



Epidemiology

Estimation of dietary intake of cadmium from cadmium in blood or urine in East Asia

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ABSTRACT

Background and aim: Cadmium (Cd) is an ubiquitous environmental toxic pollutant. As daily foods are an almost exclusive source of exposure for general populations, it is of public health importance to know the level of dietary intake of cadmium (Cd-D). The purpose of this study is to examine whether Cd in blood (Cd-B) or urine (Cd-U) correlates with Cd-D in East Asia, and in case it is, whether it is possible to estimate Cd-D from Cd-B or Cd-U. It should be added that the measurement of Cd-D is quite hand-consuming in practice.

Materials and methods: Literature was retrieved for publication on Cd-B and Cd-U in combination with Cd-D. Twenty three data sets thus obtained for East Asia were subjected to regression analysis to investigate the possibility to estimate Cd-D from Cd-B or Cd-U.

Results: In Japan and Korea, large correlation coefficients ($p > 0.7$) were observed between Cd-B and Cd-D, as well as between Cd-U and Cd-D. In China, the coefficient was > 0.7 between Cd-B and Cd-D. Furthermore, correlation was significant for Cd-B and Cd-D, as well as Cd-U and Cd-D, when 19 sets for Japan, Korea and China were combined for analysis.

Discussion: Major reasons for successful analysis may be predominant use of women-based data. Women have been less smoking than men in East Asia, and possible confounding effects of smoking on Cd exposure might be minimized.

Conclusion: Based on significant correlations, Cd-D can be estimated from Cd-B or Cd-U in East Asia.

1. Introduction

Cadmium (Cd) is a toxic element of world-wide concern for years, because it has chronic toxicities on renal tubules and then disturbs mineral metabolism in the bones [1,2]. Further problems are that this element is ubiquitous in the environment [3]. With regard to general population exposure, Cd in daily foods (Cd-D) is an almost exclusive source of exposure. The Joint FAO/WHO Expert Committee on Food Additives (JECFA) adopted the provisional tolerable monthly intake (PTMI) of 25 μg Cd/kg body weight /month [4], which suggests the importance of information on Cd-D levels in public health. Smoking and passive smoking are additional source of Cd exposure [5]. The relationship of Cd-B and Cd-U may be modified also by, e.g., iron insufficiency of the subjects [6].

Two methods [7] of food duplicate sample collection (followed by instrumental analysis for Cd) and market basket sampling (coupled with a database on Cd contents in various food materials) have been

often employed. In the practice to measure Cd-D, however, food duplicate collection is hand-consuming and nerve-taxing for sample donors, and establishment of a database on Cd in various food items are also not an easy task for the market basket method.

In a previous study in Japan, a statistically significant relationship with Cd-D ($\mu\text{g}/\text{day}$) was detected for Cd-B ($\mu\text{g}/\text{l}$) and also for Cd-U [as corrected for creatinine; Cd-Ucr ($\mu\text{g}/\text{g}$ cr)] [8], and Cd-D was successfully estimated from Cd-B as well as Cd-U [8]. As Cd-B and Cd-U have been popularly measured in environmental health as biomarkers to examine possible Cd-D intake due to pollution of the environment with Cd [1], estimation of Cd-D based on Cd-B or Cd-U may facilitate to obtain valuable Cd-D data in environmental health practice.

In the present study, investigation was conducted to examine whether the same strategy can be applied in other Asian countries, especially in East Asia.

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Table 1
Dietary intake of cadmium, cadmium in blood and cadmium in urine by area and location.

| Area No. | Area | Authors | Year | Ref. no. | Location | U/R ^a | No ^b | Cd-D (µg/day) | Cd-B (µg/l) | Cd-U (µg/g cr ^c) | Notes |
|----------|-----------------|----------------------------|------------|----------|-------------------|------------------|------------------|-------------------|-------------------|------------------------------|------------------------------------|
| 1 | Japan | Ikeda et al. | 2000 | [9] | Hokkaido | R | 51 | 18.7 | 2.17 | 5.69 | Women, mostly non-smoking |
| 2 | Japan | Ikeda et al. | 2000 | [9] | Tohoku | U + R | 145 | 20.7 | 1.42 | 3.16 | Women, mostly non-smoking |
| 3 | Japan | Ikeda et al. | 2000 | [9] | kanto-Tokai | U + R | 123 | 23.0 | 1.80 | 3.42 | Women, mostly non-smoking |
| 4 | Japan | Ikeda et al. | 2000 | [9] | Hokuriku | U + R | 75 | 53.2 | 3.74 | 7.78 | Women, mostly non-smoking |
| 5 | Japan | Ikeda et al. | 2000 | [9] | Kinki | U + R | 83 | 23.4 | 1.02 | 2.4 | Women, mostly non-smoking |
| 6 | Japan | Ikeda et al. | 2000 | [9] | Chu-shikoku | U + R | 63 | 27.0 | 2.02 | 5.27 | Women, mostly non-smoking |
| 7 | Japan | Ikeda et al. | 2000 | [9] | Kyushu-Okinawa | R | 67 | 20.9 | 1.71 | 4.1 | Women, mostly non-smoking |
| 8 | Korea | Moon et al. | 1999 | [10] | Seoul | U | 18 | 14.4 | 1.30 | 2.25 | Women, mostly non-smoking |
| 9 | Korea | Moon et al. | 1999 | [10] | Pusan | U | 38 | 24.8 | 1.40 | 2.16 | Women, mostly non-smoking |
| 10 | Korea | Moon et al. | 1999 | [10] | Chunan | U | 17 | 18.49 | 1.22 | 1.4 | Women, mostly non-smoking |
| 11 | Korea | Moon et al. | 1999 | [10] | Haman | R | 34 | 23.48 | 1.51 | 3.05 | Women, mostly non-smoking |
| 12 | Korea | Huang et al. | 2011 | [11] | 6 Districts | U + R | 643 ^d | 5.72 | 1.22 | 0.95 | Men and women including smokers |
| 13 | China | Cai et al. | 1995 | [12] | Jiangxi Province | U + R | 124 | 48.4 | 1.34 | 3.03 | Men and women including smokers |
| 14 | China | Watanabe et al. | 1998 | [13] | Shandong Province | U + R | 100 | 6.18 | 0.39 | NA ^e | Non-smoking women |
| 15 | China | Watanabe et al. | 2000 | [14] | Shaanxi Province | U + R | 150 | 6.06 | 0.46 | 2.83 | Non-smoking women |
| 16 | China | Zhang et al., Ikeda et al. | 1997, 2000 | [15,16] | Beijing | U | 50 | 9.8 | 0.73 | 2.01 | Non-smoking women |
| 17 | China | Zhang et al., Ikeda et al. | 1997, 2000 | [15,16] | Shanghai | U | 50 | 8.7 | 0.74 | 1.67 | Non-smoking women |
| 18 | China | Wang et al. | 2012 | [17] | Tianjin etc. | U | 120 | 15.5 | 0.78 | 0.34 | Men; smoking habits not described. |
| 19 | China | He et al. | 2013 | [18] | Shanghai | U | 207 | 3.28 ^f | 0.31 ^f | 1.54 ^e | Men and women including smokers |
| 20 | South-East Asia | Ikeda et al. | 1996 | [19] | Tainan | U | 52 | 10.1 | 1.11 | NA ^e | Non-smoking women |
| 21 | South-East Asia | Moon et al. | 1996 | [20] | Kuala Lumpur | U | 49 | 7.31 | 0.71 | NA ^e | Non-smoking women |
| 22 | South-East Asia | Zhang et al. | 1998 | [21] | Manila | U | 45 | 14.2 | 0.47 | NA ^e | Non-smoking women |
| 23 | South-East Asia | Zhang et al. | 1999 | [22] | Bangkok | U | 52 | 7.09 | 0.41 | 1.40 | Women, mostly non-smoking |

^a U; urban area; R; rural area.

^b No. of participants.

^c cr: creatinine.

^d Market basket Moment Moment method was applied in case of Cd-D; Cd-B & Cd-U were originally GM.

^e NA: not available.

^f Medians.

2. Materials and methods

Literature was sorted by use of PubMed with three keywords of dietary cadmium intake (Cd-D), cadmium in blood (Cd-B) and cadmium in urine (Cd-U). The article file thus obtained was supplemented with references in previous publications. The target areas were East and South-East Asia, i.e., China, Japan, Korea, Thailand, the Philippines and Malaysia, where people depend basically on rice as the source of energy for daily life. Selection of study sites was by chance of availability. The data on residents in Cd-polluted areas were excluded. Twenty-three sets [of Cd-D and Cd-B (together with Cd-U as far as available)] thus obtained are listed in Table 1, of which 7, 5, 7 and 4 sets were for Japan [9], Korea [10,11], China [12–18] and South-East Asia [19–22], respectively. The survey in Japan was originally conducted at 30 locations, and 7 regional values {combining 1 to several locations to make up a region [9]} were taken in the place of locations to balance with other areas in the set numbers. Geometric means (GMs) for the locations were also given in Table 1; the GM values were estimated by use of the moment method [23] when necessary. One and 3 GM Cd-U values were not available for China and South-East Asia, respectively (Table 1). Only Cd-U levels as corrected for creatinine concentration (i.e., Cd-Ucr) were available in some reports. Thus Cd-Ucr was employed in the present analysis, despite the recommendation by Barr et al [24] to use non-corrected observed Cd-U values.

For statistical evaluation, the relation of Cd-B (or Cd-U) with Cd-D was presented as a regression line for which Cd-B (or Cd-U) was taken as the independent variable and Cd-D as the dependent variable. Two regression lines were compared for statistical difference in intercepts, slopes, and correlation coefficients after Ichihara [25].

A preliminary analysis revealed that logarithmic conversion of the data did not improve the statistical significance in analysis results. With regard to instrumental analysis of biological materials, early time studies {e.g., [9]} employed flame atomic absorption spectrometry and then graphite furnace atomic absorption spectrometry, whereas inductively coupled-plasma mass spectrometry was used in later studies {e.g., [17]}. The data were evaluated together as it is known that the results obtained by these analytical methods are compatible to each other [26,27] with exception of ICP-MS-measure Cd-U with no removal of molybdenum from urine [28].

3. Results

The results of regression analysis by area are summarized in Table 2 in terms of intercepts, slopes, and correlation coefficients. P values were also given to show statistical significance of the correlation.

The P values were < 0.05 in cases of Eqs. 1B and 3B. In addition, correlation coefficients were > 0.7 in cases of Eqs. 1U, 2B and 2U. Knowing that P for $r = 0.7$ would be < 0.05 when the number (n) of available sets is ≥ 8 , the lack of statistical significance may be due to the small number of sets (n = 5–7) available for evaluation. Thus, both Cd-B and Cd-U may correlate with Cd-D in Japan, Korea and China, although Cd-U might correlate only poorly with Cd-D in China ($r = 0.41$, Eq. 3U).

The regression line equations were different among the three areas; statistical evaluation showed that intercepts, slopes or both were significantly different ($p > 0.05$). Nevertheless, combination of sets for Japan, Korea and China (n = 19) resulted in significant correlations ($p < 0.01$) of both Cd-B (Eq. 4B; $r = 0.77$) and Cd-U (Eq. 4U; $r = 0.65$)

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