Serum Dioxin Levels and Health Effects : A Cross-sectional Study of Japanese Incinerator Workers

Yamamoto K[1], Kudo M[1], Sakurai H[1], Takata T[2] and the Committee for Health Effects by Dioxin Exposure among Incinerator Workers

[1]Occupational Health Research and Development Center, Japan Industrial Safety and Health Association, Tokyo, Japan

[2] Japan Labour Health and Welfare Organization

【Abstract】

The aim of this study was to elucidate the blood level of dioxin congeners and health effects in Japanese incinerator workers. 827 male workers from 46 incinerators located at many geographic areas were subjected for study. Blood samples were analyzed for 7 congeners of PCDDs, 10 congeners of PCDFs and 12 congeners of Co-PCBs. Data for present health status and work history were collected using a standardized questionnaire. Data for age, BMI, smoking habit, alcohol consumption, and examination year were treated as potential confounders. Arithmetic mean of serum total dioxins(PCDDs+PCDFs+Co-PCBs) was 22.0±15.0 (pg-TEQ/g lipid), similar to the value reported for Japanese general population(25.6±17.2 pg-TEQ/g lipid). Multiple linear regression analysis showed significant positive associations between total cholesterol and PCDFs(β =0.686) , and also between calculated LDL-cholesterol and PCDDs (β =0.646) or PCDFs(β =0.719). Logistic regression analysis detected significant associations between diabetes mellitus and PCDDs or PCDFs, between hyperlipidemia and PCDDs or PCDFs or Co-PCBs, between liver dysfunction and Co-PCBs. It is suggested that, as serum dioxin concentrations were rather low and similar to those of general population, the associations found in this study between diabetes or hyperlipidemia or liver dysfunction and low level serum dioxins could be attributed to non-occupational exposure.

【Introduction】

In 1998, severe dioxin pollution of soil around a waste incinerator and high serum dioxin level of the workers of this incinerator attracted much public attention in Japan. Ministry of Labor established a Committee to investigate the dioxin exposure level and its health effects among other waste incinerator workers in Japan. This paper reports the result of the cross-sectional study of 861 workers in 46 incinerators under the supervision of the Committee.

【Material an Methods】

861 workers sampled from 46 waste incinerators (33 general waste incinerators and 13 industrial waste

incinerators) were surveyed during 7 years from 1999 to 2005. To investigate the level of exposure, blood samples (180ml) were analyzed with high resolving GC-MS for 7 congeners of PCDDs (polychlorinated-dibenzo-p-dioxins), 10 congeners of PCDFs (polychlorinated-dibenzofurans) and 12 congeners of Co-PCBs (coplanar-polychlorinated-biphenyls). Each concentration was converted to Toxic Equivalents (TEQ/g lipid) with Toxic Equivalency Factors (WHO -TEF) advocated by WHO in 1997.

To investigate the workers' health status, a standardized questionnaire including present medical illness and medical history was conducted. Physical examination was performed by internal physicians and dermatologists, especially for detecting chloracne. Measurement of blood pressure, BMI and others were conducted by co-medical staffs. Blood samples were analyzed for blood count, liver function, renal function, lipid profile, carbohydrate metabolism and immune system function. LDL-cholesterol(LDL-ch) was calculated by Friedwald method(LDL-ch=Total-cholesterol(T-ch)－HDL-ch－triglyceride/5). Multiple linear regression analyses were used to identify association between serum dioxin concentrations and laboratory findings. The regression model included age, BMI, smoking habit, alcohol consumption and examination year as confounders. Logistic regression analyses were also performed to clarify dose-response relationships between dioxin exposure and several disorders such as diabetes mellitus, hypertension, hyperlipidemia and liver dysfunction, which have been suggested as possible outcomes of dioxin exposure by previous literature.

Although examined incinerators were located at many geographic areas in Japan, blood samples were analyzed by the same laboratory to secure precision. Logarithmic transformation was done for data which did not distribute normally.

【Results and Discussion】

Female subjects (n=18) were excluded because of the small number. Moreover, 16 subjects without data for dioxin concentration were excluded. Finally 827 subjects(age:43.4 ± 11.2years) were analyzed for the relationship between PCDDs or PCDFs and health effect. On the other hand, because laboratory analysis of serum Co-PCB congeners was not completed for 20 incinerators in 1999 and 2000,only 494 subjects (age:42.4± 11.0years) at 26 incinerators from 2001 to2005 were analyzed for Co-PCBs.

Arithmetic and geometric means of lipid adjusted serum concentrations of dioxin congeners are shown in Table 1. Arithmetic mean of Total-Dioxins (PCDDs+PCDFs+CoPCBs) was 22.0±15.0(pg-TEQ/g lipid). This value is similar to the result of the study for general population in Japan(Total-Dioxins:25.6±17.2 pg-TEQ/g lipid) reported by Ministry of Environment in 2005. Some dermatological findings were observed by dermatologists, but those were not diagnosed as related to dioxin exposure.

Table 2 shows significant findings obtained by multiple linear regression. T-ch was associated with PCDFs(β =0.686) and LDL-ch was associated with TCDD(β =5.412), PCDDs(β =0.646) and PCDFs(β =0.719). Other factors associated with Total-Dioxins were suspected to have been affected by Co-PCBs because no significant

findings were detected for TCDD, PCDDs, and PCDFs.

In consideration of previous literature and results of this multiple linear regression, logistic regression analysis was performed to examine dose-response relationships between serum dioxin concentrations and suspected disorders. As a result, we could detect significant relationships between diabetes(HbA1c>5.8% or present medical illness) and PCDDs or PCDFs, between hyperlipidemia (Total-ch>=220mg/dl or TG>= 150 mg/dl or HDL-ch<40 mg/dl or present medical illness) and PCDDs, PCDFs or Co-PCBs, and, between liver dysfunction (AST> 40IU/l or ALT>45IU/l or gamma-GTP>=80IU/l or present medical illness) and Co-PCBs (Table3). We could not detect significant relationships between hypertension (SBP>=140mmHg or DBP>= 90mmHg or present medical illness) and dioxins.

Occupational exposure to dioxins was found to be rather low in this study. Therefore, the associations found in this study between diabetes or hyperlipidemia or liver dysfunction and low level serum dioxins could be attributed to non-occupational exposure.

【Acknowledgement】

We are grateful for assistances provided by ROUSAI-Hospital staffs of Japan Labour Health and Welfare Organization and secretariat staff of Occupational Health Research and Development Center of JISHA.

【Reference】

1. Arisawa K, Takeda H, Mikasa H. *J.Med.Invest* 2005;.52:10-21
2. Steenland K, Calvert G, Ketchum N, Michalek J. *Occup Environ Med* 2001;58:641-648
3. Michalek J, Ketchum N, Longnecker M. *Ann Epidemiol* 2001;11:304-311
4. Longnecker M, Daniels J.*Environ Health Perspect* 2001;109(suppl 6):871-876
5. Schecter A, Papke O, Ball M, Lis A, Brandt-Rauf P. *Occup Environ Med* 1995;52:385-387

【Members of Committee】

Masakazu Asahi /Heihachirou Aritou /Takao Iida /Iwao Uchiyama /Yasutaka Ogawa /Toshihiro Kawamoto / Suminori Kono /Haruhiko Sakurai /Tsutomu Takata /Isamu Tanaka /Kazuhiro Nomura /Tsuguya Fukui / Shaw Watanabe

Table1 Serum concentration of TCDD and other Dioxins

congener	n	arithmetic				geometric		
		mean	SD	min	max	mean	percentile	
							25	75
TCDD(pg/g lipid)	827	0.95	0.65	0.20	6.10	0.80	0.50	1.20
PCDDs(pg-TEQ/g lipid)	827	8.02	5.48	1.90	54.20	6.87	4.60	9.90
PCDFs(pg-TEQ/g lipid)	827	6.29	6.23	1.10	75.00	5.09	3.40	7.40
Co-PCBs(pg-TEQ/g lipid)	495 *	7.66	6.34	0.90	42.10	5.76	3.40	9.10
Total Dioxins(pg-TEQ/g lipid)	827	22.04	14.99	3.90	132.90	18.62	12.50	27.80

TCDD=2,3,7,8-tetrachlorodibenzo-dioxin

* 332 subject were excluded from Co-PCBs analysis (congeners data was not complete from 1999 to 2000)

Table2 Result of multiple regression analysis

Total-Dioxins

factor	β	95%CI		p-titer
		lower	upper	
Plt	-0.029	-0.06	0.00	0.04
γGTP*	0.006	0.00	0.01	<0.01
BUN	0.018	0.00	0.03	0.03
Tch	0.242	0.05	0.43	0.01
TG*	0.003	0.00	0.01	0.04
HbA1c*	0.001	0.00	0.00	0.01
LDLch	0.233	0.07	0.40	0.01

TCDD

factor	β	95%CI		p-titer
		lower	upper	
WBC*	-0.034	-0.06	0.00	0.03
Hb	0.178	0.06	0.30	<0.01
Glucose*	0.033	0.01	0.06	0.01
LDLch	5.412	1.77	9.05	<0.01

PCDDs

factor	β	95%CI		p-titer
		lower	upper	
LDLch	0.646	0.21	1.08	<0.01

PCDFs

factor	β	95%CI		p-titer
		lower	upper	
Tch	0.686	0.26	1.12	<0.01
LDLch	0.719	0.35	1.09	<0.01

PCDDs+PCDFs

factor	β	95%CI		p-titer
		lower	upper	
Tch	0.342	0.10	0.59	0.01
LDLch	0.393	0.18	0.61	<0.01

Co-PCBs

factor	β	95%CI		p-titer
		lower	upper	
SBP	0.344	0.05	0.64	0.02
DBP	0.297	0.10	0.49	<0.01
WBC*	-0.005	-0.01	0.00	0.03
Plt	-0.091	-0.18	0.00	0.05
AST*	0.014	0.01	0.02	<0.01
ALT*	0.016	0.01	0.02	<0.01
LAP*	0.007	0.00	0.01	<0.01
γGTP*	0.031	0.02	0.04	<0.01
BUN	0.061	0.01	0.11	0.02
TG*	0.017	0.01	0.03	<0.01
Glucose*	0.005	0.00	0.01	<0.01
HbA1c*	0.002	0.00	0.00	0.03
NKact	0.306	0.04	0.57	0.02
CD3	-0.153	-0.29	-0.01	0.03

* Logarithmic transformation was done to transform into normal distribution.

Adjusted for age, BMI, smoking habit(never smoker, low smoker: Blinkman Index(BI)=1-399, moderate smoker: BI=400-799, high smoker: BI>=800), alcohol consumption (never drinker, low drinker: a few times a month, moderate drinker: several times a week, high drinker: every day)and examination year.

WBC=white blood cell count, Hb=hemoglobin, Plt=platelet count, SBP=systolic blood pressure, DBP=diastolic blood pressure, AST=aspartate aminotransferase, ALT=alanine aminotransferase, LAP=leucine aminopeptidase, BUN=blood urea nitrogen, NKact=natural killer cell activity

Table3 Dose-response relationship between serum Dioxins(pg-TEQ/g-lipid) and diseases

			Diabetes				Hyperlipidemia				Hypertension				Liver Dysfunction			
factor	percentile	n	OR	95%CI lower	95%CI upper	p-titer	OR	95%CI lower	95%CI upper	p-titer	OR	95%CI lower	95%CI upper	p-titer	OR	95%CI lower	95%CI upper	p-titer
Total-Dioxins	<20	164	1.00				1.00				1.00				1.00			
	20-40	169	4.14	0.48	35.70	0.20	1.62	0.98	2.68	0.06	0.90	0.54	1.51	0.70	1.78	0.99	3.20	0.05
	40-60	162	5.80	0.71	47.76	0.10	2.22	1.29	3.82	<0.01 **	1.37	0.80	2.34	0.25	1.51	0.81	2.81	0.19
	60-80	169	11.38	1.40	92.71	0.02 *	2.94	1.65	5.22	<0.01 **	1.16	0.66	2.03	0.61	1.88	0.99	3.58	0.05
	>=80	163	15.80	1.95	128.13	0.01 *	2.43	1.34	4.40	<0.01 **	1.28	0.71	2.32	0.41	1.89	0.97	3.67	0.06
PCDDs	<20	165	1.00				1.00				1.00				1.00			
	20-40	176	1.03	0.28	3.78	0.97	1.55	0.95	2.55	0.08	1.04	0.63	1.72	0.86	1.45	0.82	2.54	0.20
	40-60	162	1.38	0.39	4.88	0.62	1.80	1.07	3.03	0.03 *	0.92	0.55	1.54	0.75	1.21	0.67	2.18	0.53
	60-80	162	2.77	0.84	9.19	0.10	2.29	1.31	3.99	<0.01 **	1.16	0.67	2.00	0.60	1.24	0.67	2.30	0.50
	>=80	162	3.65	1.09	12.21	0.04 *	2.96	1.66	5.29	<0.01 **	1.02	0.58	1.81	0.94	1.57	0.83	2.96	0.17
PCDFs	<20	168	1.00				1.00				1.00				1.00			
	20-40	163	1.27	0.28	5.72	0.75	1.68	1.01	2.80	0.04 *	1.15	0.69	1.91	0.59	1.24	0.71	2.16	0.44
	40-60	157	2.96	0.77	11.44	0.12	1.86	1.10	3.16	0.02 *	1.18	0.70	1.99	0.54	0.88	0.49	1.57	0.66
	60-80	174	3.75	0.96	14.60	0.06	1.76	1.01	3.06	0.05 *	1.15	0.66	1.99	0.63	0.96	0.52	1.76	0.89
	>=80	165	7.34	1.90	28.40	<0.01 **	1.74	0.97	3.11	0.06	1.40	0.78	2.50	0.26	1.24	0.66	2.33	0.51
Co-PCBs	<20	99	(+)				1.00				1.00				1.00			
	20-40	105	1.00				1.78	0.90	3.52	0.10	0.68	0.34	1.38	0.29	1.71	0.75	3.91	0.20
	40-60	96	1.04	0.26	4.10	0.96	2.86	1.34	6.11	0.01 *	1.02	0.48	2.16	0.95	3.58	1.50	8.55	<0.01 **
	60-80	97	2.07	0.58	7.39	0.26	3.64	1.66	8.00	<0.01 **	1.62	0.76	3.48	0.21	4.50	1.84	11.00	<0.01 **
	>=80	98	2.90	0.80	10.50	0.10	3.74	1.55	9.02	<0.01 **	1.41	0.60	3.30	0.43	4.87	1.84	12.90	<0.01 **

(+): no case of diabetes *:p<0.05, **:P<0.01
Adjusted for age, BMI, smoking habit, alcohol consumption and examination year.
Co-PCBs were analyzed for 494 subjects with complete data of congeners