THYROID HORMONE STATUS AND ITS RELATION TO DIOXINS AND PLOYCHLORINATED BIPHENYLS (PCBS) IN NEWBORNS

Shu-Li Wang[1], Yueliang L. Guo[2], Wei-Ling Chou[1], Shiang-Bin Jong[3]

[1] Division of Environmental Health and Occupational Medicine, National Health Research Institutes, 100 Shih-Chuan 1st Road, Kaohsiung 807, Taiwan. E-mail: wang21@nhri.org.tw
[2] Department of Occupational and Environmental Health, College of Medicine, National Cheng Kung University, 61 Shiao Tong Road, Tainan 704, Taiwan.
[3] Department of Nuclear Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan.

Introduction

Our previous study has established the transfer of polychlorinated dibenzo-p-dioxins, dibenzofurans and biphenyls (PCDD/DF &PCB) from mothers to their infants through placenta[1]. It is likely that the PCDD/DFs and PCBs from mothers may sustain for more than several years in the newborns. Animal studies have shown that dioxins and PCBs may have effects on thyroid hormone secretion, transport and/or actions[2]. The effects of modified thyroid hormone status may be substantial to the growth and development since the hormones are crucial during the brain maturation stage in humans[3]. Previous studies showed such endocrine disruptors through placenta might affect on the cognitive and related developments [4,5]. However the mechanism awaits further investigations[6]. The aim is to examine the association between transplacental exposure to dioxins/PCBs and thyroid hormone status in newborns.

Methods and materials

This is part of an on going study of dioxins/PCBs survey for the central population in central Taiwan. A total number of 430 subjects were interviewed at obstetric clinic, with personal data collected including reproductive and medical histories, and physical factors. Placenta and umbilical cord serum were gathered upon delivery. The newborns were carefully scored including structural and functional assessments.

A total number of 118 newborns were presented with complete data including dioxins/PCBs levels in the placenta and thyroid hormone status in the cord serum. A total number of 17 PCDD/F and 12 dioxin-like PCB congeners with World Health Organization (WHO) defined Toxic Equivalent Factors (TEF) and 6 indicator PCBs were measured by High Resolution Gas Chromatography / High Resolution Mass Spectrometry. The analytical methods used were validated at international quality control studies[7]. Thyroid and related growth hormones were measured using Radio-Immuno-Assay (RIA) methods, including Triiodothyronine (T_3), Thyroxine (T_4), Thyroid Stimulating Hormone (TSH- thyrotropin), Free T_4, T_3 uptake, thyrotropin receptor (TSHr), Thyroid Biding Globulin (TBG), Insulin-like Growth Factor-1 (IGF-1) and IGF Binding Globulin-3 (BP3). Blind duplicates were carried out for every 10 samples.

Mann-Whitney test was utilized for test of the difference in hormone levels between high and low exposure groups. Spearman correlation analyses were utilized to primarily evaluate the association between PCDD/F and PCB levels and the hormone levels. General Linear Model was utilized to examine the relation of the hormone log values to the dioxin/PCBs exposure. All statistical

analyses were carried out using Statistical Package for Social Science (SPSS 10.0).

Results and discussion

The babies were generally healthy with the mean fifth Apgar score of 10 (SD=0.9) from mothers with mean age of 29 years (Table 1). Female babies were bigger in size than males. Higher dioxin/PCB exposure group had greater mother's age and baby length. The length relation might be confounded by parity because the relation was gone in multivariate analysis. IGF-1 and BP3 levels were highly significantly associated with placenta weight, baby birth weight, head girth and Quetelet (Table 2). Gestational age was positively associated with the levels of T_3 and T_4/TBG, and negatively associated with T_3 uptake and TBG. There was no significant difference in the various thyroid hormones between upper and lower 50% exposure groups (Table 3). Total mono-ortho PCB and total PCB 138, 153 & 180 both showed significant and positive association with T_4/TBG levels (Table 4). We further found significantly increasing trend of T_3, T_4 and T_4/TBG with the increasing levels of mono-ortho-PCBs (Figure 1). We have inconsistent results from the previous study using milk levels in relation to thyroid hormone status in which no significant relations were found using the cord hormones[6]. Human milk levels of dioxins/PCBs decreased substantially with the duration of breastfeeding. Placenta analyses provided good indicators of in-utero exposure for newborns[1]. The percentage of all the congener-specific analyses for PCDD/DFs and PCBs over the detection limit is 90 % for placenta compare to 43% for the cord serum. In-utero exposure has been emphasized particularly for nuro-cognitive deficit[5]. Thus current finding are worth of noting. Dioxins/PCBs might affect on the binding of carrier protein to certain thyroid hormone. There might be different pathway between dioxins and mono-ortho-PCB/indicator PCBs in human neonates.

Table 1. General characteristics and birth outcomes by gender and dioxins/PCBs level in the pregnant women and their newborns

Mean (S.D.)	Gender (n)			Dioxin/PCBs TEq (ng/g lipid)[a]			Total
Factor (unit)	Female (61)	Male (57)	p[b]	Low (<15.08) n=59	High (≧15.08) n=59	p[b]	
Mother's age (yrs)	29.83 (4.72[b])	28.65 (4.11)	0.12	27.34 (4.06)	31.14 (4.04)	0.00	29.26(4.46)
Placenta weight (g)	**569.8 (149.8)**	**571.7 (138.6)**	**1.00**	**575.7 (165.5)**	**565.1 (119.6)**	**0.78**	**570.8(143.8)**
Placenta fat content (%)	0.75 (0.11)	0.75 (0.12)	0.90	0.75 (0.11)	0.75 (0.11)	0.95	0.75(0.11)
Gestational age (weeks)	38.63(1.85)	39.15 (1.42)	0.03	39.03 (1.83)	38.72 (1.49)	0.31	38.88(1.67)
Baby birth weight (g)	3027 (444)	3181 (416)	0.05	3029 (449)	3174(414.2)	0.07	3101(436)
Baby birth length (cm)	51.10 (2.31)	51.66 (2.46)	0.21	50.89 (2.37)	51.85 (2.34)	0.05	51.37(2.39)
Quetelet index (kg/m^2)	11.64 (1.27)	11.90 (1.18)	0.18	11.74 (1.22)	11.79 (1.25)	0.69	11.77(1.23)
Baby head girth (cm)	33.25 (1.37)	33.69 (1.21)	0.06	33.37 (1.40)	33.56 (1.21)	0.71	33.47(1.31)
Baby chest girth (cm)	32.73 (1.76)	32.94 (1.73)	0.42	32.76 (1.69)	32.91 (1.80)	0.63	32.83(1.74)
1st minute Apgar Score	8.60 (1.29)	8.32 (0.76)	0.26	8.57 (1.34)	8.36 (0.71)	0.44	8.46(1.07)
5th minute Apgar score	9.92 (1.14)	9.68 (0.47)	0.18	9.91 (1.16)	9.69 (0.46)	0.26	9.80(0.88)
Baby bilirubin (mg/dl)	8.89 (2.68)	7.93 (2.32)	0.04	8.76 (2.72)	8.07 (2.32)	0.14	8.40(2.54)

[a]: The 17 PDD/DF and 12 dioxins-like PCB congeners were measure in the placenta

[b]: Mann-Whitney test

[c]: Standard deviations were shown in parentheses

Table 2. Spearman Correlation between thyroid hormone concentrations and birth related indices

Variable	Placenta weight (g)	**Gestational age (weeks)**	Baby birth weight (g)	Baby head girth (cm)	Quetelet index (kg/m^2)	5^{th} minute Apgar score
T_3 (ng/dL)	-0.133	0.238*	0.066	0.037	0.103	-0.022
T_4 (ug/dL)	0.015	0.163	-0.032	-0.074	0.121	0.037
TSH (uU/ml)	0.283**	0.185	0.138	0.022	0.185*	0.119
T_3 uptake (%)	0.175	-0.267**	0.023	0.090	-0.077	-0.054
TBG (ng/mL)	0.234*	-0.210*	0.048	0.054	0.089	-0.201*
IGF-1 (ng/mL)	0.305**	-0.166	0.359***	0.350***	0.279**	-0.053
BP3 (ng/mL)	0.263**	0.017	0.274**	0.342***	0.247**	0.001
FT_4/T_4 ratio	0.074	-0.179#	0.042	0.019	0.045	0.043
T_4/TBG ratio	-0.178	0.266**	-0.041	-0.083	-0.005	0.187*

Spearman correlation: *** P<0.001,** p<0.01, * p<0.05, # p<0.1

Table 3. Serum cord thyroid hormone levels in high and low dioxin/PCBs exposure groups

	Dioxin/PCBs Teq			Total
Factor	Low (<15.08)	High (≧15.08)	p[a]	
T_3 (ng/dL)	55.95 (17.9)	58.67 (17.1)	0.29	57.32 (17.4)
T_4 (ug/dL)	8.49 (2.00)	9.01 (1.57)	0.13	8.75 (1.81)
TSH (uU/ml)	8.93 (6.37)	7.10 (5.42)	0.06	7.98 (5.94)
T_3 uptake (%)	29.51 (4.77)	28.45 (3.84)	0.29	28.98 (4.34)
Free T_4 (ng/dL)	0.83 (0.22)	0.81 (0.20)	0.45	0.82 (0.21)
T_4/Free-T_4 ratio	10.93 (3.61)	11.87 (4.78)	0.22	11.42 (4.27)
hGH (ng/mL)	26.92 (17.6)	22.07 (12.6)	0.25	24.41 (15.3)
TBG (ng/mL)	78.47 (36.9)	86.32 (77.0)	0.68	82.43 (60.4)
TSHr (U/L)	2.53 (4.61)	3.31 (8.18)	0.40	2.93 (6.66)
IGF-1 (ng/mL)	82.72 (37.7)	91.31 (37.5)	0.28	87.09 (37.7)
BP3 (ng/mL)	1.35 (0.69)	1.50 (0.87)	0.67	1.43 (0.78)

[a]: Mann-Whitney test

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Table 4. Correlation between PCDD/F & PCB levels and thyroid hormone concentrations

Hormone	PCDD/ PCDF	Total non-ortho PCB	**Total mono-ortho PCB**	PCB #138, #153, #180	2.3.7.8-Tetra -CDD
T_3 (ng/dL)	0.149	0.116	0.167#	0.062	0.099
T_4 (ug/dL)	0.180#	0.013	0.167#	0.215*	0.160#
TSH (uU/ml)	-0.186*	-0.194*	-0.232*	-0.098	-0.224
T_3 uptake (%)	-0.129	0.044	-0.092	-0.044	-0.122
Free T_4 (ng/dL)	-0.051	-0.105	-0.041	0.155#	-0.053
TBG (ng/mL)	-0.067	0.021	-0.174#	-0.123	-0.066
IGF-I (ng/mL)	0.084	-0.100	-0.053	-0.053	0.009
BP3 (ng/mL)	0.092	-0.115	-0.113	-0.156#	0.016
TSHr (U/L)	0.078	-0.111	-0.028	-0.104	0.105
hGH (ng/mL)	-0.168#	0.048#	-0.132	-0.100	-0.144
T_4/FT_4 ratio	0.116	0.174#	0.147	0.025	0.103
T_4/TBG ratio	0.157	-0.003	0.216*	0.189*	0.140
FT_4/TBG ratio	0.044	-0.072	0.162#	0.184*	0.031
FT_4*TSH	-0.146	-0.245**	-0.159#	0.009	-0.195*

***P<0.001,**p<0.01, *p<0.05, #p<0.1

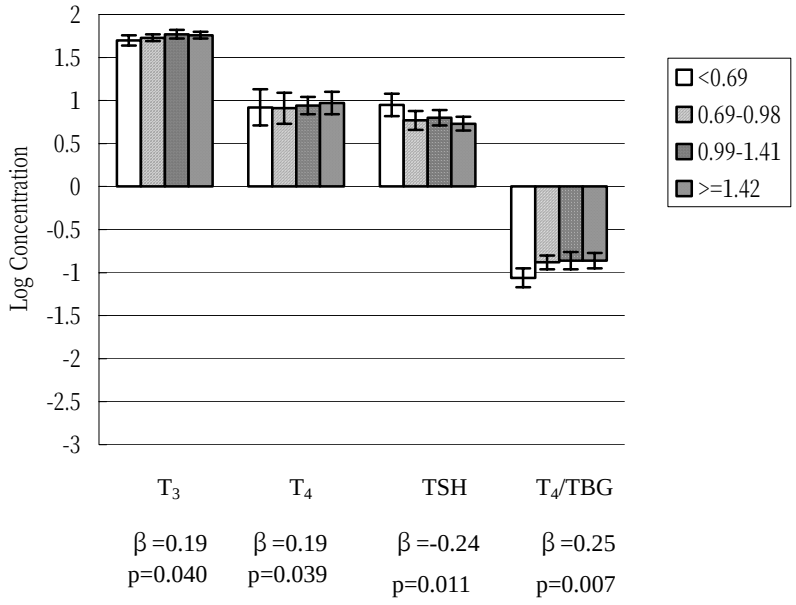

Figure 1. Log concentrations of the T_3, TSH, T_4/TBG and Free T_4/TBG in cord serum according to quartiles of mono-ortho-PCBs (ng TEq/g lipid) in placenta

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