RELATIONSHIPS OF METABOLIC SYNDROMES AND THYROID HORMONES WITH DIOXINS IN BLOOD AMONG GENERAL POPULATION IN KOREA

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Introduction

In Korea, the number of municipal and hazardous waste incinerators, as well as motor vehicles, which both emit dioxin-like compounds, has increased since 1980. Therefore, the human health risks caused by dioxin have become a matter of increasing public concern. Dioxins-like compounds accumulate in the human body and can be detected in human samples from around the world. Recently, background environmental exposure to some POPs has been reported to be associated with increased risk of diabetes (Lee et al. 2006) and metabolic syndrome (Lee et al. 2007), especially in the Asian countries (Uemura et al., 2009). In addition, the effects of organochlorines on thyroid hormone homeostasis have been studied in experimental animal and human (Turyk et al., 2007; Pelclova et al., 2006; Schantz et al., 1997).
In this study, we evaluated the associations of body burden levels of dioxins and related compounds with prevalence of metabolic syndrome and thyroid hormones in an adults who lived in urban area without reported metabolic and thyroid diseases to assess the low-dose effect in general population.

Materials and methods

Blood samples were obtained between 2002 and 2012 except 2005 from 978 volunteers living in an urban area of Korea. The annual recruitment of volunteers were 19 persons in 2002, 31 persons in 2003, 30 persons in 2004, 55 persons in 2006, 57 persons in 2007, 154 persons in 2008, 92 persons in 2009, 177 persons in 2010, 95 persons in 2011, and 179 persons in 2012. The participants who had lived in the urban area for at least 5 years were 20 ~ 80 (arithmetic average, 50) years old of age. The participants answered a detailed questionnaire regarding their sociodemographic variables, lifestyle, possible exposure through occupational and non-occupational contact, locations of their former and present residences, and their food intake patterns.

About 100 ㎖ of blood was collected without anticoagulant and centrifuged to remove cell. Quantitative assessment of PCDDs/PCDFs and co-planar PCBs in serum was analyzed by HRGC-HRMS according to US EPA 1613 method. The School of environmental Engineering, Pohang University, conducted the instrumental analysis and the Fisheries & Oceans Laboratory of Canada collaborated with our teams in the quality assurance/quality control (QA/QC) program. Calculation of PCDDs/PCDFs and co-planar PCBs body burden was made according to a subject's body weight and percentage of body fat (Schecter et al., 1998). We calculated toxic equivalents (TEQs) using the 2005 World Health Organization (WHO) toxic equivalent factors (TEFs) (Van den Berg et al., 2006).

We obtained approximately 3㎖ collected into vacationer tubes containing EDTA each participant and determined various hematology inspection such as fasting blood glucose, cholesterol, and thyroid hormones in the blood with an automatic biochemical analyzer (Sysmex SE-9000 system, Korea). Blood pressure was measured in each subject sitting at rest. If a measurement was extremely high or low or far from everyday values, we tried again after a short rest and used the second measurement as the final measurement. We assessed the prevalence of metabolic syndrome using a modification of the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) definition (NCEP, 2002). Reference ranges for thyroid stimulating hormone (TSH) and free T4 were 0.35 ~ 5.5 uU/㎖ and 0.9 ~ 2.0 ng/㎗, respectively, for the Korean Academy of Medical Sciences.

Results and discussion

A total of 978 adults were analyzed for PCDDs/Fs in individual blood samples during the 11 surveys from 2002 to 2012 except 2005. In all periods, the mean age was 50.5 (20~80) years old and the dominant volunteers were women (75.2%), non-smokers (91.0%), and more than 50 years old (59.1%). In all periods, the average concentrations of PCDDs, PCDFs and dioxins in blood were 4.54±3.45, 4.94±2.57, and 9.47±5.26 pg-TEQ05/g lipid, respectively. The ranges of body burden were 0.02~29.71 ng-TEQ05/kg-BW, 0.001~28.22 ng-TEQ05/kg-BW, and 0.05~46.32 ng-TEQ05/kg-BW of PCDDs, PCDFs, and dioxins, respectively (Table 1). The average concentrations of PCDDs/Fs in blood for non-occupationally exposed subjects were reported between 6 and 23 pg-TEQ/g lipid in a number of investigations since 2000 (Uemura et al., 2009; Wittsiepe et al., 2007). These levels were considered as background concentrations in our study (9.47±5.26 pg-TEQ05/g lipid). US EPA reported that a number of significant noncancer responses occurred at LOAEL/NOAEL/ED01s of less than 10~50 ng/kg-body weight body burden, levels that are similar to the ED01s estimated for cancer effects (US EPA, 2003). In this study, the average body burden of dioxins was 2.53 (0.05~13.9) ng-TEQ05/kg-body weight for all subjects and it is lower than the guidance of body burden by US EPA. But there are uncertainties in our study that the co-planar PCBs were not included.

Although the level of dioxins in blood by smoking habits was not significantly different, we statistically analyzed only none smokers data in order to eliminate the smoking effect. Although the dioxin levels in blood did not significantly decline over time from 2002 to 2012, the serum levels of dioxins were significantly correlated with age and BMI. For none smokers, we defined 5.6 % (5.7% for male and 5.6% for female) as having metabolic syndrome and 48.4 % (51.1% for male and 47.7% for female) as having potency metabolic syndrome. The percentage of abnormal range about TSH or free T4 value was 16.6% (14.4% for male and 17.2% for female) and that of women was significant higher than men (Table 2). The blood level and body burden of dioxins for group as having metabolic syndrome ("Yes" group) were significantly higher than those for normal group. The body burden of dioxin for high BMI group (>25 kg/㎡) was significant higher than normal group. Although there is not significant different dioxin level between normal and abnormal group, the levels of dioxin for abnormal group were slightly higher than normal group (Figure 1). Table 3 lists the non-adjusted and adjusted associations of the dioxin levels with the prevalence of metabolic syndrome and abnormality of thyroid hormone. The levels of dioxins in blood had not significant non-adjusted and adjusted associations with the effects of metabolic syndrome and thyroid hormone. For body burden of dioxin, the highest quartile of total TEQs had a high adjusted odds ratio (OR) and 95% confidence interval (CI) of 2.4 (2.1~2.7) for metabolic syndrome and 1.2 (1.0~1.7) for metabolic syndrome, respectively, compared with the referent. Uemura et al. (2009) reported that all of the TEQs of PCDDs, PCDFs, and DL-PCBs and total TEQs had significant associations with the prevalence of metabolic syndrome (OR 5.3). Turyk et al. (2007) found inverse associations of total T4 with exposure TEQs in both sexes, with stronger associations in female. Especially, the data show a dose-response in total T4 with exposure to TEQs in female, and similar to our study.

These results suggest that significant time-BMI interaction of serum dioxin levels indicates that body fat affects the reduction rate of the dioxins concentration in blood and body burden levels of dioxins are associated with metabolic syndrome and thyroid hormone homeostasis in non-occupationally exposure conditions.

Acknowledgements

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References

Lee DH, Lee IK, Song K, et al. (2006); *Diabetes Care* 29: 1638-1644

NCEP (National Cholesterol Education Program). (2002); *Circulation* 106: 3143–3421

Pelclova D, Urban P, Preiss J, et al. (2006); *Reviews on Environmental Health* 21(2): 119-138

Schantz SL, Seo BW, Moshtaghian J, et al. (1997); *Amer. Zool.* 37:399-408

Schecter A, Ryan JJ, Papke O. (1998); *Chemosphere* 37(9-12): 1807-1816

Turyk ME, Henry AA, Persky VW. (2007); *Environmental Health Perspectives* 115(8): 1197-1203

Uemura H, Arisawa K, Hiyoshi M, et al. (2009); *Environmental Health Perspectives* 117(4): 568-573

US EPA (2003); *Washington DC* http://www.epa.gov/ncea/pdfs/dioxin/nas-review/

Van den Berg M, Birnbaum L, Denison M, et al. (2006); *Toxicological Sciences* 93: 223–241

Wittsiepe J, Schrey P, Ewers U, et al. (2007); *Chemosphere* 40: 1103–1109

Table 1. Concentrations of dioxins in blood and boby burden of the subjects during 2002 – 2012

Subjects	Media	Congeners	Mean	SD	Min	Max
All (n=978)	Levels in blood (pg-TEQ05/g lipid)	PCDDs	4.54	3.45	0.06	29.71
		PCDFs	4.94	2.57	0.00	28.22
		PCDDs/PCDFs	9.47	5.26	0.14	46.32
	Body burdens (ng-TEQ05/kg-BW)	PCDDs	1.21	1.01	0.02	9.03
		PCDFs	1.32	0.79	0.00	8.44
		PCDDs/PCDFs	2.53	1.60	0.05	13.87
Non-smokers (n=889)	Levels in blood (pg-TEQ05/g lipid)	PCDDs	4.52	3.37	0.06	29.11
		PCDFs	4.95	2.57	0.00	28.22
		PCDDs/PCDFs	9.47	5.15	0.14	42.62
	Body burdens (ng-TEQ05/kg-BW)	PCDDs	1.23	0.99	0.02	9.03
		PCDFs	1.35	0.79	0.00	8.44
		PCDDs/PCDFs	2.58	1.57	0.05	12.86
Smokers (n=89)	Levels in blood (pg-TEQ05/g lipid)	PCDDs	4.73	4.18	0.36	29.71
		PCDFs	4.80	2.59	0.00	16.62
		PCDDs/PCDFs	9.53	6.31	0.65	46.32
	Body burdens (ng-TEQ05/kg-BW)	PCDDs	1.02	1.17	0.05	8.90
		PCDFs	1.00	0.74	0.00	4.98
		PCDDs/PCDFs	2.02	1.84	0.11	13.87

Table 2. Characterization of none smoker participants in this study

Contents	All (n=889)	Male (n=176)	Female (n=713)
age (years-old)	50.5	51.3	50.3
≥ 50	(58.4%)	(66.5%)	(56.3%)
BMI (kg/㎡)	23.8	24.3	23.6
> 25	(27.7%)	(36.9%)	(25.4%)
Blood pressure (㎜ Hg)			
High pressure (HP)	122	127	120
Low pressure (LP)	73	78	72
HP ≥ 140 or LP ≥ 90	(4.3%)	(11.1%)	(2.5%)
Fasting blood glucose (mg/dl)	99	102	99
>125	(4.5%)	(7.4%)	(3.8%)
Cholesterol (mg/dl)			
Total cholesterol (TC)	193	182	196
Triglycerides (TG)	124	144	118
High-density Lipoprotein Cholesterol (HDLC)	56	51	58
Low-density Lipoprotein Cholesterol (LDLC)	108	99	110
TC ≥ 250 or TG ≥ 150	(28.7%)	(39.5%)	(25.8%)
HDLC>40 in men, HDCL>50 in women, or LDLC≤160	(36.4%)	(19.0%)	(42.5%)
Metabolic syndrome [1)]			
Yes	(5.6%)	(5.7.%)	(5.6%)
Potency	(48.4%)	(51.1%)	(47.7%)
Thyroid			
Thyroid - stimulating hormone (TSH) (uU/㎖)	2.25	1.74	2.39
Free T4 (ng/㎗)	1.27	1.37	1.24
over range THS (0.35-55) or T4 (0.9-2.0)	(16.6%)	(14.4%)	(17.2%)

1) We diagnosed metabolic syndrome that "Yes" is the presence of three or more and "Potency" is the presence of one or more of five components (BMI, BP, glucose, cholesterole and lipoprotein).

Table 3. Nonadjusted and adjusted associations of the dioxin levels with the prevalence of metabolic syndrom and abnormality of thyroid hormone for none smokers

Contents	No of subjects	No of cases	OR (95% CI) Non-adjusted	OR (95% CI) Adjusted[1)]
Metabolic syndrome				
Dioxins in blood (pg-TEQ05/g lipid)				
<6.13	247	14	Referent	Referent
≥6.13 to <8.44	243	15	1.0 (0.2 ~ 1.8)	0.9 (0.5 ~ 1.3)
≥8.44 to <11.42	238	13	0.9 (0.3 ~ 1.6)	0.7 (0.3 ~ 1.1)
≥11.42	250	12	0.9 (0.3 ~ 1.7)	0.6 (0.2 ~ 1.1)
p-value			> 0.1	> 0.1
Body burden (ng-TEQ05/kg-BW)				
<1.57	268	8	Referent	Referent
≥1.57 to <2.19	222	11	1.5 (0.7 ~ 2.3)	1.2 (0.8 ~ 1.6)
≥2.79 to <3.21	253	17	2.2 (1.6 ~ 2.8)	2.1 (1.7 ~ 2.5)
≥3.212	235	18	2.4 (1.9 ~ 2.9)	2.4 (2.1 ~ 2.7)
p-value			< 0.01	< 0.01
Abnormal of thyroid hormones				
Dioxins in blood (pg-TEQ05/g lipid)				
<6.13	247	11	Referent	Referent
≥6.13 to <8.44	243	7	0.6 (0.1 ~ 1.4)	0.5 (0.1 ~ 0.9)
≥8.44 to <11.42	238	11	1.0 (0.4 ~ 1.6)	0.8 (0.4 ~ 1.2)
≥11.42	250	6	0.5 (0.1 ~ 1.0)	0.4 (0.1 ~ 0.7)
p-value			> 0.1	> 0.1
Body burden (ng-TEQ05/kg-BW)				
<1.57	268	9	Referent	Referent
≥1.57 to <2.19	222	7	0.9 (0.1 ~ 1.7)	0.8 (0.4 ~ 1.2)
≥2.79 to <3.21	253	9	1.1 (0.5 ~ 1.7)	1.0 (0.6 ~ 1.4)
≥3.212	235	10	1.3 (0.8 ~ 1.8)	1.2 (1.0 ~ 1.7)
p-value			0.06	0.04

1) Adjusted for age, sex, regional area and survey year

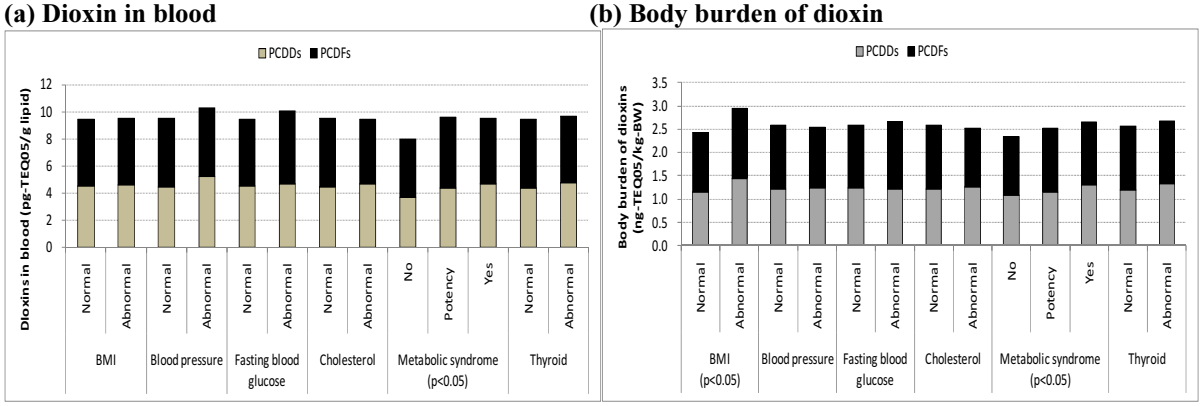

Figure 1. Comparison of dioxin levels between normal and abnormal group by the components for metabilic syndrome and thyroid hormones of none smokers