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Association Between Lifetime Cadmium Intake and Cadmium Concentration in Individual Urine

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In Japan, for cadmium (Cd)-polluted and non-polluted regions, rice represents approximately 1/2-2/3 of life-time Cd intake (LCd) (Iwao et al. 1981). The establishment of tolerable Cd concentrations in rice (RCd) is of particular importance. Our research group developed a model (Nogawa et al. 1989), and undertook studies in the Cd-polluted Kakehashi River basin to estimate tolerable limits of LCd (Hochi et al. 1995). The values calculated using various health impact indices were found to be approximately 2.0 g. Using the same method in the Jinzu River basin, the endemic region of Itai-itai disease, the values of 1.3-1.5 g for men and 1.5-1.6 g for women were calculated (Chiyoda et al. 2003).

On the other hand, investigators in the field have questioned the validity of this type of calculation for LCd as proposed by us. Their major objections to its use are that the fact that RCd fluctuates from year to year in individual rice paddies which makes it an inappropriate index of Cd exposure, and that use of the mean Cd concentration in rice collected from a hamlet as RCd ingested by the total inhabitants of that hamlet may not be suitable for the calculation of LCd at the individual level. Against this background, we undertook the present study to investigate the relationship between calculated LCd and the corresponding individual urinary Cd concentration (UCd).

MATERIALS AND METHODS

In 1981 and 1982 health examinations were conduced for all inhabitants over 50 years of age residing in the Kakehashi River basin of Ishikawa Prefecture. The 3164 participants consisted of 1419 men and 1745 women (participation rate of 91.0 %) in the Cd-polluted area and 294 participants (133 men, 161 women, participation rate of 94.0 %) in the non-polluted area. Among these, 1815 inhabitants (865 men, 950 women) who had either resided in their present hamlet since birth or who had moved into the area from a non-polluted one were selected as the subjects living in the Cd-polluted area, and all 289 inhabitants who had resided only in the non-polluted areas in the present study. Moreover, 1475 inhabitants (556 men, 919 women) over 50 years of age in two areas located in the Noto Peninsula of Ishikawa Prefecture were selected as the non Cd exposed controls. Because these areas had no history of specific Cd-pollution or Cd-exposure, the inhabitants' intake of Cd mainly derived from the foods obtained from the general environment. The data concerning age, history of residence and type of rice ingested were gathered on the basis of self-reported replies and confirmed afterwards by interview.

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Morning urine specimens collected from the participants were divided into several test tubes. To measure Cd samples were acidified by adding concentrated HNO_3. Samples were stoked at -20 ℃ until analysis. UCd was measured by graphite-furnace atomic absorption spectrometry as described Kido et al. 1984. Urinary creatinine concentration was determined by the Jaffe reaction method (Bonsnes and Taussky, 1945).

In 1974, rice was collected from the all farmers in the polluted 23 hamlets, and 35451 rice bags were stored in warehouses. According to the number of rice bags collected from each polluted hamlet, random samples were extracted before being assayed for Cd. RCd was measured by atomic absorption spectrometry after wet ashing with H_2SO_4, HNO_3, $HClO_4$ and extraction with ammonium pyrrolidine dithiocarbamate-methyl-isobutyl ketone (APDC-MIBK) (Nakashima et al. 1997).

LCd was based on the model of Nogawa (Nogawa et al. 1989) as followed;
(mean RCd per hamlet × 333.5 g + 34 μg) × 365 days × number of years of residence in present hamlet + 50 μg × 365 days × number of years living in non-polluted areas.

In the model, 333.5 g is the daily mean rice intake and 34 μg is the daily mean Cd intake from foods other than rice of the Cd-polluted Kakehashi River basin in 1970 (Ishikawa Prefecture 1976). 50 μg is the daily mean Cd intake in non-Cd-polluted regions in Japan (Yamagata 1978). The method of estimating LCd in Kakehashi River basin was the collection of a duplicate sample of the meals consumed.

UCd was expressed after correction with creatinine (cr). The values of LCd and UCd were transformed to logarithmic values.
Correlation coefficients were calculated between UCd and LCd. Moreover, the tolerable level of UCd was calculated, substituting 2.0 g which was the tolerable value of LCd calculated in our studies into the regression formula.

RESULTS AND DISCUSSION

In Table 1 are listed the number of inhabitants, their age, LCd and UCd in the Cd-exposed group and non-exposed group (Non-exposed 1) in the Kakehashi River basin and the other non-exposed group (Non-exposed 2). All values are expressed as geometric means and geometric standard deviations (arithmetic means in the case of age), with minimum and maximum values calculated according to sex.

Correlation coefficients and regression formulae between LCd and UCd calculated are shown in Table 2. Significant correlation coefficients of 0.61 and 0.59 were obtained in the men and women, respectively. When determining UCd with a substitution of a LCd of 2.0 g in the regression formula, values of 3.7μg/g cr in the men and 5.9 μg/g cr in the women obtained.

Shimbo and colleagues collected spot urine and peripheral blood specimens, and duplicate food samples eating in 24-h from 607 non-smoking, non-drinking adult women in 30 survey sites all over Japan in 1991-1998. They investigated the correlations between the respective Cd concentrations (Shinbo et al. 2000). They noted that Cd concentration in blood (BCd) correlated closely with UCd, and both BCd and UCd with Cd concentration in foods, and concluded that both BCd and UCd can serve as biomarkers of environmental Cd exposure.

Table 1. Differences of life-time cadmium intake and cadmium concentration in urine among Cd-polluted and non-polluted (Non-polluted 1) areas in the kakehashi River basin and the other non-polluted areas (Non-polluted 2) according

				LCd (g)				UCd (μg/g cr)			
Sex	Subjects	N	Mean age (y.o.	GM	GSD	Min	Max	GM	GSD	Min	Max
Males	Cd-exposed	865	62.4	3.119	1.496	1.016	7.516	5.33	1.79	0.82	49.55
	Non-exposed (1)	130	62.5	1.127	1.151	0.912	1.644	2.12	1.69	0.55	8.57
	Non-exposed (2)	556	66.6	1.205	1.138	0.912	1.66	2.48	1.8	0.21	15.92
Females	Cd-exposed	950	63.7	3.02	1.503	1.107	7.987	8.45	1.7	0.91	261.22
	Non-exposed (1)	159	63.9	1.151	1.169	0.912	1.734	3.12	1.7	0.41	18.41
	Non-exposed (2)	919	65.3	1.183	1.138	0.912	1.644	3.91	1.78	0.1	30.62

LCd: Life-time Cd intake; UCd: Urinary Cd concentration; N: Number of subjects examined; GM: Geometric mean; Min: Minimam value; Max: Maximum value; Cd-exposed: Subjects living in the Cd-polluted Kakehashi River basin; Non-exposed (1): Subjects living in non-polluted area in the Kakehashi River basin; Non-exposed (2): Subjects living in the other non-polluted areas; The values of life-time Cd intake and urinary Cd concentration were transformed to logarithmic values.

Table 2. Correlation coefficients with life-time cadmium intake and cadmium concentration in urine and allowable values of urinary cadmium concentration by sex.

Sex	N	Correlation coefficient	Regression formula	UCd (μg/g cr) *
Males	1551	0.61 c	$y = 0.748x + 0.344$	3.7
Females	2028	0.59 c	$y = 0.723x + 0.551$	5.9

*: UCd value was calculated that a LCd of 2.0 g was substituted in the regression formula. N: Number of subjects examined; c: $p < 0.001$; The values of life-time Cd intake and urinary Cd concentration were transformed to logarithmic values.

Kido and coworkers reported the study on RCd and LCd obtained from the population in the same area, the Kakehashi River basin. These researchers calculated the mean RCd in individual hamlets and LCd from the mean number of years of residence in Cd-polluted hamlets, and reported the finding of high correlations (0.93 in men, 0.88 in women) between LCd in 12 groups divided according to the level of mean UCd and residence time in polluted area (Kido et al. 1992). Although this was the first valuable study to focus on the association between these two variables, the individual values for LCd and UCd used at that time were not provided.

In the present study, to the study group of Kido (Kido et al. 1992), data pertaining to the residents of other non-polluted regions in the same prefecture (Non-exposed 2) were recently added. Using individual LCd calculated using the formula of Nogawa (Nogawa et al. 1989), high correlation coefficients ($p < 0.001$) of 0.61 in men and 0.59 in women were obtained with UCd of the corresponding individuals. The correlation coefficients in the present study seemed to be lower than value in Kido's study, since degree of freedom in the present study was much larger than that in the Kido's study. We thought the correlation coefficients were high enough to demonstrate the close relationship between LCd and UCd. Furthermore, when correlation coefficients between LCd and UCd in each Cd-polluted hamlet on individual basis, out of 23 hamlets significant correlation coefficients were obtained for men and women in 12 and 9 hamlets, respectively. Accordingly, these results demonstrate clearly that LCd of the inhabitants of a hamlet can be calculated by using the mean RCd in that hamlet. Moreover, using the obtained regression formula to calculate UCd corresponding to the 2.0 g, which we previously determined to be the tolerable limits of LCd (Nogawa et al. 1989; Hochi et al. 1995), values of 3.7 μg/g cr and 5.9 μg/g cr were obtained for the men and women, respectively. These values are in close agreement with the tolerable UCd of 1.6-3.0 μg/g cr for men and 2.3-4.6 μg/g cr for women calculated by Hayano in the inhabitants of polluted regions in the Kakehashi River basin (Hayano et al. 1996).

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