ASSOCIATION BETWEEN BIRTH OUTCOME AND POLYBROMINATED DIPHENYL ETHER LEVELS IN BREAST MILK FROM CENTRAL TAIWAN

[1] How-Ran Chao, [2] Shu-Li Wang, and [3] Olaf Päpke

[1]Department of Environmental Science and Engineering, National Pingtung University of Science and Technology, Neipu, Pingtung, Taiwan
[2]Division of Environmental Health and Occupational Medicine, National Health Research Institutes, Zhunan, Maoli, Taiwan
[3] ERGO Research Laboratory, Hamburg 22305, Germany.

Introduction

Polybrominated diphenyl ethers (PBDEs) are lipophilic and toxic pollutants with high persistence to biodegradation in the environment.[1] From the previous studies, [2,3] body burden of dioxins, polychlorinated biphenyls, and organochlorine pesticides are obviously decreased in the reports from several developed countries during these two decades. In contrast, PBDE levels in human specimens show significant correlations with the time of sample collection. [3]

The congeners of PBDEs are widespread in the global environment from the manufacture or disposal. [4] PBDEs have been found in dust, [5] fish, [6] vegetable, [7] aquatic mammals, [8] territorial mammals on land including humans. [9] Few reports in Taiwan are focused on PBDE levels in the environment or in the biota. The levels of PBDEs in the ambient air collected near the metal recycling plants were ranged from 23 to 53 pg/m^3 in Taiwan in 1992. [10] The PBDE congeners were found in the air, soil, sediment, and fish samples in Taiwan. [11] To my knowledge, the data in human exposure to PBDEs are limited in Taiwan until now. Taiwanese Environmental Protection Administration (EPA) has legislated to ban the use of PCBs and OCPs and to meet the strict standards of dioxins emission, but the use of PBDEs is not restricted in Taiwan.

Little is known about the human adverse health effects of PBDEs even though they have been widely used for two decades. PBDEs and PCBs may induce similar carcinogenic, neurotoxic, reproductive, and immunotoxic effects due to the similarity of chemical structure and lipophilic properties. Several evidences have shown hepatotoxicity, embryotoxicity, thyroid, and behavioral effects in animal studies. [12,13]

Breast milk is one of the best human specimens for biomonitoring of PBDEs because they can reflect the maternal body burden and infant with postnanal exposure. Very little has been reported in the in-vivo PBDEs effects for female reproduction and birth outcome and most of these published papers mainly deal with effects on thyroid hormone homeostasis and neurodevelopments. In the present study, the measurements of PBDEs in breast milk from central Taiwan were compared to those from other countries. We also found the association between PBDE levels and infant birth outcome (i.e. birth weight) or maternal menstruation effects (i.e. menstrual cycle length).

Methods and Materials

The study participants were selected from the cohort of the dioxin survey described previously.[14] Subjects were healthy pregnant women recruited from a medical center in the suburban area of Taichung located in central Taiwan during December 2000 and November 2001. The participants answered a detailed questionnaire, including age, height, weight, parity, health, dietary habit and socioeconomic data in table 1. Breast milk was collected approximately two weeks after the delivery and milk samples were stored at –20^{o}C refrigerator. The milk samples of 25 ml were shipped frozen to ERGO laboratory in Germany for chemical analysis. Chemical analysis for PBDEs in breast milk was described in detail previously.[15,16] The extract was identified and quantified by high-resolution gas chromatograph equipped with high-resolution mass spectrometry (HRGC/HRMS: HP GC5890 II / VG-AutoSpec) using a DB-5 column (J&W Scientific) for gas chromatographic separation. Typical HRGC and HRMS conditions had been published previously.[16] The

congeners of 12 PBDEs (IUPAC 17, 28, 47, 66, 85, 99, 100, 138, 153, 154, 183, 209) were measured to determine the levels in human milk and the correlated factors.

The limits of detection (LODs) of PBDEs were performed from 0.01 to 0.4 ng/ g lipid. Recovery measured for the internal standards added normally range from 60 to 120%. The blank tests of solvents and glassware were regularly checked. The original concentrations were corrected by the recovery rates of the internal standards. For quality control, a set of standard, blank, and pooled breast milk samples were inserted each batch of approximately 10 samples. Measurements below LODs were recorded as half-LOD values in the present study. The PBDE daily intake was calculated for a breastfed newborn after delivery based on birth weight, PBDE concentrations and lipid content in breast milk, and the consumption of 500 g milk per day. We assumed that the PBDEs absorption rate in the intestinal tract was the same as dioxins absorption rate of 0.95.[17]. Spearmen's rank correlation coefficients were initially used to find the correlations between individual PBDEs and maternal and infant demographic parameters or the associated factors. The measurements of PBDEs were log-transformed to fulfill the normal distribution by the Kolmogorov-Smirnov method for further parametric analyses. When two groups (i.e. birth weight) were compared, Student *t*-tests were used. Multiple linear regressions were used to evaluate differences in two groups (i.e. birth weight) after maternal age, maternal pre-pregnant BMI, and parity were adjusted. Analyses were carried out using the Statistical Package for Social Science (SPSS) 13.0 version.

Results and Discussion

The distribution of PBDE congeners was presented in Fig. 1. The mean and median of total PBDEs was 3.93 (SD= 1.74) and 3.65 ng/g lipid, respectively. The predominate PBDE congeners of BDE-47 and BDE-153 were 61.0% consisting of total PBDEs. Most measurements of BDE-17, BDE-138, and BDE-183 were below LODs. The estimated daily intake of PBDEs for a breastfed newborn after delivery was 20.6 ng/kg (body weight: b.w.)/day. Concentrations of 12 PBDE congeners were not correlated with maternal age (r= -0.099~0.289, p>0.05) and pre-pregnant BMI (r= -0.010~-0.347, p>0.05). No significant difference in PBDE concentrations between primiparous and multiparous breast milk from our population.

Elevated PBDE levels in breast milk were correlated with lower birth weight and length, head and chest circumference, and Quetelet's index in Table 1. Mothers nursing their newborns with lower Quetelet's index (≤ 11.8 kg/m^2 ; geometric mean (GM) PBDEs = 5.27 ng/g lipid) had the significantly higher PBDE concentrations in their beast milk than those with higher Quetelet's index (> 11.8 kg/m^2 ; GM PBDEs= 2.94 ng/g lipid) after maternal age and pre-pregnant BMI and parity were adjusted (p= 0.015). We found that higher PBDE levels (GM= 5.03 ng/g lipid) in breast milk from mothers with newborns' breast circumference ≤ 32.5 cm were compared to lower PBDE levels (GM= 3.02 ng/g lipid) from mothers with newborns' breast circumference > 32.5 cm (p= 0.004) after maternal age and pre-pregnant BMI and parity were adjusted.

Table 2 shows that women with menstrual cycle length lower than 30 days (GM= 4.59 ng/g lipid) had significantly higher concentrations of PBDEs compared to those higher than 30 days (GM= 3.08 ng/g lipid, p= 0.028). Levels of BDE-99 and BDE-209 in breast milk were negatively associated with the prolonged the longest length of menstrual cycle (p= 0.025) and duration of menstrual bleeding per cycle (p= 0.048), respectively. After adjusting for maternal age and pre-pregnant BMI and parity, no significant differences in total PBDEs or individual PBDE congeners were found between three pairs of two reproductive groups.

Very few long-term monitoring of PBDEs in the environment and biota is performed in Taiwan. Taiwanese researchers and government is still to pay greatly attention to dioxins exposure. Levels of PBDEs in the environment and human bodies in Taiwan are comparable to those in the neighbouring country of China, which has begun to environmentally and biologically monitor PBDEs. The environmental and healthy assessment of PBDEs for the long-term monitoring is essential Taiwan due to the adverse health effects on thyroid hormone and neurobehavior particularly for the infants. Our future studies will continuously investigate PBDE levels in human specimens and further assess the infant neurodevelopment related to PBDEs exposure.

Acknowledgements

This study was supported by a grant (NSC93-2320-B-273-003) from National Science Council, Taiwan. The

authors are indebted to the research teams in National Health research Institutes and Department of Safety Health and Environmental Engineering of Chung Hwa College of Medical Science and Technology in Taiwan. The authors also acknowledge ERGO Forschungsgesellschaft mbH in Germany for their assistance for PBDEs analysis.

References

1. Legler J and Brouwer A. (2003) Environ Int 29, 879.
2. Päpke O. (1998) Environ Health Perspect 106 (Suppl 2), 723.
3. Norén K and Meironyté D. (2000) Chemosphere 40, 1111.
4. de Wit CA. (2002) Chemosphere 46, 583.
5. Wilford BH, Shoeib M, Harner T, Zhu J, Jones KC. (2005) Environ Sci Technol 39, 7027.
6. Christensen JH, Glasius M, Pecseli M, Platz J, Pritzl G. (2002) Chemosphere 47, 631.
7. Ohta S, Ishizaka D, Nishimura H, Nakao T, Aozasa O, Shimidzu Y, Ochiai F, Kida T, Nishi M, Miyata H. (2002) Chemophere 46, 689.
8. de Boer J, Wester PG, Klamer HJC, Lewis WE, Boon JP. (1998) Nature 394, 28.
9. Mazdai A, Dodder NG, Abernathy MP, Hites RA, Bigsby RM. (2003) Environ Health Perspect 111, 1249.
10. Watanabe I., Kawano M, Wang Y, Chen Y, Tatsukawa R. (1992) Organohalogen Comp 9, 309.
11. Peng Z.-H. Master Thesis, Department of Chemistry, Chung Yuan University, Chungli, Taiwan, 2002.
12. International Program on Chemical Safety, Environ Health Criteria 162. Geneva: World Health Organization, 1994.
13. Zhou T, Ross DG, DeVito MJ, Crofton KM. (2001) Toxicol Sci 61, 76.
14. Chao HR, Wang SL, Lee CC, Yu HY, Lu YK, Päpke O. (2004) Food Chemical Toxicol 42, 1299.
15. Schecter A, Pavuk M, Päpke O, Ryan JJ, Birnbaum L, Rosen R. (2003) Environ Health Perspect 111, 1723.
16. Päpe O, Fürst P, Herrmann T. (2004) Talanta 63, 1203.
17. Dahl P, Lindström G, Wiberg K, Pappe C. (1995) Chemosphere 30, 2297.

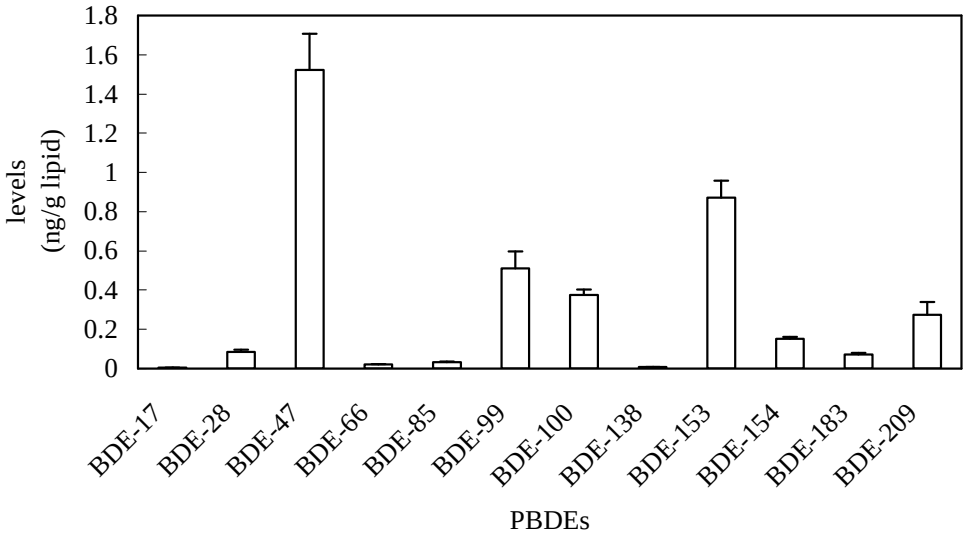

Figure 1. The distributed congeners of PBDEs in human milk were from central Taiwan. The data were presented as mean ± standard error (SE).

Table 1. The relation of PBDE levels in breast milk and birth outcome of their offspring from central Taiwan (n=20)

	BDE-47	BDE-85	BDE-99	BDE-100	BDE-153	BDE-209
Birth weight						
≤3.05 kg (n=7)	2.15 (1.57-2.95)[a]	0.034 (0.017-0.069)	0.727 (0.419-1.26)	0.451 (0.347-0.586)	0.948 (0.704-1.28)	0.346 (0.128-0.936)
>3.05 kg (n=13)	1.05 (0.837-1.32)	0.019 (0.012-0.032)	0.296 (0.211-0.422)	0.318 (0.283-0.357)	0.717 (0.527-0.976)	0.105 (0.062-0.178)
p value	0.001^{**b} (0.001^{**c})	0.151 (0.067)	0.004** (0.001**)	0.004** (0.007**)	0.207 (0.181)	0.015* (0.004**)
Birth length						
≤50.0 cm (n=8)	1.67 (0.988-2.81)	0.033 (0.021-0.051)	0.629 (0.383-1.03)	0.432 (0.330-0.563)	0.940 (0.696-1.27)	0.306 (0.137-0.683)
> 50.0 cm (n=12)	1.18 (0.935-1.48)	0.019 (0.016-0.035)	0.303 (0.200-0.459)	0.318 (0.285-0.355)	0.705 (0.512-0.971)	0.103 (0.056-0.192)
p value	0.130 (0.148)	0.162 (0.198)	0.021* (0.040*)	0.012* (0.025*)	0.182 (0.276)	0.024* (0.033*)
Head circumference						
< 33.0 cm (n=7)	1.68 (1.11-2.52)	0.025 (0.013-0.048)	0.454 (0.269-0.768)	0.391 (0.311-0.492)	0.838 (0.577-1.33)	0.185 (0.058-0.592)
≥ 33.0 cm (n=13)	1.20 (0.886-1.63)	0.023 (0.013-0.040)	0.382 (0.235-0.618)	0.343 (0.287-0.410)	0.766 (0.580-1.01)	0.147 (0.079-0.275)
p value	0.163 (0.274)	0.791 (0.576)	0.616 (0.521)	0.334 (0.433)	0.690 (0.697)	0.671 (0.401)
Breast circumference						
≤ 32.5 cm (n=7)	1.95 (1.37-2.76)	0.032 (0.015-0.068)	0.686 (0.371-1.27)	0.455 (0.351-0.590)	0.901 (0.658-1.23)	0.343 (0.126-0.933)
> 32.5 cm (n=13)	1.11 (0.845-1.46)	0.020 (0.012-0.033)	0.306 (0.215-0.435)	0.316 (0.283-0.354)	0.737 (0.539-1.01)	0.105 (0.062-0.179)
p value	0.012* (0.015*)	0.241 (0.126)	0.011* (0.05*)	0.002** (0.003**)	0.369 (0.266)	0.016* (0.003**)
Quetelet's index						
≤ 11.8 kg/m^2 (n=10)	1.75 (1.30-2.37)	0.033 (0.021-0.054)	0.605 (0.387-0.948)	0.416 (0.336-0.514)	0.894 (0.622-1.28)	0.259 (0.126-0.532)
> 11.8 kg/m^2 (n=10)	1.04 (0.756-1.44)	0.017 (0.009-0.031)	0.272 (0.180-0.410)	0.311 (0.274-0.351)	0.700 (0.522-0.937)	0.098 (0.049-0.198)
p value	0.015* (0.024*)	0.060 (0.043*)	0.008* (0.009*)	0.015* (0.031*)	0.249 (0.307)	0.043* (0.019*)

[a] Geometric mean (95% of confidence intervals)
[b] *p* value in Student-*t* test
[c] *p* value in a multiple regression test after maternal age, maternal pre-pregnant BMI, and parity were adjusted
$^{*}p<0.05$, $^{**}p<0.005$, $^{***}p<0.001$

Table 2. PBDE levels in breast milk associated with reproductive effects in Taiwanese general population

	BDE-47	BDE-99	BDE-100	BDE-153	BDE-209
Menstrual cycle length					
< 30 days (n=10)	1.58 (1.11-2.25)[a]	0.572 (0.373-0.878)	0.419 (0.334-0.526)	1.06 (0.825-1.36)	0.293 (0.129-0.662)
≥ 30 days (n=10)	1.26 (0.886-1.80)	0.302 (0.175-0.524)	0.322 (0.279-0.372)	0.642 (0.468-0.882)	0.104 (0.056-0.195)
p value	0.322[b] (0.586[c])	0.056 (0.104)	0.035* (0.072)	0.013* (0.064)	0.032* (0.073)
The longest length of menstrual cycle					
< 38 days (n=11)	1.51 (1.11-2.04)	0.559 (0.383-0.817)	0.382 (0.316-0.461)	0.912 (0.658-1.26)	0.212 (0.091-0.494)
≥ 38 days (n=9)	1.27 (0.821-1.99)	0.267 (0.142-0.500)	0.342 (0.270-0.433)	0.696 (0.500-0.968)	0.124 (0.066-0.234)
p value	0.483 (0.449)	0.025* (0.056)	0.411 (0.466)	0.213 (0.333)	0.303 (0.506)
Duration of menstrual bleeding per cycle					
< 5 days (n=3)	1.09 (0.326-2.35)	0.54 (0.44-0.64)	0.392 (0.036-3.54)	1.25 (0.751-2.08)	0.663 (0.231-1.90)
≥ 5 days (n=17)	1.38 (1.08-1.78)	0.393 (0.271-0.570)	0.354 (0.311-0.415)	0.752 (0.597-0.946)	0.136 (0.081-0.227)
p value	0.532 (0.537)	0.565 (0.664)	0.998 (0.995)	0.146 (0.176)	0.048* (0.091)

[a] Geometric mean (95% of confidence intervals)
[b] *p* value in Student-*t* test
[c] *p* value in a multiple regression test after maternal age, maternal pre-pregnant BMI, and parity were adjusted
$^{*}p<0.05$, $^{**}p<0.005$, $^{***}p<0.001$