Changes in Cadmium Exposure among Persons Living in Cadmium-Contaminated Areas in Northwestern Thailand: A Five-Year Follow-Up

Witaya Swaddiwudhipong MD*, Pranee Mahasakpan BSc, MPH*,
Thippawan Funkhiew BPH*, Pisit Limpatanachote MD**

** Department of Community and Social Medicine, Mae Sot General Hospital, Tak, Thailand*
*** Department of Internal Medicine, Mae Sot General Hospital, Tak, Thailand*

Objective: *To determine changes in cadmium exposure among persons aged 15 years and older who lived in the 12 cadmium-contaminated villages in northwestern Thailand.*
Material and Method: *Urinary cadmium was measured among villagers in 2004. An exposure reduction campaign was conducted soon afterwards, and in 2009, urinary cadmium was measured among people living in the same villages. The survey participants were asked about their smoking status and consumption of rice grown locally in cadmium-contaminated areas. Both were the two main routes of cadmium exposure in these villages.*
Results: *Seven thousand six hundred ninety seven and 6,748 persons participated in the first and second surveys, respectively. The proportion of current smokers was higher in the first survey (34.9%) than the second survey (31.5%). The proportion of persons who consumed rice grown locally decreased from 88.0% in the first survey to 50.5% in the second survey. Of persons who consumed rice grown locally, the proportion of those with urinary cadmium $\geq$ 2 μg/g creatinine increased from 55.5% in the first survey to 61.3% in the second survey. Of persons consuming rice purchased from other areas, the proportion of those with urinary cadmium $\geq$ 2 μg/g creatinine decreased from 46.7% in the first survey to 35.6% in the second survey. In both surveys, the adjusted odds ratio for increasing prevalence of high urinary cadmium associated with consumption of locally grown rice was greater than that for tobacco smoking.*
Conclusion: *Urinary excretion of cadmium significantly decreased after environmental cadmium exposure was reduced.*

Keywords: *Cadmium, Cadmium exposure, Rice consumption, Smoking*

J Med Assoc Thai 2010; 93 (10): 1217-22
Full text. e-Journal: *http://www.mat.or.th/journal*

Cadmium is widely distributed in the earth's crust. This metal is commonly found in zinc ore deposits and a common by-product of zinc mining. Cadmium is an important public health concern due to its toxic effects to many organs[1-6]. The kidney is considered the critical target organ for chronic exposure to cadmium. The principal environmental sources of cadmium exposure for the general population are food and cigarettes. Crops grown in cadmium-contaminated soil may contain elevated cadmium levels[1,4]. Long-term excessive oral exposure can cause chronic cadmium toxicity. The tobacco plant naturally accumulates high cadmium content in its leaves. Therefore, cigarette smoking is an important additional source of cadmium exposure for smokers. Cadmium can be measured in blood for acute exposure and in urine for chronic exposure and body burden[1-6]. Urinary excretion of cadmium is usually < 2 μg/g creatinine in a population without excessive exposure to cadmium.

In Mae Sot District, Tak Province, northwestern Thailand, some rice fields were irrigated with water from two creeks that ran through a zinc mine that was operated for more than 20 years. About 69.2% of 91 sediment samples from the creeks and 85.0% of 1,090 paddy soil samples contained cadmium content above the maximum permissible level of 3.0 mg/kg during the surveys in 2001-2004[7-9]. Of the 1,067 samples of rice grain grown in these paddy fields, 83.0% had cadmium levels exceeding the acceptable level of 0.2 mg/kg (range between < 0.1 and 7.7)[7-9]. The cadmium-contaminated areas were discovered in the

Correspondence to:
Swaddiwudhipong W, Department of Community and Social Medicine, Mae Sot General Hospital, Tak 63110, Thailand.
Phone: 055-531-229, Fax: 055-533-046
E-mail: swaddi@hotmail.com

12 villages of the district. Since the majority of inhabitants consumed locally grown rice and other crops, they were at risk for cadmium-induced toxicity. A population screening survey for cadmium exposure using urinary cadmium measurement was first conducted in 2004 among inhabitants aged 15 years and older living in these cadmium-contaminated villages. Of the 7,697 adults examined, 47.2% had urinary cadmium levels 2-4.9 μg/g creatinine and 7.2% had cadmium concentrations ≥ 5[10]. A significant proportion of those with high cadmium exposure had renal dysfunction and/or bone toxic effects[11-14]. The survey revealed that urinary cadmium excretion significantly ($p < 0.01$) increased with increasing age, being female, tobacco smoking, and consumption of rice grown in these contaminated areas[10].

Between 2004 and 2006, the government purchased all rice grown in these contaminated areas and supported the production of non-food crops. Sugar cane for ethanol production was the main crop grown in the areas. The inhabitants were educated about the toxic effects of cadmium and the benefit of exposure reduction by cessation of consumption of crops, particularly locally grown rice, and quitting smoking. However, some inhabitants continued to grow some rice for their own consumption. A similar population screening survey for urinary cadmium measurement was carried out in 2009 to determine changes in cadmium exposure among inhabitants who lived in these cadmium-contaminated villages. This report compares cadmium exposure data from surveys in 2004 and 2009.

Material and Method

The screening survey for cadmium exposure was conducted among inhabitants living in the 12 cadmium-contaminated villages. The measurements were done first in 2004 and then in 2009. Persons aged 15 years and older were the subjects of both surveys. Details of the community preparation for both surveys were reported previously[10,15]. The study protocols of both surveys were approved by the Mae Sot Hospital Ethical Committee and oral informed consent was obtained from the inhabitants before they participated in the survey.

In each village, all persons aged 15 years and older were identified and interviewed by trained health workers. The questionnaire collected information about age, sex, address, smoking status, and consumption of rice grown locally in contaminated areas or purchased from other areas. A 30-ml sample of second morning urine was obtained from each participant for measurements of cadmium and creatinine. Urinary cadmium content was determined by a graphite tube atomic-absorption spectrometer (Varian Model AA280Z, USA) by the national laboratory at the Thailand Ministry of Public Health. This laboratory has been certified for toxicological analyses in biological materials by the German External Quality Assessment Scheme. Urinary creatinine concentration determined by an auto-analyzer (Konelab 30, Thermo Electron Corporation, Finland) was used to adjust for urinary excretion of cadmium.

The distributions of variables were expressed in percentages of the study persons. The arithmetic mean and standard deviation were used to summarize the quantitative variables. The geometric mean was used when the logarithms of the observations were more likely to distribute normally than the observations themselves. The Chi-square test was used for comparison between proportions. The analysis of variance or the Mann-Whitney U-test was used for comparison between means. Multiple linear regression analysis was used to determine the correlations of urinary cadmium with age, sex, tobacco smoking, and consumption of rice grown in contaminated areas. Multiple logistic regression analysis was used to determine the associations between prevalence of elevated urinary cadmium (≥ 5 μg/g creatinine) and age, sex, smoking, and consumption of rice grown in contaminated areas. A p-value of less than 0.05 was considered statistical significant.

Results

Seven thousand six hundred ninety seven persons participated in the first survey in 2004 and 6,748 in the second survey in 2009, giving response rates of 79.6% and 71.7%, respectively. About 14.7% in the first survey and 18.2% in the second survey refused to be screened and claimed that they were healthy. The remainders were not at home during the study period.

Table 1 shows the characteristics of the study population surveyed in 2004 and 2009. The participants of the second survey had a significantly ($p < 0.01$) higher mean age and a greater proportion of women than the first survey persons. In the first survey, the age of the study persons ranged from 15 to 95 years in men and from 15 to 97 years in women. In the second survey, their age ranged between 15 and 92 years in both genders. The proportion of current smokers was higher in the first survey (34.9%) than the second

Table 1. Characteristics of the study population surveyed in 2004 and 2009

Characteristics	2004	2009	p-value
Total no. surveyed	7,697	6,748	
Age (years)			
Mean ± SD*	44.0 ± 16.1	47.0 ± 15.9	<0.01
Sex			
Male (%)	47.6	44.8	<0.01
Female (%)	52.4	55.2	
Smoking status			
Never (%)	50.7	55.3	
Former (%)	14.4	13.2	<0.01
Current (%)	34.9	31.5	
Rice consumption			
Rice grown locally in contaminated areas (%)	88.0	50.5	<0.01
Rice purchased from other areas (%)	12.0	49.5	
Urinary cadmium (μg/g creatinine)			
Mean ± SD**	2.1 ± 2.9	1.9 ± 2.4	<0.01

* Arithmetic mean ± standard deviation
** Geometric mean ± standard deviation

Table 2. Distribution and mean of urinary cadmium in the population surveyed in 2004 and 2009, by consumption of rice grown in contaminated or other areas

Year	Rice consumption	No. surveyed	Urinary cadmium (μg/g cr)*			Mean ± SD**	p-value
			< 2	2-4.9	≥ 5		
2004	Rice grown locally in contaminated areas	6,770	44.5 (41.9)	47.7 (49.3)	7.8 (8.8)	2.1 ± 3.0	<0.01
	Rice purchased from other areas	927	53.3 (48.6)	43.6 (46.6)	3.1 (4.7)	1.7 ± 2.7	
2009	Rice grown locally in contaminated areas	3,411	38.7 (39.4)	43.0 (41.8)	18.3 (18.8)	2.4 ± 2.3	<0.01
	Rice purchased from other areas	3,337	64.4 (62.3)	29.2 (30.7)	6.4 (7.0)	1.5 ± 2.3	

* Expressed as a percentage of the number surveyed
Numbers in parentheses were percentages adjusted for age, sex, and smoking
** Geometric mean ± standard deviation

survey (31.5%). The proportion of persons who consumed rice grown in cadmium-contaminated areas decreased from 88.0% in the first survey to 50.5% in the second survey. Persons of the second survey had a significantly ($p < 0.01$) lower mean level of urinary cadmium than those of the first survey.

Table 2 presents distributions and means of urinary cadmium among persons in each survey categorized by consumption of rice grown in cadmium-contaminated or purchased from other areas. Of persons who consumed rice grown in contaminated areas, 55.5% in the first survey had urinary cadmium levels ≥ 2 μg/g creatinine. This proportion increased to 61.3% in the second survey. The mean urinary cadmium level of these persons in the second survey was also significantly ($p < 0.01$) higher than that in the first survey. Of persons who reported consumption of rice purchased from other (uncontaminated) areas, the proportion of those with urinary cadmium levels ≥ 2 μg/g creatinine decreased from 46.7% in the first survey to 35.6% in the second survey. A significantly ($p < 0.01$) lower mean level of urinary cadmium was also observed among these persons in the second survey than those in the first survey.

Table 3 presents the correlations of urinary cadmium with age, sex, tobacco smoking, and consumption of rice grown in contaminated areas by multiple linear regression analysis. In both surveys,

Table 3. Multiple linear regression analysis of the determinants of urinary cadmium in the population surveyed in 2004 and 2009

Independent variables*	Urinary cadmium (μg/g creatinine)			
	2004		2009	
	β**	p-value	β**	p-value
Age	0.031	<0.01	0.049	<0.01
Sex	0.571	<0.01	0.970	<0.01
Smoking	0.373	<0.01	0.431	<0.01
Rice consumption	0.600	<0.01	1.299	<0.01
Adjusted r^2	0.05		0.17	

* Age (years), sex (male = 0, female =1), smoking (never = 0, ever = 1), and rice consumption (purchased from other areas = 0, grown in contaminated areas = 1)
** Regression coefficient

urinary excretion of cadmium significantly ($p < 0.01$) increased with increasing age, being female, tobacco smoking, and consumption of rice grown locally. The analyses of both survey data similarly indicated that a correlation coefficient for cadmium exposure via consumption of locally grown rice was greater than uptake from smoking.

Multiple logistic regression analysis was used to determine the associations between prevalence of urinary cadmium ≥ 5 μg/g creatinine and study independent variables including age, sex, tobacco smoking, and consumption of rice grown in contaminated areas (Table 4). The present study revealed that the prevalence of urinary cadmium ≥ 5 μg/g creatinine significantly ($p < 0.01$) increased with increasing age, being female, tobacco smoking, and consumption of rice grown locally. In both surveys, the adjusted odds ratio for increasing prevalence of high urinary cadmium associated with consumption of locally grown rice was greater than that for tobacco smoking.

Discussion

Data from the first survey in 2004 indicated that most inhabitants living in the contaminated areas consumed rice grown locally and nearly all of the remainder purchased rice from Mae Sot markets, which contained products from both contaminated and uncontaminated areas. Following the cadmium exposure reduction campaign, about half of the inhabitants stopped consumption of locally grown rice in the second survey. Urinary cadmium levels were found to decrease among those who had stopped consuming rice grown locally in these contaminated areas. Decreased urinary cadmium excretion after reduction of environmental cadmium exposure was similarly observed in follow-up studies among exposed populations in Japan and Belgium[16-19]. In contrast, the present study found a significant increase in urinary cadmium levels among those who continued to consume locally grown rice. An increase in urinary cadmium excretion was possibly due to prolonged cadmium exposure via contaminated food in the study persons. It is therefore important to reduce the source of cadmium exposure in this population. In addition to massive health education on cessation of contaminated food, particularly rice, measures on reduction in cadmium uptake by crop plants and improvement in

Table 4. Logistic regression analysis of the determinants of prevalence of urinary cadmium ≥ 5 μg/g creatinine in the population surveyed in 2004 and 2009

Independent variables*	Urinary cadmium ≥ 5 μg/g creatinine			
	2004		2009	
	Odds ratio	95% CI	Odds ratio	95% CI
Age	1.028	1.021-1.034	1.046	1.040-1.052
Sex	1.837	1.509-2.236	2.661	2.218-3.193
Smoking	1.410	1.134-1.752	1.410	1.175-1.690
Rice consumption	2.089	1.498-2.910	3.680	3.103-4.364

* Age (years), sex (female/male), smoking (ever/never), and rice consumption (grown in contaminated areas/purchased from other areas)

the soil contamination are essential since some inhabitants may prefer to consume locally produced rice.

Tobacco smoking was found to contribute an important additional source of cadmium exposure for smokers in the study population. In both surveys, urinary excretion of cadmium was positively correlated with smoking, after adjusting for other co-variables. Although the proportion of current smokers was reduced following the cadmium exposure reduction campaign, smoking remained prevalent in the study population as shown in the second survey. A variety of community-based prevention programs, including media-based programs, school-based programs, and smoking cessation services, should be developed for maximum impact against tobacco smoking in the community.

The present study revealed a correlation between increasing urinary cadmium levels and consumption of rice grown in contaminated areas, after adjusting for other co-variables, in both 2004 and 2009 surveys. The strength of correlation for cadmium exposure via consumption of rice grown locally was greater than uptake from tobacco smoking. These findings implicated that dietary cadmium was the principal source of excessive cadmium exposure in the study population.

The cadmium levels in the body commonly increase with age[1,4]. Women generally have higher cadmium concentrations than men, which can be explained by increased gastrointestinal absorption of cadmium due to low body iron stores in women[1,3,4]. Increases in urinary cadmium levels with age and being females were similarly found in the present study. Since increased urinary cadmium excretion coincides with an increase in body burden, the elderly and women should be the target for assessment of chronic cadmium poisoning.

Acknowledgement

The authors wish to thank Dr. Alden Henderson of the Field Epidemiology Training Program, Bureau of Epidemiology, Thailand Ministry of Public Health, for his assistance in editing the manuscript.

References

1. World Health Organization. International programme on chemical safety: environmental health criteria 134. Cadmium. Geneva: WHO; 1992.
2. Jarup L. Cadmium overload and toxicity. Nephrol Dial Transplant 2002; 17(Suppl 2): 35-9.
3. Patrick L. Toxic metals and antioxidants: Part II. The role of antioxidants in arsenic and cadmium toxicity. Altern Med Rev 2003; 8: 106-28.
4. Agency for Toxic Substances and Disease Registry. Toxicological profile for cadmium (draft for public comment). Atlanta: US Department of Health and Human Services, Public Health Service; 2008.
5. Bernard A. Cadmium & its adverse effects on human health. Indian J Med Res 2008; 128: 557-64.
6. Satarug S, Garrett SH, Sens MA, Sens DA. Cadmium, environmental exposure, and health outcomes. Environ Health Perspect 2010; 118: 182-90.
7. Pollution Control Department. Cadmium contamination in Mae Tao Creek, Mae Sot District, Tak Province. Bangkok: Thailand Ministry of Natural Resources and Environment; 2004.
8. National Research for Environmental and Hazardous Waste Management, Chulalongkorn University. Distribution of cadmium and absorption by rice plants in areas nearby the zinc mine in Mae Sot District. Bangkok: Chulalongkorn University; 2005.
9. Simmons RW, Pongsakul P, Saiyasitpanich D, Klinphoklap S. Elevated levels of cadmium and zinc in paddy soils and elevated levels of cadmium in rice grain downstream of a zinc mineralized area in Thailand: implications for public health. Environ Geochem Health 2005; 27: 501-11.
10. Swaddiwudhipong W, Limpatanachote P, Mahasakpan P, Krintratun S, Padungtod C. Cadmium-exposed population in Mae Sot District, Tak Province: 1. Prevalence of high urinary cadmium levels in the adults. J Med Assoc Thai 2007; 90: 143-8.
11. Teeyakasem W, Nishijo M, Honda R, Satarug S, Swaddiwudhipong W, Ruangyuttikarn W. Monitoring of cadmium toxicity in a Thai population with high-level environmental exposure. Toxicol Lett 2007; 169: 185-95.
12. Limpatanachote P, Swaddiwudhipong W, Mahasakpan P, Krintratun S. Cadmium-exposed population in Mae Sot District, Tak Province: 2. Prevalence of renal dysfunction in the adults. J Med Assoc Thai 2009; 92: 1345-53.
13. Nambunmee K, Honda R, Nishijo M, Swaddi-wudhipong W, Nakagawa H, Ruangyuttikarn W. Bone resorption acceleration and calcium re-absorption impairment in a Thai population with

high cadmium exposure. Toxicol Mech Methods 2010; 20: 7-13.
14. Swaddiwudhipong W, Limpatanachote P, Nishijo M, Honda R, Mahasakpan P, Krintratun S. Cadmium-exposed population in Mae Sot district, Tak province: 3. Associations between urinary cadmium and renal dysfunction, hypertension, diabetes, and urinary stones. J Med Assoc Thai 2010; 93: 231-8.
15. Swaddiwudhipong W, Mahasakpan P, Limpatana-chote P, Krintratun S. Correlations of urinary cadmium with hypertension and diabetes in persons living in cadmium-contaminated villages in northwestern Thailand: a population study. Environ Res 2010; 110: 612-6.
16. Iwata K, Saito H, Moriyama M, Nakano A. Renal tubular function after reduction of environmental cadmium exposure: a ten-year follow-up. Arch Environ Health 1993; 48: 157-63.
17. Cai Y, Aoshima K, Katoh T, Teranishi H, Kasuya M. Renal tubular dysfunction in male inhabitants of a cadmium-polluted area in Toyama, Japan-an eleven-year follow-up study. J Epidemiol 2001; 11: 180-9.
18. Nawrot TS, Van Hecke E, Thijs L, Richart T, Kuznetsova T, Jin Y, et al. Cadmium-related mortality and long-term secular trends in the cadmium body burden of an environmentally exposed population. Environ Health Perspect 2008; 116: 1620-8.
19. Kobayashi E, Suwazono Y, Honda R, Dochi M, Nishijo M, Kido T, et al. Serial changes in urinary cadmium concentrations and degree of renal tubular injury after soil replacement in cadmium-polluted rice paddies. Toxicol Lett 2008; 176: 124-30.

การเปลี่ยนแปลงในการได้รับสารแคดเมียม ในประชากรที่อาศัยอยู่ในพื้นที่ปนเปื้อนสารแคดเมียม ในพื้นที่ตะวันตกเฉียงเหนือของประเทศไทย: การติดตาม 5 ปี

วิทยา สวัสดิวุฒิพงศ์, ปราณี มหาศักดิ์พันธ์, ทิพวัลย์ ฟั่นเขียว, พิสิฐ ลิมปธนโชติ

วัตถุประสงค์: *เพื่อศึกษาการเปลี่ยนแปลงในการได้รับสารแคดเมียม ในประชากรอายุ 15 ปีขึ้นไปที่อาศัยอยู่ในพื้นที่ปนเปื้อนสารแคดเมียมรวม 12 หมู่บ้าน ในพื้นที่ตะวันตกเฉียงเหนือของประเทศไทย*
วัสดุและวิธีการ: *ได้ตรวจหาระดับแคดเมียมในปัสสาวะของประชากรในพื้นที่ดังกล่าวในปี พ.ศ. 2547 หลังจากนั้นได้มีการรณรงค์เพื่อลดการได้รับหรือสัมผัสสารแคดเมียม ต่อมาในปี พ.ศ. 2552 ได้มีการตรวจหาระดับแคดเมียมในปัสสาวะของประชากรในพื้นที่ ประชากรที่สำรวจได้รับการสอบถามเกี่ยวกับการสูบบุหรี่ และการบริโภคข้าวที่ปลูกในพื้นที่ปนเปื้อนสารแคดเมียม ซึ่งเป็นสองทางหลักในการได้รับสารแคดเมียม*
ผลการศึกษา: *ได้สำรวจประชากรครั้งแรกรวม 7,697 ราย และครั้งที่สองรวม 6,748 ราย พบว่าประชากรในการสำรวจครั้งแรกร้อยละ 34.9 ยังสูบบุหรี่อยู่ ซึ่งสูงกว่าร้อยละ 31.5 จากการสำรวจครั้งที่สอง ส่วนประชากรที่ยังบริโภคข้าวที่ปลูกในพื้นที่ปนเปื้อนสารแคดเมียมได้ลดลงจากร้อยละ 88.0 จากการสำรวจครั้งแรก เหลือร้อยละ 50.5 จากการสำรวจครั้งที่สอง สำหรับกลุ่มที่ยังบริโภคข้าวที่ปลูกในพื้นที่ปนเปื้อน พบว่าร้อยละ 55.5 มีระดับแคดเมียมในปัสสาวะ $\geq$ 2 ไมโครกรัม/กรัมครีเอตินิน จากการสำรวจครั้งแรก และเพิ่มเป็นร้อยละ 61.3 จากการสำรวจครั้งที่สอง ส่วนกลุ่มที่บริโภคข้าวที่ซื้อจากที่อื่น พบว่าผู้ที่มีระดับแคดเมียมในปัสสาวะ $\geq$ 2 ไมโครกรัม/กรัมครีเอตินิน ได้ลดลงจากร้อยละ 46.7 จากการสำรวจครั้งแรก เป็นร้อยละ 35.6 จากการสำรวจครั้งที่สอง ผลการวิเคราะห์ข้อมูลจากการสำรวจทั้งสองครั้ง พบว่าการบริโภคข้าวที่ปลูกในพื้นที่ปนเปื้อน มีโอกาสทำให้ความชุกของผู้ที่มีระดับแคดเมียมในปัสสาวะสูงเพิ่มขึ้น ได้มากกว่าจากการสูบบุหรี่*
สรุป: *ระดับแคดเมียมในปัสสาวะของประชากรที่สำรวจได้ลดต่ำลงอย่างมีนัยสำคัญทางสถิติ ในกลุ่มที่ได้รับสารแคดเมียมลดลง*