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Short Communication

Short-term Changes in Cadmium in Feces, Blood and Urine after Dietary Cadmium Intake in Young Japanese Females

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Diet and smoking are the major routes of cadmium (Cd) intake[1]. In Japanese populations, dietary Cd intake is higher than in other countries, for example, China[2], Finland[3], Germany[4], Malaysia[5], and Sweden[6].

In determining a tolerable daily/weekly intake of Cd from foods and beverages, the rate of absorption of Cd from the digestive organs is a crucial factor, but it remains controversial. To design a human volunteer experiment for assessing the absorption rate, a preliminary experiment was performed to clarify short-term intake-output balance of Cd and to estimate better biological monitoring parameters for Cd absorption.

Subjects and Methods

Subjects

Three non-smoking young Japanese female volunteers (age 23–25 yr old, height 155–165 cm, weight 50–61 kg) were recruited for this study because the rate of absorption of Cd from the digestive organs was reported to be higher in females than in males, because the health effects appeared to be more severe in females than in males in cases of Itai-Itai disease, and because the body burden due to past Cd intake was expected to be small in a young population. All of the subjects were informed of the toxicity of Cd, the purpose and significance of the volunteer experiment, the benefits of the experiment for human health, and their rights as experiment volunteers. Each agreed to participate and signed the form of informed consent approved by the Ethical Review Committee, School of Medicine, Keio University. All volunteers underwent pre-experiment medical checks including hematological, serum biochemical and urinary examinations. They were also requested to complete self-administrated questionnaires to examine past illness and subjective symptoms. These medical checks showed no health problems in any of the volunteers.

Experimental outline

Two lots of rice containing 0.004 ppm of Cd (Rice L) and 0.340 ppm of Cd (Rice H) were kindly supplied by the Ministry of Agriculture, Forestry and Fisheries. Considering nutritional balance and Cd concentrations in 519 foods and beverages previously measured[7], a registered dietitian chose foods and beverages with minimal levels of Cd for side dishes, and made two kinds of meals, Meal L consisting of Rice L as the staple food and the side dishes, and Meal H consisting of Rice H and the same side dishes.

Three volunteers were requested to eat the same amount of Meal L (7.50 ± 2.84 μg Cd/d) for 12 experimental days, and the same amount of Meal H (52.44 ± 2.84 μg Cd/d) from the 13th day to the 17th day. Cd-free beverages were freely drunk. During the 1st to the 17th day, all urine and feces excreted and meals ingested from 0 to 24 o'clock were collected, and blood was sampled approximately 1 hour after breakfast on days 0, 3, 6, 9, 11, 13, 16 and 19 in metal-free heparinized syringes and glass tubes.

Sample treatment and Cd analysis

Cd intake from the daily meals (Cd-I), Cd in feces (Cd-F), Cd in urine (Cd-U) and Cd in blood (Cd-B) were measured by means of a flameless atomic absorption spectrophotometer (AAS) (Hitachi Z-5010, Hitachi, Japan)[8]. Meals or feces and highly purified water were put together into a food mixer and were mingled for more than 15 or 5 min. The mixed samples were dried by the freeze-drying method, and 50 mg of the dried samples was digested with 2 m*l* of highly purified nitric acid (Suprapur Nitric Acid 65%, Merck) using the microwave wet-ash technique (EthosPlus/MDR2, Milestone Inc, USA). The aliquot was diluted, and Cd was determined by flameless AAS. After 10-time dilution of blood with 0.2% Triton X and 4-time dilution of urine with 0.5% highly purified nitric acid, the samples were put directly into the flameless AAS.

The quality of the Cd analysis was certified by the 28th intercomparison programme for occupational-medical and environmental-medical toxicological analyses in biological materials performed by the German Society for Occupational and Environmental Medicine e.V.

Results

Cd-I, Cd-F, Cd-U and Cd-B during the experimental

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Table 1. Dietary Cd intake and Cd in biological specimens

Day	Cd-I (μg/d)	Cd-F (μg/d) M ± SD	Cd-B (μg/*l*) M ± SD	Cd-U (μg/d) M ± SD
0	–	–	0.112 ± 0.060	–
1	9.0	–	–	0.315 ± 0.174
2	10.5	19.0 ± 11.8	–	0.271 ± 0.104
3	3.0	22.8 ± 13.6	0.108 ± 0.066	0.323 ± 0.231
4	6.7	14.0*	–	0.310 ± 0.126
5	8.4	6.8*	–	0.291 ± 0.127
6	9.0	19.6 ± 7.2	0.091 ± 0.055	0.359 ± 0.131
7	10.5	15.8 ± 15.1	–	0.274 ± 0.023
8	3.0	11.8 ± 7.1	–	0.342 ± 0.097
9	6.7	8.4 ± 4.4	0.076 ± 0.049	0.382 ± 0.123
10	8.4	9.3 ± 5.3	–	0.360 ± 0.070
11	9.0	7.6 ± 3.6	0.076 ± 0.052	0.376 ± 0.085
12	10.5	9.6 ± 2.0	–	0.290 ± 0.104
13	48.0	4.7 ± 1.9	0.076 ± 0.052	0.272 ± 0.155
14	51.6	13.9 ± 10.5	–	0.318 ± 0.132
15	53.3	33.6 ± 16.1	–	0.219 ± 0.100
16	53.9	24.1 ± 12.6	0.087 ± 0.054	0.256 ± 0.100
17	55.4	23.8 ± 11.6	–	0.335 ± 0.082
18	–	–	0.102 ± 0.053	–

– : not examined. * : n=1. Cd-I, Cd-F, Cd-B, Cd-U : See text.

period are shown in Table 1 and their changes are illustrated in Figs 1a–d. During the 12-d intake of Meal L, Cd-F gradually decreased (Fig. 1b). The average amount of Cd-F of three volunteers from the 9th to the 13th day was 7.24 μg/d (SD 3.24), which was almost the same amount of Cd-I as from Meal L. Cd-B in each volunteer decreased from 1.8, 0.8, and 0.7 μg/*l* on day 0 to 1.3, 0.5 and 0.4 μg/*l* in the morning of the 13th day, corresponding to ca. 25, 35 and 48% reductions (Fig. 1e), and was almost completely stable from the 9th to the 13th day (Fig. 1d). The trend in Cd-U reduction during the intake of Meal L was unclear and the variation in Cd-U was larger than that in Cd-B and Cd-F in all three volunteers. (Fig. 1c)

With the intake of Meal H from day 13 until day 17, Cd-B sharply increased toward the Cd-B on day 0, and Cd-F also clearly increased with a one- or two-day delay. Cd-U seemed to increase from day 15 with a two-day delay (Fig. 1c).

Discussion

The major routes of exposure to Cd are food intake, e.g. crops and shellfish, and smoking[1]. In a non-Cd polluted area in Japan, rice as well as shellfish is the major source of Cd intake. In Asian and Western countries, the amount of Cd-I was estimated to be smaller than 20 μg/d except for Korea[9]. In Japan, however, Watanabe *et al.*[10] calculated that Cd-I was 25.5 μg/d in 1991–97, though Cd-I in this period was two-thirds of that (37.5 μg/d) in 1977–1981. Cd-I from Meal H used in this study was 2 times higher than that detected by Watanabe *et al.*[10], but not extraordinarily high because Cd in Rice H was lower than the guideline level of Cd for rice, 0.4 ppm, distributed to general food markets by the Japanese Government.

Changes in Cd-F during the intake of Meal L suggest that the short-term input-output balance of Cd seems to become almost even after ca. 10-d intake of meals containing a low and steady level of Cd, though the inter-daily or inter-individual variation is not negligible. As far as we know, an input-output balance study of Cd like this has not been published in both occupational and environmental settings.

Cd-B and Cd-U were used to estimate recent and chronic occupational exposure to Cd, respectively[1, 11]. In this study, Cd-B responded in a timelier and quicker fashion than Cd-U to the change in Cd-I. This finding clearly shows that Cd-B is a better biological monitoring index of the short-term fluctuation in dietary Cd intake than Cd-U in a non-occupationally Cd-exposed population.

Because the number of study subjects was only three and all of them were young females with an undoubtedly small body burden of Cd, we should pay enough attention

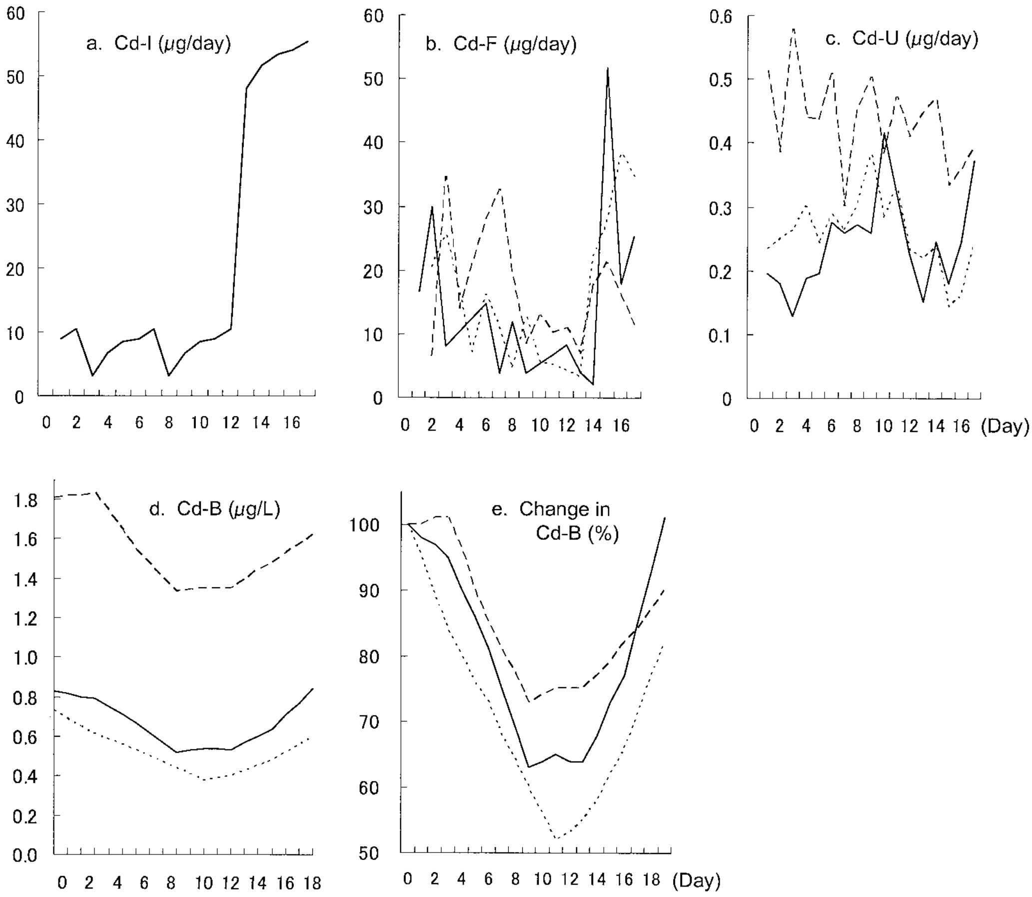

Fig. 1. Change in Cd-I, Cd-F, Cd-U, and Cd-B in 3 young female volunteers.
Cd-I, Cd-F, Cd-U, Cd-B: See text.

when we apply these results to populations with specific characteristics such as those of aged females, occupationally Cd-exposed workers, and the general population in heavily Cd polluted areas.

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