DIOXIN IN BREAST MILK OF VIETNAMESE MOTHERS AND STEROID HORMONE IN SALIVA OF THEIR INFANTS

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Introduction

Dioxin is known as risk factor of various kinds of adverse health effects including cancer, diabetes mellitus and cardiovascular disease. Hormone levels are also known to be altered by low-dose exposure to TCDD, and foetal death can occur after high-dose exposure. Likewise, animal studies have established an association between maternal TCDD exposure and immune deficiencies, decreased estradiol and progesterone levels and altered serum testosterone levels. A related study has shown that exposure of rodents and other species to TCDD leads to changes in steroid hormone levels¹. A recent study showed that biosynthesis of androgens, cortisol, and aldosterone is altered by dioxin-like PCB126 in human adrenocortical H295R cells². There is a great deal of concern regarding the adverse effects of polychlorinated dibenzodioxins (PCDD) and polychlorinated dibenzofurans (PCDF) present in Agent Orange and other herbicides on Vietnam's population and ecosystems³⁻⁶. We have already shown that found the inverted U-shaped relationship between dioxins in breast milk and salivary cortisol or cortisone and also the U-shaped relationship between dioxins in breast milk and salivary estradiol of Vietnamese primiparae in a hot spot and a non-exposed area^{7, 8}. However, it is not clarified if dioxin induces adverse effects on steroid hormone levels of Vietnamese infants. Therefore, the purpose of this study was to determine the adverse health effect of dioxin exposure on steroid hormone of Vietnamese infants.

Materials and methods

This study was carried out in Phu Cat district, Binh Dinh province and Kim Bang district, Nam province in Vietnam. Phu Cat airbase is one of three main dioxin hot spots in Vietnam and is located in southern Vietnam. Kim Bang district is located in northern Vietnam and did not experience herbicide operations during the war, and was

chosen as the control site. Breast milk samples were obtained from lactating females aged between 20 and 30 years from both districts in September 2008. One hundred and twenty three lactating females (60 from Phu Cat district and 63 from Kim Bang district) participated, who had recently given birth to their first or second child. All lactating females consented to donate milk samples (10-20 mL) and were breast-feeding infants aged from 4 to 16 weeks. In August 2011, about 0.25.0.8 ml of saliva samples of their infants who grew up about 3 years old were collected in the morning (between 8:00 and 10:00 AM) by using hormone free cotton. One hundred and eleven infants (52 from Phu Cat district and 59 from Kim Bang district) participated. All samples were stored at –70 °C until analysis. Breast milk samples were analyzed following previously reported procedures⁹. Cortisone, cortisol and dehydroepiandrosterone (DHEA) were analyzed as salivary steroid hormone of infants. The medical ethics committee of Kanazawa University approved this study (Permission No; Health-89), and informed consent was obtained from each participant. All statistical analyses were performed using the JMP[®]9 software package (SAS Institute, Japan).

Results and discussion

Comparison of salivary steroid hormone of 3 year infants in hot spot and non-exposed area divided by sex was shown in Table 1 and 2. Salivary DHEA of both sexes was significantly lower in hot spot than non-exposed area. Relation between dioxin in breast milk and each steroid hormone in saliva divided by sex was shown in figure. Significant negative correlation between dioxin and DHEA was shown in both sexes after removing of one or two distant values although no significant relationship was found between dioxin and cortisone or cortisol. The majority of data from epidemiological studies pertaining to effects of TCDD on the human male reproductive system have been collected from cohort exposed as adults¹⁰. This is the first report to find out that dioxin induces the inhibition of DHEA synthesis in infants. It is necessary to observe these infants consecutively and also increase the number of infants.

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References:

1. Peterson RE, Theobald HM, Kimmel GL. (1993); Cri Rev Toxicol. 23(3): 283-335

2. Li, LA, Wang PW. (2005) Toxicol Sci. 84: 1-11

3. Dwernychuk LW, Cau HD, Hatfield CT, Boivin TG, Hung TM, Dung PT, Thai N. (2002) *Chemosphere*. 47(2): 117-37

4. Schecter A, Quynh T, Päpke O, Tung KC, Constable JD. (2006) J Occup Environ Med. 48(4): 408-13

5. Mai TA, Doan TV, Tarradellas J, de Alencastro LF, Grandjean D. (2007) Chemosphere. 67(9): 1802-7

6. Kido T, Maruzeni S, Suzuki H, Odamae Y, Muranaka M, Naganuma R, Tawara K, Nishijo M, Nakagawa H, Hung TM, Thom LTH, Dung PT, Nhu DD, Oka H, Noguchi K. (2008) *Persistent Organic Pollutants (POPs) Research in Asia*. 444-50

7. Nhu DD, Kido T, Naganuma R, Suzuki H, Kuroda N, Honma S, Tai PT, Maruzeni S, Nishijo M, Nakagawa H, Hung NN, Son LK. (2010) *Toxicol Environ Chem*.92(10): 1939–52

8. Nhu DD, Kido T, Hung NN, Thom LTH, Naganuma R, Son LK, Honma S, Maruzeni S, Nishijo M, Nakagawa H. (2011) *Toxicol Environ Chem*.93(4): 824–38

9. Tawara K, Nishijo M, Maruzeni S, Nakagawa H, Kido T, Naganuma R, Suzuki H, Nhu DD, Hung NN, Thom LTH. (2011) *Chemosphere*. 84: 979–86

10. Schecter A, Gasiewicz TA. (2003) Dioxins and Health 2nd Eds. Wiley-Interscience. 391-9

Table 1 Comparison of salivary steroid hormone of 3 year male infants between hot spot and non-exposed area

		Male			
		Hot spot	-	Non-exposed	-
Indicators	n	Median (inter-quartile range)	n	Median (inter-quartile range)	p Value
Cortisone (ng/mL)	29	3.32 (1.83-5.17)	27	2.88 (2.02-4.36)	0.48 1)
Cortisol (ng/mL)	29	0.49 (0.22-0.86)	27	0.37 (0.2-0.58)	0.25 1)
DHEA (pg/mL)	29	39 (30-60)	27	69 (34-102)	0.02 2)*

Table 2 Comparison of salivary steroid hormone of 3 year female infants between hot spot and non-exposed area

	Female						
		Hot spot	Non-exposed		_		
Indicators	n	Median (inter-quartile range)	n	Median (inter-quartile range)	p Value		
Cortisone (ng/mL)	23	2.74 (1.32-6.0)	32	3.14 (2.04-3.83)	0.7 1)		
Cortisol (ng/mL)	23	0.39 (0.21-0.98)	32	0.39 (0.25-0.66)	0.85 1)		
DHEA (pg/mL)	23	32 (25-55)	32	77 (54-118)	< 0.001		

Note: Hormone levels were transformed into log10 to improve normality first. After checking normal distribution by good-of-fitness, only DHEA have normal distribution in both areas. ¹⁾ Wilcoxon rank sum test, ²⁾ t-test

Figure Association of dioxin in breast milk of mothers and steroid hormone in saliva of their 3 year old infants

