Cadmium Levels in Liver, Kidney, and Lung of Northeastern Thais without Occupational Exposure to Metals

ระดับแคดเมียมในตับ ไต และปอด คนไทยภาคตะวันออกเฉียงเหนือ ที่ไม่ได้ประกอบอาชีพสัมผัสโลหะ

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ABSTRACT

Cadmium (Cd) is one of ten chemicals considered by the World Health Organization to be of major public health concern. This study aimed to assess levels of Cd exposure in residential populations without occupational Cd exposure in northeastern Thais. Samples were obtained from 38 donated cadavers in the Department of Anatomy, Khon Kaen University. Tissues were analyzed for Cd levels with f atomic absorption spectrometer. The overall mean values for cadmium in the liver, kidney, and lung were 1.18, 12.09, and 0.22 μg/gm wet tissue weight, respectively. The Cd concentration in tissues of females was significantly higher than that of males. On the other hand, the Cd levels in the kidney and lung of male smokers was higher than male non-smokers. The present findings represent the first data-bases of Cd levels in kidney and liver of general population in Thailand without occupational exposure.

บทคัดย่อ

แคดเมียมเป็นโลหะ 1 ใน 10 ที่องค์การอนามัยโลกกำหนด ว่าเป็นสาเหตุหลักของปัญหาสาธารณสุข วัตถุประสงค์ของการศึกษานี้เพื่อประเมินระดับของการสัมผัสแคดเมียมในคนไทย ภาคตะวันออกเฉียงเหนือ ซึ่งเป็นผู้ที่ไม่ได้ประกอบอาชีพสัมผัสแคดเมียม ตัวอย่างเนื้อเยื่อได้จากศพผู้บริจาคร่างกาย จำนวน 38 ร่าง จากภาควิชากายวิภาคศาสตร์ มหาวิทยาลัยขอนแก่น เนื้อเยื่อถูกวัดปริมาณแคดเมียมโดยเครื่อง อะตอมมิกแอบซอร์พชัน สเปกโตรมิเตอร์ ค่าเฉลี่ยระดับแคดเมียมในตับ, ไต และปอด คือ 1.18, 12.09 และ 0.22 ไมโครกรัมต่อ กรัมน้ำหนักเปียก ตามลำดับ พบการสะสมแคดเมียมในเพศหญิงสูงกว่าเพศชาย อย่างมีนัยสำคัญทางสถิติ และระดับแคดเมียมในไต และปอดของผู้ที่สูบบุหรี่สูงกว่า ผู้ที่ไม่สูบบุหรี่อย่างมีนัยสำคัญทางสถิติ การศึกษานี้เป็นข้อมูลพื้นฐานแรก ของระดับแคดเมียมในตับ ไต และปอด ในคนไทยภาคตะวันออกเฉียงเหนือ

Key Words: Cadmium, Thailand

คำสำคัญ: แคดเมียม ประเทศไทย

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Introduction

Cadmium (Cd) is one of the most heavily cumulative toxics with an estimated half-life of more than 10 years in man. Once absorbed, Cd irreversibly accumulates in human body, in particularly in kidneys and other vital organs such the lungs or the liver. The kidney contains the highest concentrations of Cd, and it is considered as the critical organ whatever the source is and portal of entry of Cd (Bernard, 2004). In addition to the direct cytotoxic effects that can lead to apoptotic and/or necrotic events, Cd has potent carcinogenic effects in target organs (Zalups & Ahmad, 2003). Cd occurs naturally in some rock phosphate fertilizers. Industrial uses of the metals and agricultural activities have led to dispersion of Cd at trace levels into the environment and human foods (Satarug et al., 2002). In non-occupationally primary exposure sources of Cd for the general population include food and tobacco smoking. The highest concentrations of Cd are found in internal organs of mammals, mainly in the kidneys and liver (offals) as well as in some species of fish, mussels and oysters, especially when caught in polluted seas. Consumption of staple foods such as wheat, rice also significantly contributes to human exposure. In the industry, Cd exposure is mainly by inhalation although significant amounts of Cd can be ingested via contaminated hands or cigarettes (Bulmer et al., 1938; Nicaud & Lafitte, 1942).Tobacco smoking is an important additional source of exposure for smokers. Since one cigarette contains approximately 1 to 2 μg Cd, smoking one pack per day results in a daily uptake of Cd that approximates that derived from food. When exposure is by inhalation, it is estimated that between 10 and 50 per cent of Cd is absorbed, depending on the particle size and the solubility of Cd compounds. In the case of Cd in tobacco smoke (mainly in the form of CdO), an average of 10 per cent of Cd is absorbed (Friberg, 1950; WHO, 1992; Bernard & Lauwerys, 1986; Nordberg et al., 2007). The Cd body burden, negligible at birth, increases continuously during life until approximately the age of about 60-70 yr from which Cd body burden levels off and can even decrease (Järup et al., 1998). Non-workplace exposure to cadmium has been linked to a number of adverse health effects attributable to distinct pathological changes in a variety of tissues and organs (IPCS, 1992; Bellinger et al., 2001; Järup et al., 1998). These include the development and/or progression of diabetic renal complications, hypertension, osteoporosis, leukaemia and cancer in several organs such as the lung, kidney, urinary bladder, pancreas, breast and prostate. Adverse health effects by Cd exposure in non-occupational populations include interactions with diabetes, osteoporosis and renal toxicity, particularly impairment of renal tubular re-absorption function (Satarug et al., 2003). The study of Cd levels in human organs in Thailand wich may be one of the health effect factors has never been reported. Therefore, this study was conducted among non-occupational Cd-exposed Thai populations residing in northeastern, an area without reports of Cd contamination.

Objectives of the study

The aim of the present study was to investigate the levels of Cd in the kidney liver and lung in northeastern Thais without Occupational Exposure to Metals, and further the correlation among tissue Cd levels, sex, age and smoking behavior.

Methodology

The study protocol was approved by the Ethics Committee of the Faculty of Medicine, Khon Kaen University. Samples of the kidney liver and lung were obtained from 38 donated cadavers of anthropologic autopsies carried out in the Department of Anatomy within Khon Kaen University. All of subjects had been residents of northeastern, Thailand. Subjects were excluded from the study if they had one of the following criteria: not domiciled in the northeast, blood - borne communicable diseases, cadavers had not been kept at 4 °C and historical data is not available. A questionnaire was used to evaluate exposure to Cd including questions on demographic data, residency period, general heath, history of chronic disease and smoking status of cases were obtained from donated relative. The sample were analyzed at the Department of Biochemistry, Faculty of Medicine, Khon Kaen University. Wet tissue samples of the kidney liver and lung were weighed approximately 10 gm. The tissue sample were rinsed in ice-cold normal saline. The medulla and cortex of the kidney samples were dissected apart. The samples were dissected into smaller sizes and were then oven-dried at 70ºC for 48 hr. We then weighed dried samples to 4 decimal points to estimate the water content in each sample. Dried samples were digested in 65% HNO3 and equilibrated to a boiling water bath temperature for 24 hr. Samples were then analyzed for Cd with the flame atomic absorption spectrometer. The quality assurance of this analysis for tissue Cd levels were assessed with a Cd standard solution (TraceCERT©, Sigma).

Statistical analysis was performed using SPSS package for Windows version 17.0. The strength of correlation between the variables and between ages was determined by Pearson's correlation coefficient. The distribution of Cd levels in kidney liver and lung prior to statistical test, and the significance levels of differences in mean values of these variables among subjects in different groups were assessed by one-way analysis of variance. Comparison of qualitative data was done by the chi-square test. Statistical significance was set at $\alpha = 0.05$ for all test.

Results

In this study, samples of lung, liver, and kidney were collected from the same anatomical sites in cadavers, although in our pilot study we found that there was no difference in tissue cadmium concentrations that could be attributable to sampling locations.

Table 1 Characteristics of subjects in the sample population. Data are presented as mean ± SD and (range) or number (percent) values

Parameters	Total subjects (N = 38)	Males (n =23)	Females (n =15)
Number of subjects, n (%)	38 (100%)	23(60.5%)	15 (39.5%)
Age (years)	64.1 ± 14.1 (39-90)	64.5 ± 14.5 (44-90)	63.6 ± 14.0 (39-83)
Body weight (kg)	55.7 ± 10.1 (38-80)	58.3 ± 9.8 (38-80)	51.7 ± 9.4 (40-70)
Occupation, n (%)			
Official	14 (36.8)	8 (21.1)	6 (15.8)
Farmer	8 (21.1)	4 (10.5)	4 (10.5)
Merchant	7 (18.4)	3 (7.9)	4 (10.5)
Housewife	6 (15.8)	3 (7.9)	3 (7.9)
Laborer	3 (7.9)	3 (7.9)	0 (0)
Smoke, n (%)			
Ever	8 (21.1)	8 (21.1)	0 (0)
Never	30 (78.9)	15 (39.4)	15 (39.4)

The sample population comprised 23 males and 15 females (age range: 39–90 yr). The overall mean age for the sample population was 64.1 yr. The mean ages for males and females were 64.5 yr and 63.6 yr, respectively.

Twenty three (60.5%) of these subjects were 60 years and older. The majority of study subjects were government officers (36.8%); other occupations including farmers (21.1%), merchants (18.4%), housewives (15.8%) and laborers (7.9%). About 21% of the total populations surveyed were smokers and all of them were male are shown in Table 1.

The mean and ranges values for the levels of Cd (expressed in µg/gm wet tissue weight) found in the liver, kidney, and lung as a function of smoking are shown in Table 2. The mean Cd content in liver, kidney, and lung was 1.88, 12.09 and 0.22 µg/gm wet tissue weight, respectively. The total mean estimated liver, kidney and lung Cd amount was higher in female (1.35 µg/gm in the liver, 12.57 µg/gm in the kidney, and 0.28 in the lung) than in male (1.03 µg/gm in the liver, 11.71 µg/gm in the kidney, and 0.21 in the lung). And he difference between genders was statistically significant in liver Cd (p = 0.01) and in lung Cd (p = 0.23).

Table 2 Cadmium concentrations (µg/gm wet tissue weight) in kidney liver and lung samples from the sample population

Descriptors	Liver Cd			Kidney Cd			Lung Cd		
	Smoker (range)	Non-smoker (range)	Total (range)	Smoker (range)	Non-smoker (range)	Total (range)	Smoker (range)	Non-smoker (range)	Total (range)
Male	8/1.22±0.67 (0.32 - 2.55)	15/0.87±0.40 (0.12 - 1.49)	23/1.03±0.53 (0.12 - 2.55)	8/14.14±2.08 (9.44-16.09)	15/10.10±3.68 (3.13 - 16.64) *	23/11.71±3.76 (3.13 - 16.64)	8/0.28±0.27 (0.24-0.32)	15/0.18±0.18 (0.13-0.23) †	23/0.21±0.57 (0.13- 0.32)
Female	NS	15/1.35±0.44 (0.37-2.17) §	15/1.35±0.44 (0.37 - 2.17) §§	NS	15/12.57±3.55 (6.13 - 18.42) **	15/12.57±3.55 (6.13 - 18.42)	NS	15/0.28±0.25 (0.18-0.33) ††	15/0.28±0.25 (0.18-0.33)
Total	8/1.22±0.67 (0.32 - 2.55)	30/1.22±0.48 (0.12 - 2.17)	38/1.18±0.53 (0.12 - 2.55)	8/14.14±2.08 (9.44 -16.09)	30/11.30±3.77 (3.13 -18.42) ***	38/12.09±3.62 (3.13 - 18.42)	8/0.28±0.27 (0.24-0.32)	30/0.20±0.36 (0.13-0.33) †††	38/0.22±0.47 (0.13-0.33)

Note: each descriptor shows n/mean ± SD (range), NS: no sample

§ Indicates statistically significant difference of liver Cd levels from male nonsmoker at p =0.01

§§ Indicates statistically significant difference of liver Cd levels from total male at p =0.046

* Indicates statistically significant difference of kidney Cd levels from male smoker at p =0.002

** Indicates statistically significant difference of kidney Cd levels from male nonsmoker at p =0.02

*** Indicates statistically significant difference of kidney Cd levels from smoker at p =0.001

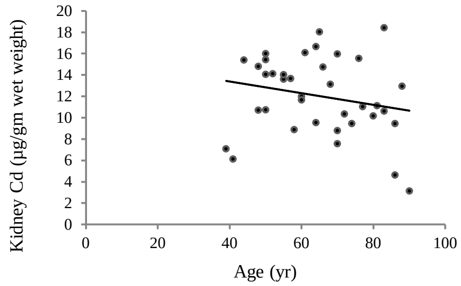
† Indicates statistically significant difference of lung Cd levels from male smoker at p < 0.001

†† Indicates statistically significant difference of lung Cd levels from male nonsmoker at p =0.002

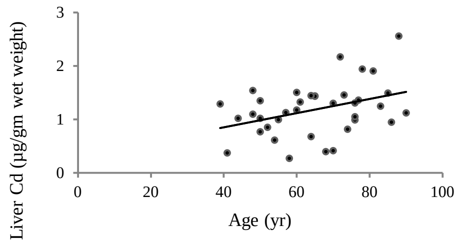
††† Indicates statistically significant difference of lung Cd levels from smoker at p < 0.001

Pearson's correlation analysis revealed significant correlations between age and Cd levels in the liver, kidney, and lung. Pearson's correlation coefficient (r) indicated the strength of association between age and Cd levels found in each organ. A positive correlation was significance between age and lung Cd (p = 0.02) and the correlation coefficients for the liver and kidney were .36,and -.25 respectively (Fig. 1). We controlled for age, and the resulting correlation coefficient values that show positive correlation between liver-kidney Cd (r = 0.47, p = 0.009) and between liver and lung (r = 0.16, p = 0.47) (Fig. 2).

a. Relationship between age and levels of cadmium in kidney



b. Relationship between age and levels of cadmium in liver



c. Relationship between age and levels of cadmium in lung

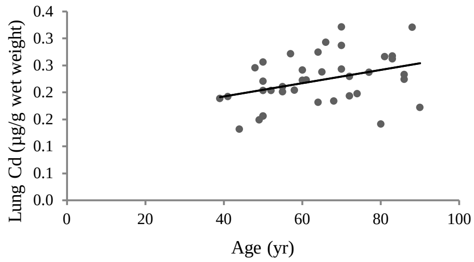
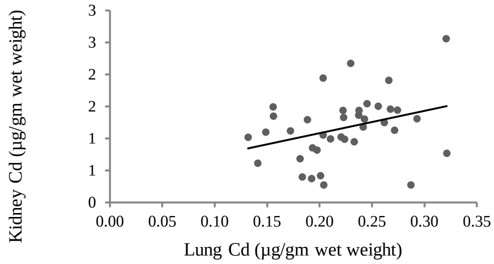
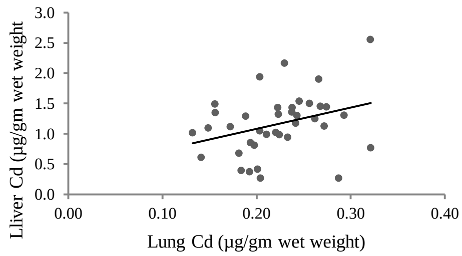


Fig. 1 Correlation between age and kidney (Panel 1a), and liver (Panel 1b), and lung (Panel 1c)

a. Lung- kidney Cd



b. Lung- liver Cd



c. Liver-kidney Cd

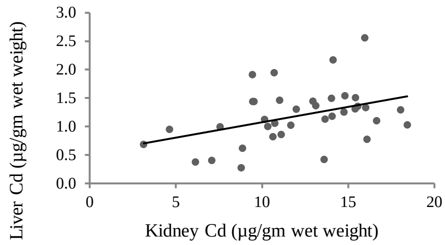


Fig. 2 Correlation between levels of cadmium in lung and kidney (Panel 2a), in lung and liver (Panel 2b), and in liver and kidney (Panel 2c)

About 21% of the total populations surveyed were smokers and all of them were male. The male smoker population exhibited higher Cd levels (1.22 µg/gm in the liver, 14.14 µg/gm in the kidney and 0.28 µg/gm in lung) than male non-smoker (0.87 µg/gm in the liver, 10.10 µg/gm in the kidney, and 0.18 in the lung). The difference in Cd levels between male smokers and male non smokers was statistically significant in kidney Cd ($p = 0.01$) and in lung Cd ($p < 0.001$), and so was the kidney Cd difference between male non smoker (10.10 µg/gm) and female non smoker (12.57 µg/gm) ($p = 0.046$) and the difference in the lung Cd between male non smoker (0.18 µg/gm) and female non smoker (0.28 µg/gm) ($p = 0.002$). Subjects who smokers (14.14 µg/gm in the kidney, and 0.28 in the lung) had higher Cd levels in kidney and lung than non smokers (12.57 µg/gm in the kidney, and 0.28 in the lung) ($p = 0.001$ for the kidney, $p < 0.001$ for the lung).

Discussion

In the present study, the highest renal cadmium level of approximately 18.42 µg/gm was found in females, and liver-cadmium levels were 70% higher in females than males (Table 2). The reasons for these three differences are unclear at present. These data may suggest that there is a higher absorption rate in females than in males. Increased absorption of cadmium from a shellfish diet was found in females who had low body iron stores (Flanagan et al., 1978; Vahter et al., 1996). And there has been a study suggesting that the higher kidney Cd concentration may be due to a mobilization of Cd from the liver and other tissues to accumulate into the kidney (Satarug et al., 2002).

Age related increases in renal cadmium accumulation and preferential renal accumulation found in our sample population were consistent with many other human autopsy studies conducted on nonoccupationally exposed individuals (Tiran et al., 1995; Lyon, 1999; Elinder et al., 1976). In this sample population, kidney-cadmium concentrations increased progressively with age, reaching a peak of approximately 18.42 µg/gm in the 41–50-yr age group. Kidney-cadmium concentrations tended to decrease in the 51+ yr and older. Such a decrease in renal cadmium levels in the 51+-yr may represent decreases in exposure to cadmium in relatively more recent times and/or loss of cadmium from the kidneys. This loss may be caused by cadmium induced damage or age-related degeneration of the kidney.

This study found the difference in Cd levels between male smokers and male non smokers was statistically significant in kidney Cd and in lung Cd. These findings suggest that tobacco leaves, which are known to naturally accumulate high Cd concentrations, can contribute to another important source of Cd-exposure to human being (WHO, 1992). These data may suggest that there is a higher absorption rate in females than in males. Increased absorption of cadmium from a shellfish diet was found in females who had low body iron stores (Flanagan et al., 1978). In general, females have lower body iron stores than males, and, therefore, increased body burdens of cadmium in females may result from increased absorption (Vahter et al., 1996).

Conclusions

The present study represents the first finding of Cd levels in the liver, kidney and lung of residential population without occupational Cd exposure in the northeastern Thailand.

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