LONGITUDINAL ANALYSIS OF BLOOD DIOXIN LEVELS OF RESIDENTS OF TWO AREAS IN JAPAN

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Abstract

To investigate the recent changes in background exposure to dioxin-related compounds, the concentrations of polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), and dioxin-like polychlorinated biphenyls (PCBs) in the blood of selected residents from Districts A and B were examined from 2002 to 2006. For the longitudinal analysis of these concentrations, we used the generalized estimating equation (GEE). The PCDDs+PCDFs concentration decreased, but the concentrations of dioxin-like PCBs declined less over 5 years. A significant time×body mass index (BMI) interaction suggests that the reduction rate of blood PCDDs+PCDFs concentration of subjects who have more than 75 percentile of BMI is lower than that of subjects having less than 75 percentile of BMI from 2002 to 2004. From reports on the dietary dioxin intake, the total amount of daily dioxin intake decreased but the percentage of dioxin-like PCBs in the daily dioxin intake increased yearly from 1999 to 2004. The reason for the difference in the 5-year change in blood concentrations between PCDDs+PCDFs and dioxin-like PCBs may be explained by yearly change in the dietary dioxin intake.

Introduction

Humans has been exposed to low levels of polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and dioxin-like polychlorinated biphenyls (PCBs) through food, water, and the atmosphere. More than 90% of exposure occurred through food, but the dietary intake of dioxins has been below the upper limit of tolerable daily intake (TDI) of dioxins and dioxins related compounds, which was set at 1-4 pg Toxicity Equivalency Quantity (TEQ)/kg/day by the World Health Organization (WHO)[1]. There were reports on the association between exposure to background levels of dioxins and dioxin-related compounds and health effects such as diabetes, endometriosis, altered thyroid function, and defective neurodevelopment of infants. However, the results of the association studies shown in these reports are heterogeneous and inconclusive[2].

To clarify the recent background levels of exposure to PCDDs, PCDFs and dioxin-like PCBs, we measured the blood concentrations of these compounds in the general population from 2002 to 2006, and analyzed these results longitudinally.

Materials and Methods

We used the survey conducted by the Ministry of the Environment Government of Japan. Sixty-eight subjects were selected from residents of Districts A and B. Twenty-two female and 14 male subjects were selected from District A, and 25 female and 7 male subjects were selected from District B. They were included in the cohort from 2002 to 2006. The previous job, dietary and smoking habits, and body weight and height of each subject were obtained from a questionnaire survey in 2002. The concentrations of 7 PCDDs, 10 PCDFs and dioxin-like PCBs were repeatedly measured in blood samples from 2002 to 2006. Calculation of the 2,3,7,8-TCDD toxicity equivalency quantity (TEQ) of the dioxin analogues in the analyzed samples was carried out on the basis of the toxicity equivalent factor (TEF) revised by the World Health Organization in 2005[3].

For the longitudinal analysis, the generalized estimating equation (GEE) approach was used to analyze the repeated measurements. The dependent variable was concentrations of PCDDs +PCDFs or dioxin-like PCBs for each year, with the main explanatory factor being the time variable (continuous or categorical for the 5-year change), and with the model adjusted for age, body mass index (BMI), and sex. Five subjects were excluded from the analysis, as their weights or heights were unknown. Because the distribution of the blood concentration of dioxins is skewed, log-transformed concentrations were also used as the dependent variable. The models also included an interaction term between BMI and time. An exchangeable correlation structure was used to adjust for the correlation between repeated measurements. The analyses were performed using Proc Genmod in SAS (version 8.2, SAS, Inc., Cary, NC). Marginal means and standard errors (SEs) of concentrations at each time point were calculated using the least square means option of the Genmod procedure.

Results and Discussion

Forty-three subjects were included in the cohort in 2002, and 9 subjects in 2003, 8 subjects in 2004, 3 subjects in 2005, and 5 subjects in 2006 were added to the cohort. There were no significant differences in sex ratio, age, and BMI among these 5-year groups. The means and standard deviations (SDs) of the subjects` ages were 54.1 (7.7) for females and 57.9 (8.6) for males. The means and SDs of BMIs were 22.0 (2.6) for females and 23.8 (2.4) for males. We measured the blood concentrations of 43 subjects in 2002, 38 in 2003, 51 in 2004, 42 in 2005, and 46 in 2006.

Firstly, we examined the GEEs given that the time variable is continuous, and show the estimates for PCDDs+PCDFs and dioxin-like PCBs in Table 1. Age and BMI were positively associated with the blood concentrations of both PCDDs+PCDFs and dioxin-like PCBs. The blood concentrations of PCDDs+PCDFs significantly decreased with time, but that of dioxin-like PCBs did not changed over 5 years.

Table 1. Estimates of GEE analyses for PCDDs+PCDFs and dioxin-like PCBs.

	PCDDs+PCDFs			Dioxin-like PCBs		
	Estimate	SE	p-value	Estimate	SE	p-value
Intercept	-37.141	8.512	<0.0001	-25.806	7.205	<0.001
Time	-0.876	0.231	<0.001	-0.147	0.272	0.588
Age	0.649	0.150	<0.0001	0.438	0.110	<0.0001
BMI	0.876	0.285	0.002	0.569	0.199	0.004
Female	1.218	2.200	0.580	-2.106	1.704	0.217

Secondly, we examined the GEEs with the time variable being categorical, and the change in the marginal mean concentration with standard error (SE) for PCDDs+PCDFs is shown in Figure 1. We obtained the estimates and their 95% confidence intervals (CIs) for the time variable as follows, -2.082 (95%CI -3.195 -0.969) for 2004, -1.758 (95%CI -3.239 -0.278) for 2005, and -3.273 (95%CI -4.707 -1.839) for 2006 as compared with that of 2002.

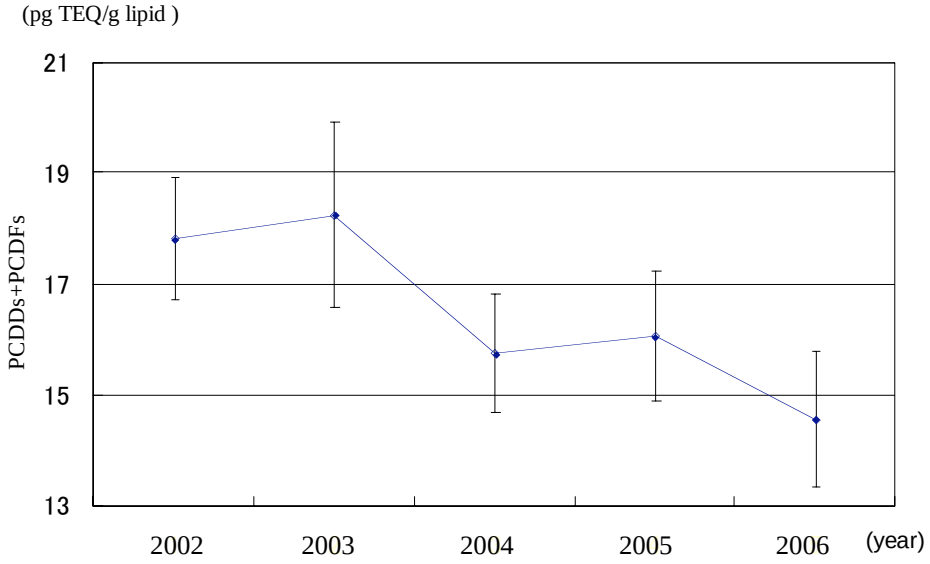

Figure 1. Marginal means of blood concentrations for PCDDs+PCDFs. Values are expressed as means ± SE.

We applied GEE to the log-transformed concentrations of PCDDs+PCDFs, and obtained a significant time×BMI interaction. BMI is transformed to a new categorical variable which has a value 1 if the BMI is more than 75 percentile (BMI=24.35), and has value 0 for others. The concentrations of PCDDs+PCDFs in the blood of subjects who have higher BMI declined less than those of others from 2002 to 2004.

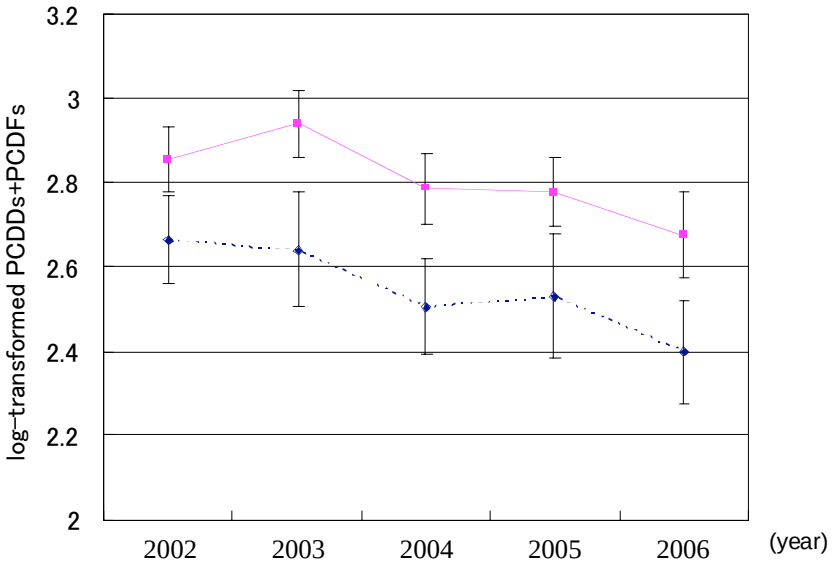

Figure 2. Marginal means of log -transformed concentrations of PCDDs+PCDFs. : BMI_ 75 percentile (n=16), : BMI<75 percentile (n=47).

We examined the GEEs for dioxin-like PCBs with the time variable being categorical, and the change in the marginal mean concentration with standard error (SE) is shown in Figure 3.

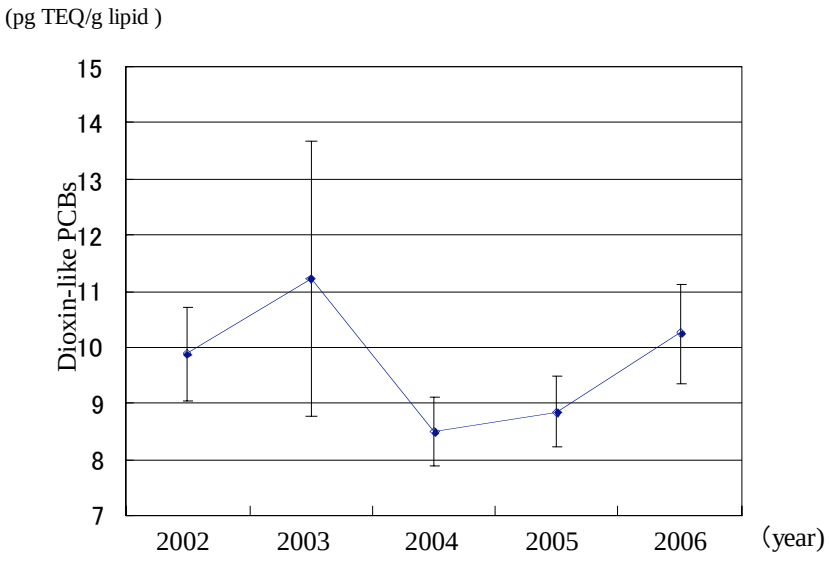

Figure 3. Marginal means of blood concentrations of dioxin -like PCBs. Values are expressed as means ± SE.

Only in 2004 did the mean blood concentration of dioxin-like PCBs in 2004 become less than that in 2002, but that in 2006 became the same as that in 2002.

From the result of the significant time×BMI interaction, the reduction rate of blood PCDDs+PCDFs concentration for subjects who have more than 75 percentile of BMI is lower than that of others from 2002 to 2004. It is considered that body fat affected the reduction rate of blood PCDDs+PCDFs concentration.

More than 90% of exposure occurs through food. Sasamoto et al. measured the dietary intake of dioxins consisting of PCDDs, PCDFs and dioxin-like PCBs through foods retailed in the metropolitan Tokyo area from1999 to 2004 by the total diet-market basket method[4]. They showed that the daily dioxin intake of an adult with an average body weight of 50 kg was 2.18 pg TEQ/kg/day in 1999, 1.87 pg TEQ/kg/day in 2000, 1.25 pg TEQ/kg/day in 2001, 1.60 pg TEQ/kg/day in 2002 and 2003, and 1.55 pg TEQ/kg/day in 2004. They also showed that the percentage of dioxin-like PCBs in the daily intake of dioxins increased yearly, and suggested that the reduction rate of dioxin-like PCBs was lower than those of PCDDs and PCDFs in foods, particularly in fish and shellfish. Their results showing the yearly change in dietary intakes of dioxins may explain the reason for the difference in the 5-year change in blood concentrations between PCDDs+PCDFs and dioxin-like PCBs. Nations where fish and shellfish are consumed in large quantities should put particular importance to dioxin-like PCBs.

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