REDUCTION OF DIOXINS AND POLYCHLORINATED BIPHENYLS (PCBs) IN HUMAN BODY USING COLESTIMIDE

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Introduction

The accumulation of persistent lipophilic organic pollutants in human body is of great concern since many of these compounds may elicit adverse health effects on humans.[1,2] Dioxins or polychlorinated biphenyls(PCBs) are one of these chemicals. Exposure to dioxins, especially to 2,3,7,8-tetrachloro-dibenzo-*p*-dioxin (TCDD), has been reported to cause adverse health effects and developmental toxicity to fetuses.[3] Adverse health effects of PCB exposure include neurological disorders, carcinogenic effects and diminished reproductive and immunologicalfunctions.[4] The health effects of extreme high exposure to PCBs in humans are known as Yusho or Yu-Cheng.[5]

It has been also reported that once dioxins or PCBs are absorbed into human body, dioxins/PCBs are excreted into the intestinal tract and reabsorbed into the body. Thus, dioxins or PCBs circulate between the intestinal tract and the body organs such as liver and adipose tissue, etc.[6]

Although the half-life of the dioxins or PCBs in the human body was described to be 3 to 25 years [5,7], there are very few drugs or methods to exclude them from the human body. Therefore, it is necessary to establish a new method to reduce them and prevent possible adverse health effects for future generations.

Colestimide is an anion-exchange resin with an imidazolium salt on an epoxide polymer skeleton that exhibits pharmacological usefulness in hyperlipoproteinemia. Colestimide has been reported to absorb bile acids and other lipophilic compounds.[8] Recently, we have reported pilot study to reduce dioxins in the human body using colestimide.[9] In this short paper, we investigated (i) whether colestimide reduces blood PCB level also, and (ii) correlation of reduction rate between dioxin and PCB concentration in blood level after colestimide treatment.

Material and Methods

Samples

Blood samples were collected from eight male and two female subjects who diagnosed as hyperlipoproteinemia. This study has been approved by the “Congress of Medical Bioethics” of Chiba University, and the samples were obtained after receipt of written informed consent. The number of the Congress of Medical Bioethics of Chiba University is No. 108. Their mean age was 57.3 (±9.4) years old.

Measurement

The blood dioxin/PCB level of each subject was assessed before and six months after the treatment started. All of them were treated with colestimide (3 g/day) for six months. Fifty mL of blood sample was taken from each subject.

*Dioxin Analysis:*Each congener of polychloro-dibenzo-*p*-dioxin (PCDD), polychlorodibenzofran (PCDF), and coplanar PCB (co-PCB) was measured by the method proposed by the Japanese Ministry of Health, Labour and

Welfare, using gas-chromatography/mass spectrometry.[9]

Total PCBs Analysis: Five grams of blood sample was prepared for PCB analyses and measured by GC-ECD (GC-17A, Shimadzu Co., Kyoto, Japan).

Statistical Analysis

Data are expressed as mean (± standard deviation [SD]). Pair-wise differences were computed by paired Student's *t*-test.

Results and Discussion

Eighteen blood samples including before and after the colestimide treatment were analyzed (Table1). Two samples from one male subject who stopped taking colestimide at one month of this study were excluded from the data. The mean dioxin level and PCB level in the blood samples before the treatment was 44 ± 25 pg-TEQ/g-fat and 260 ± 160 ng/g-fat, respectively. Six months later, the mean dioxin level and PCB level was significantly ($p<0.05$) lowered to 35 ± 16 pg-TEQ/g-fat and 200 ± 110 ng/g-fat, respectively. Hence, both dioxin and PCB levels were decreased about 20% on average. The maximum decrease was about 40%.

Table 1. Dioxin and PCB concentrations before and after the colestimide treatment

	Dioxins (pg-TEQ/g-fat)			PCBs (ng/g-fat)		
Volunteer	Before	After	Reduction	Before	After	Reduction
1	50	40	20%	240	190	21%
2	19	21	-11%	110	130	-18%
3	43	36	16%	190	190	0%
4	57	35	39%	360	200	44%
5	20	17	15%	73	63	14%
6	40	31	23%	260	230	12%
7	100	74	26%	580	430	26%
8	40	32	20%	360	280	22%
9	27	26	4%	130	120	8%
mean	44	35	17%	260	200	14%
SD	25	16	14%	160	110	18%

It was found that when the concentration level of dioxins before the treatment was higher, the stronger the effect of colestimide (R=0.63) (Fig. 1A). Similar results were found about PCB (R=0.64) (Fig 1B). On the other hand, the subject who stopped taking colestimide showed an increase in blood dioxin or PCB level six months later (dioxin: 44.0 to 54.0 pg-TEQ/g-fat, PCBs: 370 to 460 ng/g-fat). The reduction rate of blood dioxin concentration after colestimide treatment was significantly correlated with the reduction rate of blood PCB level (R=0.91) (Fig. 2).

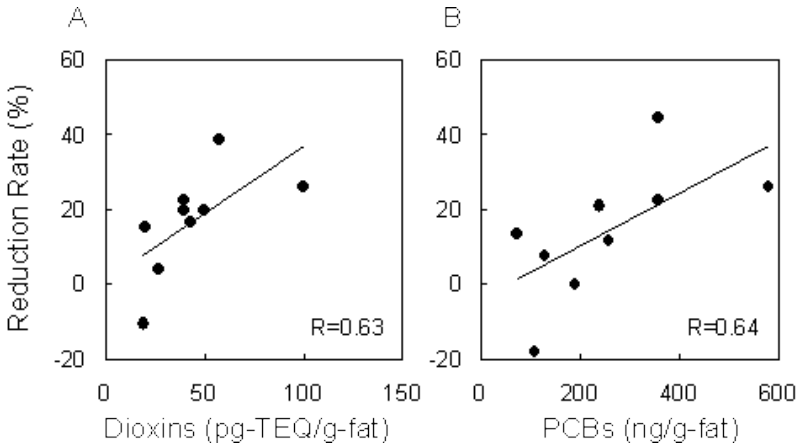
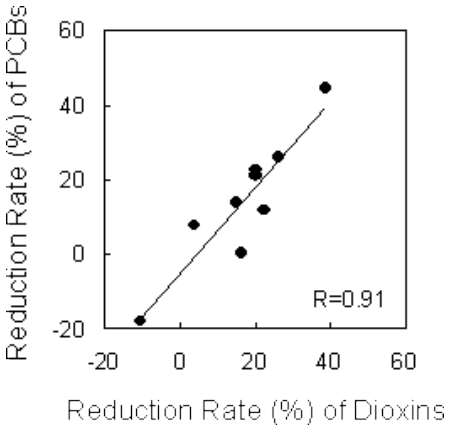


Figure 1

Correlation between initial concentrations of dioxins (A) / PCBs (B) and reduction ratio (%) of dioxins (A) / PCBs (B) after colestimide treatment.



Figure

Correlation of reduction rates of dioxin and PCB level after colestimide treatment. Data is expressed as percentage of the concentration after treatment compared to those before treatment. A significant correlation was found between dioxin and PCB. (R=0.91)

In this study, the results indicate that colestimide can decrease not only the blood dioxin level, but also PCB level in humans. It is possible that colestimide absorbs dioxins/PCBs in gastro-intestinal tract, inhibits reabsorption of dioxins/PCBs and increases excretion of dioxins/PCBs out of the human body.

Multiple persistent lipophilic organic pollutants are detected in modern human body.[10,11] Our present data suggest that colestimide can absorb lipophilic compounds non-selectively. It is possible that other persistent lipophilic organic pollutants such as organochlorine compounds are also absorbed and decreased by using colestimide.

It is required to establish the methods of decreasing the levels of dioxins, PCBs and other organic pollutants in human body. If the study is designed as to decrease the dioxin/PCB level in human body, and if the subjects receive proper counseling what to eat and what to be avoided to eat, then it is possible to decrease the level of dioxins/PCBs more effectively. Both dioxins and PCBs are easily transferred from mother to fetus through placenta,[11] so if the concentration level in human blood can be decreased before pregnancy, colestimide can help to prevent possible adverse health effect for future generations.

Acknowledgements

This work is supported by grants from Ministry of Education, Culture, Sports, Science and Technology (Government of Japan).

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