MINI REVIEW

Time trend of cadmium intake in Korea

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Received: 12 October 2015 / Accepted: 9 February 2016 / Published online: 22 February 2016 - The Japanese Society for Hygiene 2016

Abstract

Objectives The aim of this study was to elucidate past and current levels of cadmium (Cd) intake among the general populations in Korea.

Methods For this purpose, publications reporting dietary intake of cadmium (Cd-D), cadmium concentration in blood (Cd-B) and that in urine (Cd-U) in Korea were retrieved through literature survey for a period from 1975 to 2015.

Results In practice, 9, 21 and 14 articles were available on Cd-D, Cd-B and Cd- U_{cr} (Cd-U as corrected for creatinine concentration), respectively. Linear regression analyses of the reported values as a function of years (i.e., the year when each survey was conducted) showed steady decreases in all of the three exposure markers of Cd-D, Cd-B and Cd-U_{cr}. Factors possibly contributing for the reduction were discussed including the government-set guideline of 0.2 mg/kg for rice and changes in food habits among general populations.

Conclusions There have been steady decreases in Cd-D, Cd-B and Cd-Ucr. The current estimates for Cd-D, Cd-B and Cd-U_{cr} were 6.0–7.4 μ g/day, 0.73–0.83 μ g/L and $0.60 - 0.95$ µg/g cr, respectively.

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Keywords Cadmium in diet - Cadmium in blood - Cadmium in urine - General population - Korea - Time trend

Introduction

It was previously observed that cadmium (Cd) contents in rice to be consumed in Korea were among the high group in rice-dependent Asian areas $[1, 2]$ $[1, 2]$ $[1, 2]$ $[1, 2]$. In fact, surveys by food duplicate collection [\[3](#page-8-0)] in two large cities in Korea in 2000 disclosed that the Cd intake was at the level of 21 µg/day, which was the second highest among 13 areas surveyed in Asia [[4\]](#page-8-0). Cd has insidious toxicities primarily on the renal tubules and then bone tissues after long-term exposure through daily foods [\[5–7](#page-8-0)]. Consumption of rice, a traditional staple food in Korea [\[8](#page-8-0)], indeed accounted for 23 % $[9]$ $[9]$ to 25 % $[10]$ $[10]$ of total dietary Cd intake. Thus, current dietary Cd intake levels in combination with chronological changes apparently deserve studies from environmental health viewpoints.

The present study was initiated to obtain an answer to this question of public health importance. The results will be presented in this article. A preliminary report has been published [[11\]](#page-8-0).

Materials and methods

All data were cited from existing articles, and approval of the study by an institutional review board was considered to be unnecessary.

Two databases of PubMed and KoreaMed (established by Korean Association of Medical Journal Editors) were searched for publications with two keywords of Korea and

^a NA not avaiable: Cd-D was estimated based on other food intake data such as national statistics and numbers of cases were not available

 b Adjusted for a body weight of 63 kg for a total of adult men and women [[16](#page-8-0)]</sup>

 \degree Adjusted for a reported mean body weight of 56.4 kg for adult women [[16](#page-8-0)]

^d Year of publication

cadmium. In practice, 22 and 25 articles, respectively, were identified as those with data on 1; cadmium in daily (24-h) foods (Cd-D in lg/day or lg/kg body weight/day), 2; cadmium in peripheral blood (Cd-B in μ g/L), or 3; cadmium in urine or preferably as cadmium in urine as corrected for creatinine concentration (Cd-U and Cd-U_{cr}). The articles retrieved through KoreaMed were limited to those either in English, or in Korean with an English abstract. However, publications from Korean government were written only in Korean. Other articles in English were also cited as necessary.

Smirnov's test for extreme value and Pearson's correlation coefficient were employed as necessary. In some articles, Cd-D, Cd-B or Cd-U_{cr} values were provided in terms of arithmetic means (AMs) and arithmetic standard deviations (ASDs) [or arithmetic standard errors (ASEs)], and the geometric mean values (GMs) were calculated by use of the moment method $[12]$ $[12]$ for uniformity in the data compilation, considering that Cd-D, Cd-B and Cd- U_{cr} may distribute log-normally rather than normally.

It should be noted that the reports cited were limited to those on areas where there was no known Cd pollution. In studies on Cd-exposed residents in vicinity of abandoned mines and non-exposed control subjects (e.g., [\[13–15](#page-8-0)]), the values for the controls were included in the analyses whereas the exposed cases were not.

Survey years were cited as described in the original publications. In case the survey year was not given, the year of publication was taken in the place.

In some reports, Cd-D was presented in terms of µg/day. To convert to the µg/kg body weight/day basis, an average body weight of 63 kg was assumed for a total of adult men (69.6 kg) and women (56.4 kg) [\[16](#page-8-0)].

In collecting Cd-D data on China, attention was paid to limit to rice-depending southern part of China. It is known that people in the northern half depend primarily on wheat rather than rice.

In calculating the estimates for 2000 and 2015 based on the regression equations established in this work, intercepts

Table 2 Cadmium in peripheral blood

Table 2 continued

Originally the AM and ASD (or ASE) were given, from which GM was estimated by the moment method [[12](#page-8-0)]

^b Year of publication in place of the survey year

 C MHWAK Ministry of Health, Welfare and Family Affaires, Korea

^d KNHEBE Korean National Human Exposure and Bio-monitoring Examination

^e KNHANES Korean National Health and Nutrition Examination Survey

^f KEHSCA Korean Environmental Health Survey in Children and Adolescents

and slopes were taken down to several digits below the decimal points. This was necessary because the multipliers were in the order of thousand (i.e., 2000 and 2015).

Results

Data retrieved from 1980 to 2015 were summarized in three tables, one each for Cd-D (Table [1](#page-1-0)), Cd-B (Table [2\)](#page-2-0) and $Cd-U_{cr}$ (Table [3\)](#page-4-0). The scale of studies were various when expressed by number of subjects studied, i.e., from less than 20 to nearly 5000. In some Cd-D studies, Cd-D was estimated taking advantage of e.g., national data on food consumption and the number of cases studied was not available (shown as NA in Table [1\)](#page-1-0).

Time trend in Cd-D

Search for publication on Cd-D gave 9 articles including 3 Cd-D estimation reports $[1, 11, 20]$ $[1, 11, 20]$ $[1, 11, 20]$ $[1, 11, 20]$ $[1, 11, 20]$ $[1, 11, 20]$ $[1, 11, 20]$. The surveys were conducted in 10 individual regions together with one whole country survey. The articles are summarized in Table [1,](#page-1-0) in which GM Cd-D values were given both on per day and per kg body weight per day bases, together with years of survey and the number of cases studied. The first report was published in 1980 [\[17](#page-8-0)] and the latest one was in 2011 [\[24](#page-8-0)].

When the data collected were listed in the order of year of survey (Table [1\)](#page-1-0), it became clear that no data were available for about 15 years from 1980 till 1994 (the first reported value was an estimate). Nevertheless, the two parameters of survey year and Cd-D closely related to each other (Fig. [1\)](#page-5-0) when the correlation was examined for 1980 to 2011. The regression analysis showed a negative (i.e., $\langle 0 \rangle$ slope indicating a decreasing trend as a function of time (see Eq. 1 in Table [4](#page-5-0) for the equation of the regression line). The correlation coefficient ($r = -0.586$) was significant ($p < 0.01$)

Time trend in Cd-B

In total, 21 articles were available on Cd-B (Table [2](#page-2-0)). Many of the cited articles reported Cd-B on more than one group of subjects, and accordingly Cd-B in 38 groups of people in non-polluted areas were available after exclusion of duplication in reporting such as men and women separately and also in combination.

The data were reported first in 1985 [\[25](#page-8-0)] and the reporting continued till present [\[15](#page-8-0)]. Perusal of data following the flow in time disclosed that there was an exceptionally high value of 5.8 lg/L reported in late 1980s [[27\]](#page-8-0) (Table [2](#page-2-0)), but the general trend of decrease was observable till recent years. The slope of the calculated regression line (Fig. [2\)](#page-6-0) was negative and the correlation coefficient, $r = -0.575$, was statistically significant ($p < 0.01$) (Eq. 3 in Table [4](#page-5-0)) When the Cd-B of 5.8 μ g/L reported in 1987 [\[27](#page-8-0)] (Table [2](#page-2-0)) was taken as an outlier to be excluded ($p<0.01$ by Smirnov' test for extreme value), recalculation excluding the case gave an substantially greater absolute value for r of $|0.625|$ (with a negative slope of -0.0369 µg/L/year) to show closer clustering around the regression line although the slope became less steep (Eq. 4 in Table [4\)](#page-5-0).

Time trend in Cd-U_{cr}

Search for $Cd-U_{cr}$ was also rewarding, and 14 articles reporting Cd-U_{cr} values were identified. After exclusion of duplication cases (as described above), 28 groups with Cd- U_{cr} values were available (Table [3](#page-4-0)). Reading through the data following the time suggested that the values in excess of $2 \mu g/g$ cr were found mostly in earlier years (e.g., before 2000) and typically in coastal areas such as Haman (e.g., [[18,](#page-8-0) [33](#page-9-0)]). Reversely, Cd-U_{cr} was often around 1 μ g/g cr or below in the years after 2010. A regression analysis showed a timedependent decrease also for $Cd-U_{cr}$ (Eq. 5 in Table [4](#page-5-0)). Scattering around the regression line was however rather

References	Ref. No.	No. of cases studied	$Cd-U_{cr}$ (μ g/g cr) (GM)	Year of survey	Note
Hwang et al.	$[27]$	72	2.5^{a}	1987 ^b	Women
Lee and Kim	$[41]$	77	1.99	1992^b	No correction for CR
Yeon et al.	$[29]$	160	1.19	1992 ^b	Men
Ibid.		243	1.87	1992^b	Women
Ibid.		403	1.60	1992^b	$Men + women$
Moon et al.	$[18]$	18	2.25	1994	Seoul
Ibid.		38	2.16	1994	Pusam
Ibid.		17	1.40	1994	Chunan
Ibid.		34	3.05	1994	Haman
Ibid.		107	2.26	1994	Total
Lee et al.	$[42]$	426	0.74	1997	School children
Ibid.		250	1.29	1999	School children
Ibid.		249	1.48	2000	School children
Moon et al.	$[19]$	38	1.69	2000	Children
Ibid.		38	1.56	2000	Mothers
Watanabe et al.	$[21]$	33	2.54	2003-2004	Kindergarten children in Seoul
Ibid.		37	0.99	2003-2004	Kindergarten children in Jeju City
Ibid.		18	1.01	2003-2004	Kindergarten children in Jeju village A
Ibid.		20	0.88	2003-2004	Kindergarten children in Jeju village B
Ibid.		108	1.30	2003-2004	Kindergarten children, total
Chung et al.	$[13]$	88	0.88	$2005^{\rm b}$	Control areas
MEK ^c	$[43]$	126	2.08 ^d	2007	Middle-sized city
Moon et al.	$[33]$	88	2.59	2007-2008	Coastal areas
Ibid.		180	1.81	2007-2008	Inland areas
Ibid.		268	2.04	2007-2008	Total
Lee et al.	$[44]$	5087	0.61	2008	$KNSEPHBe$; men + women
Yun et al.	$[14]$	73	0.59	2010^b	Controls (Village B)
Ibid.		74	0.65	2010^b	Controls (Village D)
Ibid.		147	0.62	2010^b	Controls (Villages $B + D$)
Huang et al.	$[24]$	239	1.04	2011 ^b	\geq 20 year-old men
Ibid.		404	0.89	2011^{b}	\geq 20 year-old women
Ibid.		643	0.95	2011 ^b	\geq 20 year-old men + women
Yang et al.	$[15]$	457	1.40	$2015^{\rm b}$	Controls

Table 3 Cadmium concentration in urine as corrected for creatinine concentration

^a Originally the AM and ASD (or ASE) were given, from which GM was estimated by the moment method [[12](#page-8-0)]

^b Year of publication

^c MEK Ministry of Environment, Korea

 d µg/L

^e KNSEPHB Korea National Survey for Environmental Pollutants in Human Body in 2008

remarkable (Fig. [3\)](#page-6-0) with $r = -0.490$, although the coefficient was statistically significant ($p < 0.01$).

Discussion

The present analyses of published reports on Cd-D in Korea clearly demonstrated that there has been steady reduction since 1980s (Table [1](#page-1-0)). The results of analyses for time trends in Cd-B and Cd-U are also in agreement with the observation on Cd-D. It should be added that dietary Cd is an almost exclusive Cd exposure source for general populations [[4\]](#page-8-0). A similar trend of time-depending decrease in Cd-D was reported also for Japan, a neighboring and another rice-depending country in East Asia [\[45](#page-9-0), [46](#page-9-0)].

To confirm the above-stated observation, several statistical analyses were conducted in parallel. With regard to Table 4 Regression line

Fig. 1 Time trend in cadmium in dietary intake. Each *dot* represents a GM value observed in one group of study subjects. The line in the middle is a calculated regression line (for equation, see Eq. 1 in Table 4), and the two dotted curves show the 95 % range

the databases, study years were not always available. Both the years of surveys and the years of publications were reported in 8, 8, and 13 articles on Cd-D, Cd-B and Cd-Ucr, respectively. The differences between the years of survey and the years of publication did not distribute normally or log-normally, and medians were 5.5, 5.5 and 3 years in the order. The years of surveys were tentatively estimated by subtracting the median values from the publication years for the reports in which no survey years were given. The survey years thus estimated were subjected (in combination with survey years reported in other publications) to regression analyses between survey years and Cd-exposure parameters (i.e., Cd-D, Cd-B or Cd- U_{cr}) (Case B in Table 4). The parameters (including slopes) of the regression lines thus obtained (Eqs. 6 to 10) did not differ

In the equation $Y = \alpha + \beta X$, X is the year of survey and Y is the parameter shown in the table

 $^{\rm a}$ Unit for Y

^b Number of groups in Case A and Case B, and number of individuals in Case C

^c Case A: the publication year is taken as the survey year when the survey year is not reported

^d Case B: in absence of report on the survey year, the survey year is estimated by subtracting 5.5, 5.5 and 3.0 years from the publication year in cases of Cd-D, Cd-B and Cd-Ucr, respectively. There is no significant difference ($p > 0.05$) in intercepts, slopes and correlation coefficients between Eqs. 1 and 6, Eqs. 2 and 7, Eqs. 3 and 8, Eqs. 4 and 9, and Eqs. 5 and 10

^e Case C: calculation was made as in Case A, except that the analysis is made in a number-weighted manner taking the number of individuals into consideration

 f Five studies are not included because the Cd-D is estimated taking advantage of e.g., national statistics of</sup> food consumptions and the number of participating subjects are not available

^g After exclusion of one group of extreme cases ($p < 0.01$ by Smirnov's test for extreme value)

Fig. 2 Time trend in cadmium concentration in peripheral blood. Notes are as under Fig. [1](#page-5-0). For the regression line equation, see Eq. 3 in Table [4](#page-5-0)

Fig. 3 Time trend in cadmium concentration in urine as corrected for creatinine concentration. Notes are as under Fig. [1](#page-5-0). For the regression line equation, see Eq. 5 in Table [4](#page-5-0)

significantly ($p > 0.05$) from the corresponding values for Eqs. 1 to 5 (Case A, in which the year of survey was taken as a surrogate of the pear of survey when necessary). Thus, the effects of the surrogate use (i.e., the use of publication years in place of survey years as necessary) should be small.

As the number of cases was various depending on the groups from less than 20 to nearly 5000 (Tables [1,](#page-1-0) [2](#page-2-0), [3](#page-4-0)), number-weighted analyses were conducted in parallel (Case C in Table [4](#page-5-0)). In Cd-D, case numbers were not available in 2 studies [[11,](#page-8-0) [17\]](#page-8-0) for 5 estimated Cd-D, as stated above. Correspondingly, Case A analysis was conducted also with selected groups (i.e., excluding these studies) (Eq. 2 in Table [4\)](#page-5-0) in addition to the analysis with all groups (Eq. 1) for better comparison with the results from Case C (Eq. 11). Accordingly, regression analysis for Cd-D was conducted also in Case C analysis excluding these studies $[11, 17]$ $[11, 17]$ $[11, 17]$ $[11, 17]$, the studies for which case numbers were missing (Eq. 11 in Table [4\)](#page-5-0). In Cd-B, one study [[27\]](#page-8-0) gave extremely high GM Cd-B value and excluded as an outlier group. Thus, Case C analyses for Cd-B were conducted including and also excluding this outlier group (Eqs. 12 and 13).

Perusal of Table [4](#page-5-0) revealed that both intercepts and slopes in Case C analyses differed to some extent from the corresponding results of group-based Case A and Case B analyses. Nevertheless, all slopes were negative with $p<0.01$ –0.05 for correlation coefficients to suggest timedependent decreases.

There have been several factors which have been contributing to the reduction. Korea Food and Drug Administration set a guideline for Cd in rice at 0.2 mg/kg in 2012, and marketing of rice containing Cd at the concentration in excess of this guideline has been prohibited by law [\[47](#page-9-0)]. In addition, there has been a gradual reduction in rice consumption by general public due to changes in food habits. According to the national data, consumption of rice in 2005 and 2013 was 80.7 and 67.2 kg/person/year [[48\]](#page-9-0), indicating reduction by about 17 % in these 8 years (rice weight was assumedly for pre-cooked weight). From rice-cultivation technology side, efforts have been made to reduce Cd contents in rice by use of ameliorants, especially in Cdcontaminated rice fields in the vicinity of abandoned metal mines, e.g., [\[49](#page-9-0), [50](#page-9-0)].

To compare with the past and current levels in Cd-D, $Cd-B$ and $Cd-U_{cr}$ in Korea, literature survey was made for the levels in other countries in 2000–2015 (Table [5\)](#page-7-0). For this purpose, estimation for the levels in Korea in 2000 and 2015 was also presented, taking advantages of regression equations in Case A (Eqs. 1, 3 and 5), Case B (Eqs. 6, 8 and 10) and Case C analyses (Eqs. 11, 12 and 14) given in Table [4](#page-5-0). Table [5](#page-7-0) shows that regional differences were much more remarkable than time-dependent changes. Thus, it was apparent that Cd exposure has been higher in Asia than in Europe and in USA. Within Asia, all of Cd-D, Cd-B and Cd- U_{cr} were highest for Japan, and Korea is essentially the 2nd-highest, although there were substantial reductions in the estimates of three exposure parameters in 2015 as compared with the estimates in 2000.

In 2013, Joint FAO/WHO Expert Committee on Food Additives (JECFA) adopted 25 µg/kg body weight/month as the provisional tolerable monthly intake (PTMI) for Cd [\[65](#page-10-0)]. Assuming that the average body weight for adult Korean population is 63 kg [\[16](#page-8-0)] and that a month consists of 30 days, 25 µg/kg body weight/month is approximately equivalent to $52.5 \mu g/day$. Thus, the current estimate for Cd-D, $6.0-7.4 \mu g/day$ (the bottom three rows in Table [5](#page-7-0)), is about 11–14 % of the PTMI.

There may be several limitations in the present study. The first point is on the instrumental methods for Cd determination. Early time studies used flame atomic absorption spectrometry, whereas later studies employed graphite furnace atomic absorption spectrometry and then inductively coupled plasma mass spectrometry. Compatibility between the last two methods was previously confirmed [\[60](#page-9-0)] but no information was available with regard to

^a Year of publication

^b Geometric means unless otherwise specified

 \degree Estimates taking advantake of Eqs. 1, 3 and 5 in Table [4](#page-5-0)

^d Estimates taking advantake of Eqs. 6, 8 and 10 in Table [4](#page-5-0)

^e Estimates taking advantake of Eqs. 11, 12 and 14 in Table [4](#page-5-0)

 f An average body weight of 63 kg $[16]$ $[16]$ $[16]$ is assumed for adult men and women in Korea

 g GM was clculated from AM and ASD by use of the moment method [\[12\]](#page-8-0)

 h Median in μ g/L</sup>

 i Median in μ g/g cr

^j The minimum and the maximum of GMs for 17 countries in Europe

the first method and other two methods. Secondly, only body weight was taken into consideration in evaluating the Cd-D values across men, women and children, despite the fact that children need energy (in terms of foods) not only for their daily life but for growth. It is also known through experiences that men used to take more rice (and therefore more Cd) than women. On this point, it should be added that preliminary analyses with adult populations only gave essentially the same decreasing trends in Cd-D, Cd-B and Cd-Ucr with the present analyses in which adult people and children were taken together (data not shown). Thirdly, a well-known confounding factor of smoking as a non-occupational source of Cd burden [\[6](#page-8-0)] was not taken into

account. The original objectives of most studies cited were elucidation of Cd burdens on general Korean populations, and studies on selective evaluation of non-smokers were very limited. The fourth point is on the comparability of Cd-B and Cd- U_{cr} between adults and children. There is no confirming report if Cd-D intake at the same level gives comparable Cd-B both for adults and for children. The same point may need to be taken as a study limit when Cd-U_{cr} values for adults and children were taken together in trend analyses. It is known that aged people have higher Cd-Ucr possibly because Cd has accumulated in the kidney cortex in reflection of years in life [\[66](#page-10-0)]. Similarly but to the opposite direction, children may have lower $Cd-U_{cr}$

because of shorter time for Cd accumulation. Therefore, it is one of the limitations of the present study that the data on Cd-D, Cd-B and Cd- U_{cr} for adults and children were intermingled.

In conclusion, literature survey for time trend in Cd-D made it clear that there has been a gradual decrease in the intake to the estimated current level of $6.0-7.4$ μ g/day or $0.09-0.12$ µg/kg body weight/day (with assumption of 63 kg for body weight $[16]$), although Cd intake among general populations in Korea was once reported to be high in the past. Results of statistical analyses for trends in other two exposure parameters of Cd-B and Cd-U (as corrected for creatinine level) were in agreement with the above conclusion on Cd-D. The corresponding estimates for two exposure markers are $0.77-0.83 \mu g/L$ for Cd-B and 0.60–0.95 μ g/g cr for Cd-U_{cr}.

Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflicts of interest.

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