0.114	0.010	5.59E-14
1,2,3,7,8 PeCDD	0.484	0.053	3.13E-11	0.16	0.020	4.61E-10
1,2,3,5,7,8 HxCDD	0.474	0.036	4.08E-16	0.182	0.013	2.00E-16
1,2,3,4,6,7,8 HpCDD	0.421	0.045	1.58E-11	0.147	0.014	1.21E-12
OCDD	0.228	0.029	2.01E-14	0.079	0.009	2.54E-11
2,3,4,7,8 PeCDF	0.469	0.040	3.10E-14	0.174	0.015	5.65E-14
1,2,3,6,7,8 HxCDF	0.629	0.069	2.73E-11	0.130	0.019	3.34E-08
1,2,3,4,6,7,8 HpCDF	0.611	0.093	8.93E-08	0.210	0.024	8.97E-11

*Levels in CB as response variable