ESTIMATION OF PENTA-CHLORODIBENZOFURAN (PECDF) HALF LIFE IN YUSHO PATIENTS

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ABSTRACT

Yusho (oil disease) was a food poisoning incident that occurred in Japan. The causative agents of *Yusho* are currently considered to be polychlorinated biphenyls (PCBs) and their by-products, such as dioxins. The purpose of this study was to estimate the 2,3,4,7,8-penta-cholorodibenzofuran (PeCDF) half-life in *Yusho* patients. The present study revealed two groups of patients: one with decreasing PeCDF blood levels and another with high PeCDF blood levels. Thus, there were two groups: one showing a half-life of approximately seven years and the other showing no reduction in PeCDF levels over time.

INTRODUCTION

Yusho (oil disease) was a food poisoning incident that occurred in western Japan in 1968[1,2]. The causative agents of *Yusho* are currently considered to be polychlorinated biphenyls (PCBs) and their by-products, such as dioxins including 2,3,4,7,8-penta-cholorodibenzofuran (PeCDF)[1,2,3]. Recent advancements in techniques to measure dioxins including PeCDF has made it possible to determine the levels of dioxins in a regular blood sample. Thus the blood levels of dioxins have been measured in *Yusho* patients during medical check-ups since 2001[4]. In the present study, we attempted to estimate the PeCDF half-life from the PeCDF blood levels measured during medical check-ups.

MATERIAL AND METHODS

1. Subjects

The PeCDF blood levels were measured in 162 patients who had five or more *Yusho* medical check-ups from 2001 to 2006. Thirty eight and 124 patients underwent an annual check-up for the last six or five years, respectively.

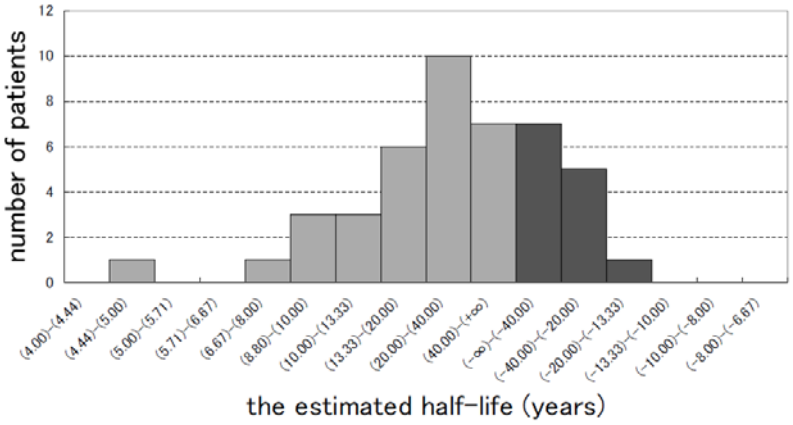

Figure 1. Distribution of PeCDF half-lives in patients with blood levels ≥ 200 pg/g lipid. The vertical and horizontal axes represent the number of patients and the estimated years of half-life, respectively. Gray columns are the patients whose PeCDF levels were reduced over time. Black columns were the patients whose PeCDF levels increased over time.

2. Analysis Method

Linear regression analysis was performed with the binary logarithm of PeCDF blood levels in *Yusho* patients as the dependent variable and the measurement year as the independent variable using the following function: $\log_2 C_{year} = a \cdot \text{year} + b$. The linear coefficient determined in this analysis is the reciprocal of the half-life. For example, if the slope is –1, the dependent variable decreases by 1 and the PeCDF blood level is halved in 1 year, thus the half-life is 1 year. If the slope is –0.1, the dependent variable decreases by 1 and the PeCDF blood level is halved in 10 years, thus the half-life is 10 years.

RESULTS

1. PeCDF Half-lives in Patients with Five or More Check-ups

Figures 1, 2 and 3 indicate the number of patients who fall into each 0.025 portion of a slope interval. The horizontal axis represents the estimated years of half-life. During the medical check-ups, PeCDF was measured using a single measuring device. Thus, we assume that there was minimal error in the measurements of PeCDF during the medical check-ups.

2. PeCDF blood level: 200 pg /g lipid or higher

Figure 1 shows a histogram with a bell-shaped distribution of the estimated half-life in the 44 patients with PeCDF blood levels of 200 pg/g lipid or higher. The estimated half-lives in 10 patients were 20–40 years, and

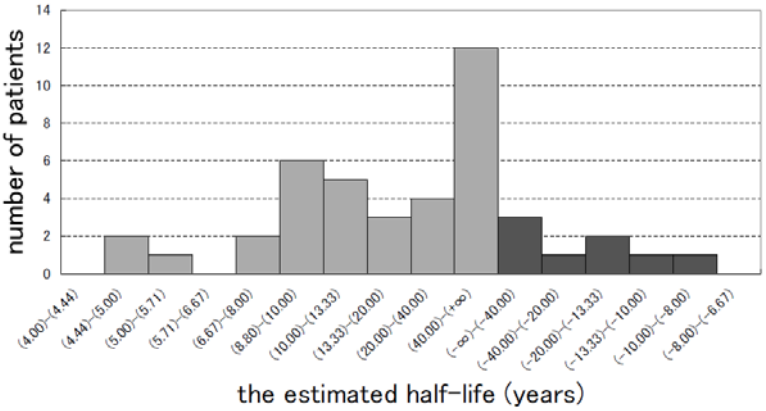

Figure 2. Distribution of PeCDF half-lives in patients with blood levels of 50–200 pg/g lipid. The vertical and horizontal axes represent the number of patients and the estimated years of half-life, respectively. Gray columns: the patients whose PeCDF levels reduced. Black columns: the patients whose PeCDF levels increased.

this range was the highest in frequency of this group. Seven patients had half-lives of 40 years or longer. Surprisingly, 13 patients (black columns in Figure 1) showed increasing PeCDF levels. From this group, 7 patients had an estimated PeCDF doubling period of 40 years or longer and 5 patients had a 20–40 year doubling period, while 1 patient had a 13–20 year doubling period.

3. PeCDF blood level: 50 – 200 pg/g lipid

There were 43 patients in this group (Figure 2). The highest in frequency was observed in the range of estimated half-lives of 40 years or longer in 12 patients, suggesting that the actual PeCDF concentration in the body may not change much. The ranges of estimated half-life of 8–10 years and 10–13 years contained 6 and 5 patients, respectively. Similar to the 200 pg/g lipid or higher PeCDF group, 8 patients showed increasing PeCDF levels (black columns in Figure 2).

4. PeCDF blood level: 20 – 50 pg/g lipid

The frequency distribution of the patients showed both increasing and decreasing tendencies in PeCDF blood levels (Figure 3). The half-lives in some patients were separated from the bulk of the group. Three patients were within the half-life range of 5–6.67 years, while 6 patients had a PeCDF doubling period of 13–20 years. The changes in this group may correspond to a state where the excretion and natural increase in PeCDF were balanced in the body.

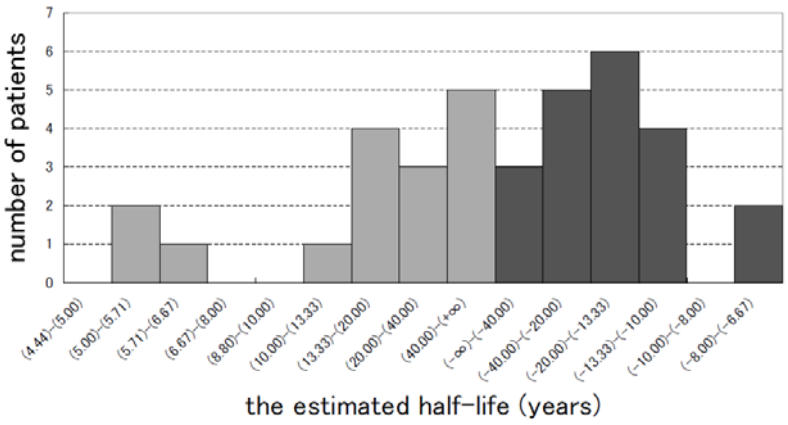

Figure 3. Distribution of PeCDF half-lives in patients with blood levels of 20–50 pg/g lipid. The vertical and horizontal axes represent the number of patients and the estimated years of half-life, respectively. Gray columns are the patients whose PeCDF levels are reduced. Black columns are the patients whose PeCDF levels increased.

DISCUSSION

The literature has reported that the half-life of PeCDF is shorter when the blood level of PeCDF is higher, and is longer when the blood level is lower[5,6]. Leung et al. estimated the half-life based on the data from five *Yusho* patients and three *Yucheng* patients, and reported that the half-life was 1.1 years in the high blood level cases and 7.2 years in the low blood level cases[7]. They concluded that the half-life of PeCDF was dependent on blood level and age. However, our results of estimated PeCDF half-lives were inconsistent with these previous reports. We calculated the half-life of PeCDF using medical check-up data from over 100 *Yusho* patients. Our results showed that the half-life of PeCDF varied among the patients. Even in the patients group with the higher PeCDF concentration (200 pg/g lipid or higher), approximately 40% of patients showed that the blood levels of PeCDF were maintained at high levels. In the patient group with a blood level of 50–200 pg/g lipid, there were two peaks in the half-lives, indicating relatively shorter or longer half-lives. Thus, we conclude that the present study revealed two types of patients as shown in Figure 4 (Patient A and B): patients whose PeCDF is decreasing at the rate that is consistent with a normal half-life (approximately seven years) and the other showing less than expected reduction in PeCDF levels over time. The results led us to think that a more complicated model is necessary to explain PeCDF excretion in humans because the present result cannot be explained with the conventional model of blood level-dependent PeCDF excretion alone. Further studies are necessary to clarify this result.

In conclusion, we have estimated the half-life of PeCDF in blood based upon measurements obtained from 2001 to 2006 medical check-ups of *Yusho*. Our data show that there is a group of patients whose PeCDF blood levels do not decrease in accordance with the reported half-life.

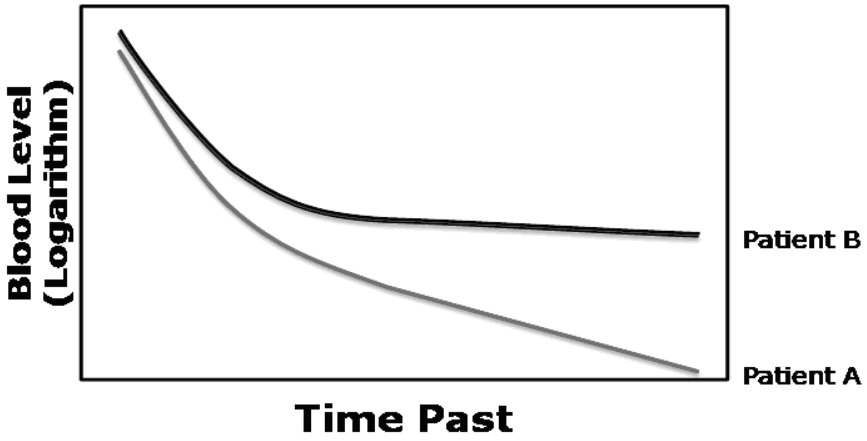

Figure 4. The schema of changes in blood PeCDF levels in two types of typical *Yusho* patients

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