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Blood and Urine Cadmium Levels in Relation to Demographic and Life Style in Middle Aged and Elderly Men

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Background levels of cadmium in food, water, and ambient air may not be a health concern for the general population except for smoking individuals or individuals in industry producing or using cadmium. Chronic exposures, however, can be a major concern because cadmium has a tendency to accumulate, primarily in the kidneys and the liver and affect primarily the kidneys, cardiovascular system, and skeletal system (Waalkes and Rehm 1994; Järup et al. 1998). Cadmium also has been associated with an increased frequency of prostate carcinoma (Lee and White 1980; Pearce et al. 1987; Elghamy et al. 1990; Järup et al. 1998).

The incidence of prostate carcinoma has become the most frequently diagnosed cancer for men in some Western countries (American cancer Society 1999; Black et al. 1997; Haas and Sakr 1997). But, a low rate of prostate carcinoma occurs among Asians (Sung et al. 1999). This disease accounted for only 2.2% of all cancer deaths in Taiwan versus 14% among American men's in 1995. Potential risk factors for the disease include environmental and life-style factors. Among these factors, cadmium's association was less conclusive (Järup et al. 1998).

Given that the occurrence of prostate carcinoma has an association with the exposure to cadmium, and the great difference in the incidence of the disease between Asian men and Western men, there may be a difference between them in cadmium burden. Few investigations have been conducted to measure the cadmium level in Asian populations. This study was to assess the levels of blood cadmium (BCd) and urine cadmium (UCd) of selected men aged 50 and above who live in northern Taiwan and identify factors that may have an association with the cadmium burden. This would allow us to establish baseline knowledge of human cadmium exposure for a further study in the relationship between prostate cancer and cadmium exposure.

MATERIALS AND METHODS

This investigation was conducted at a health examination center. This center has been established since 1994 to deliver clinical preventive services for routine health examinations. Urine and blood specimens are collected to routinely determine levels of creatinine, uric acid, nitrite, serum triglycerides, serum total

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cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol, blood calcium and iron, liver function, renal function and diabetes screening. However, cadmium exposure is not routinely assessed.

We restricted the study population to man aged 50 and above, and selected them as convenience samples from June to September 1999. We explained the purpose of the study to male clients and invited whoever was eligible in age criteria. With consent, specimens for cadmium measures were collected while they were at the health examination center, in addition to specimens collected for the routine screening examinations. Each participant completed also a self-reported questionnaire to provide personal information such as demographic characteristics, lifestyle factors, dietary characteristics and limited personal and family histories of health.

Urine was convenient to be collected in a sterile, plastic collection cup and transferred the required 10ml sample to a conical-bottom plastic tube free of cadmium contamination. Blood specimens of 2-3ml were collected in pre-screened heparin tubes also from lots verified to be free of cadmium contamination. Both urine and blood specimens were stored at 4℃ if analyzed in a week, or at -20℃ if not analyzed within a week. At the analyses, 100ul of blood and 900ul of matrix modifier (0.2% nitric acid, 0.5% Triton®-x-100 and 0.2%$(NH_4)_2$ HPO_4) and 100ul of urine and 200ul of matrix modifier were prepared for analyses. Samples, quality control specimens, and standards prepared with matrix modifier were analyzed for cadmium on a Perkin-Elmer Model 5100 PC atomic absorption spectrometer with Zeeman background correction (Sampson, 1999; Sharma et al 1982). For quality control, blood reference samples (NYCOMED PHARMA AS, Oslo, Norway) were used. Urine cadmium analysis was verified every other month using Inter-laboratory Comparison program, Le Centre de toxicologie du Québec (Sainte-Foy, QC, Canada). The recovery rates for spike tests were 100.7±3.5% for urine analysis and 100.9 ±3.6% for blood analysis.

The data analysis was conducted with SAS 6.12 (Cary, NC) beginning with descriptive analysis of demographic and lifestyle variables of the participants. Classical statistical parameters, including mean and standard deviation, geometric mean (GM) and standard deviation, median and range, were computed for cadmium levels in the specimens. We also used multivariate logistic regression model to identify risk factors of elevated cadmium levels.

RESULTS AND DISCUSSION

We considered age as an important factor influencing cadmium burden in human and education, occupation, diet and lifestyle as other potential risk factors. Because the study participants practice annual routine health examination, it is not surprising that about 22% participants received college or graduate education. Younger individuals (ages 50-59) were more likely to work as white-collar employees than older men. (Table 1) Among individuals ages 70 and above,

Table 1. The demographic characteristics of study participants by age

Characteristics	Age (years)			Total
	50-59 N=144	60-69 N=105	70+ N=46	N=295
	N (%)	n (%)	n (%)	n (%)
Education (Years)				
≦9	61 (42.4)	61 (58.1)	21 (45.7)	143 (48.5)
10-15	42 (29.2)	27 (25.7)	14 (30.4)	83 (28.1)
>15	39 (27.0)	15 (14.3)	10 (21.7)	64 (21.7)
Missing	2 (1.4)	2 (1.9)	1 (2.2)	5 (1.7)
p-value*				0.09
Occupation				
White collar	94 (65.3)	48 (45.7)	14 (30.4)	156 (52.9)
Blue collar	33 (22.9)	29 (27.6)	5 (10.9)	67 (22.7)
None	12 (8.3)	27 (25.7)	23 (50.0)	62(21.0)
Missing	6 (4.2)	1 (0.9)	3 (6.5)	10 (3.4)
p-value*				0.001
Smoking				
No	73 (50.7)	48 (45.7)	46 (39.1)	139 (47.1)
Quit>5 years	15 (10.4)	16 (14.4)	14 (30.4)	45 (15.3)
Quit≦5years	12 (8.3)	12 (10.6)	3 (6.5)	27 (9.1)
Yes	43 (29.9)	28 (26.7)	11 (23.9)	82 (27.8)
Missing	1 (0.7)	1 (0.9)	0 (0.0)	2 (0.7)
p-value*				0.01
Alcohol				
No	86 (57.6)	57 (54.3)	31 (67.4)	174 (60.0)
Quit	8 (5.5)	12 (11.4)	5 (10.9)	25 (8.5)
Yes	47 (32.6)	32 (30.5)	10 (21.7)	89 (30.2)
Missing	3 (2.1)	4 (3.8)	0 (0.0)	7 (2.4)
p-value*				0.28

*p-value of Chi-square test

41.3% of them remained active at work. They were less likely than younger ones to be current smokers (39.1% vs. 50.7%), but more likely to have quit the smoking habit longer than 5 years. Apparently, lifestyles of study participants varied among age groups. Although, drinking habit did not vary substantially among men of these age groups.

Both arithmetic and geometric means showed BCd and UCd levels of study subjects tended to increase as age increased, although trends were not significant in the Wilcoxon rank-sum test (Table 2). Geometric means show that the BCd levels increased from 0.78 ug/L for younger individuals to 0.93 ug/L for the oldest individuals. The values of UCd for the corresponding groups were 0.74 ug/g creatinine and 0.92 ug/ g creatinine. The overall geometric means were 0.83 ug/l for BCd and 0.82 ug/g creatinine for UCd. Cadmium levels in blood for normal population are usually between 0.1 ug/L and 1.0 ug/L for nonsmoker and 1.0-4.0 ug/L for smokers (Sharma, 1982; Järup, et al. 1998). Our study population seemed to have the BCd levels similar to Italian (dell'Omo et al. 1999), but might have slight higher UCd level than American (Paschal et al. 2000).

Some other chemicals may influence the body burden of cadmium. A low intake of dietary calcium, iron, zinc, and copper may account for increased susceptibility to bone effect at cadmium exposure (Klaassen, 1996). Flanagan (1978) also found iron deficiency increases the cadmium absorption in the gastrointestinal tract. Table 2 also shows blood iron levels decreased as age increased, indicating a negative association with cadmium burden. The levels in blood calcium did not vary substantially.

If not by inhalation exposure in the workplace, food and cigarette smoke are the largest sources of cadmium exposure for general population (Järup et al. 1998). Cadmium from cigarette smoke is in very small size of particles and consequently 50-100% are deposited in the alveoli (Nordberg, 1985). Cigarette smoke inhalation is thus the largest source of cadmium exposure. This study also found that BCd level was higher in smokers than in nonsmokers (1.09 ug/L vs. 0.73 ug/L in GM) (Table 3). The level for those who had quit the habit for less than 5 years was similar to that for current smokers. Current alcohol drinking also elevated the BCd level. Blue-collar employees had higher BCd levels probably due to occupational exposure. It is also possible that blue-collar employees are more likely smokers (Yen, et al.1994). Further analyses also showed that subjects who had received less education were more likely smokers and blue-collar employees (data not shown). Therefore, it is not surprising that study participants receiving 9 years or less education had the highest levels of BCd (GM=0.96 ug/L) and UCd (GM=0.91 ug/g cre.). Those with 16 years and above of education had the lowest levels of BCd (GM=0.69 ug/L) and UCd (GM=0.70 ug/g cre.). Current smokers also had a higher UCd level, except former smokers, who had the lowest level in urine. UCd levels reflect most total body burden of cadmium and part of recent exposure (Bernard and Lauwerys, 1986). On the other hand, BCd levels indicate principally the recent exposure to cadmium (Lauwerys et al. 1994; Roels et al. 1989).

Based on the data, half of participants in this study had their BCd at the level of 0.84 ug/L or higher, and one fourth of subjects had UCd at the level of 1.73ug/g creatinine or higher. Table 4 shows multivariate logistic regression model identifying factors associated with elevated levels of BCd and UCd. Cadmium levels did not associate substantially with occupation, alcohol consumption, blood iron and shellfish consumption. Compared with men aged 50-59 years, the odds ratios of higher UCd level were 2.0 for men aged 60-69, and 3.4 for men aged 70 and above. There was also a similar trend by age in the relationship with elevated BCd, but with the evidence of less strong. This phenomenon may reflect that recent exposure to cadmium is not associated with age significantly, but the total body burden is significantly age associated. This finding is consistent with previous finding (Bernard and Lauwerys 1986; Lauwerys et al. 1994).

Table 2. Cadmium, calcium, and iron in blood and cadmium in urine by age

	Age (Years)			Total
	50-59	60-69	70+	
Blood cadmium(ug/l)				
N	142	105	46	293
Mean±Sd	1.16±1.10	1.18±0.89	1.33±1.15	1.19±1.04
Median	0.8	0.88	0.92	0.84
GM (GSD)	0.78 (0.96)	0.87 (0.85)	0.93 (0.89)	0.83 (0.91)
5^{th}-95^{th} percentile	0.13-3.35	0.19-3.01	0.27-3.62	0.15-3.35
p-value				0.48
Urine cadmium (ug Cd/g cre)				
N	144	105	46	295
Mean±Sd	1.24±1.92	1.44±1.47	1.67±1.82	1.38±1.76
Median	0.86	1.11	1.06	0.94
GM (GSD)	0.74 (1.05)	0.91 (1.06)	0.92 (1.21)	0.82 (1.08)
5^{th}-95^{th} percentile	0.10-3.32	0.12-3.44	0.09-5.96	0.10-4.05
p-value				0.13
Blood calcium (mg/dL)				
N	144	104	46	294
Mean±Sd	9.04±0.37	9.06±0.36	9.07±0.40	9.05±0.37
Median	9.0	9.0	9.05	9.0
GM (GSD)	9.03 (0.04)	9.06 (0.04)	9.06 (0.04)	9.04 (0.04)
5^{th}-95^{th} percentile	8.5-9.7	8.5-9.7	8.4-9.9	8.5-9.7
p-value				0.75
Blood iron (mg/dL)				
n	144	104	46	294
Mean±Sd	116.15±41.64	108.85±36.71	99.37±29.70	110.90±38.62
Median	116.5	107.5	102.0	111.0
GM (GSD)	108.06 (0.40)	101.97 (0.39)	93.62 (0.39)	103.52 (0.40)
5^{th}-95^{th} percentile	57.0-190.0	56.0-168.0	46.0-133.0	53.0-177.0
p-value				0.03

p-value: of Wilcoxon rank-sum test; SD: standard deviation; GM:geometric mean; GSD: geometric standard deviation.

Table 3. The statistics for levels of cadmium in blood and urine by demographic characteristics

	Blood cadmium (ug/L)			Urine Cadmium (ug Cd/g cre.)		
	n	Median	GM (GSD)	n	Median	GM (GSD)
Education (Years)						
≦9	142	0.98	0.96 (0.91)	143	1.05	0.91 (1.02)
10-15	82	0.79	0.76 (0.91)	83	0.85	0.74 (1.16)
＞15	64	0.72	0.69 (0.87)	64	0.76	0.70 (1.04)
p-value*	0.02			0.10		
Occupation						
White collar	154	0.79	0.74 (0.93)	156	0.86	0.75 (1.06)
Blue collar	67	1.04	1.05 (0.82)	67	1.05	0.84 (1.07)
Others	62	0.83	0.83 (0.93)	72	1.10	0.89 (1.06)
p-value*	0.047			0.38		
Smoking						
No	139	0.66	0.73 (0.94)	139	0.80	0.71 (1.03)
Quit＞5 years	45	0.70	0.66 (0.96)	45	0.70	0.65 (1.07)
Quit≦5years	26	1.16	1.09 (0.54)	27	1.18	0.93 (1.06)
Yes	81	1.19	1.09 (0.87)	82	1.27	1.08 (1.08)
p-value*	0.0002			0.004		
Alcohol						
No	174	0.79	0.75 (0.97)	174	0.81	0.73 (1.12)
Quit	25	1.00	0.93 (0.93)	25	1.00	0.62 (1.29)
Yes	87	0.88	0.95 (0.75)	89	1.18	1.03 (0.85)
p-value*	0.14			0.08		
Fish and Shellfish						
＜1(dish/week)	35	0.88	0.88 (0.95)	35	0.86	0.65 (1.23)
1-6	196	0.79	0.77 (0.87)	198	0.9	0.78 (1.01)
≧7	48	1.04	1.05 (0.97)	48	1.12	1.02 (1.12)
p-value*	0.06			0.21		

Cre.: creatinine; *p-value of Wilcoxon rank-sum test.

Table 4 also shows current smokers were 2.5 times more likely than nonsmoker to have higher cadmium level in urine. There was no risk to have BCd level > 0.84 ug/L for men who had quit smoking for longer than 5 Years. The risk with elevated BCd level was significant for active smokers (OR=3.2, 95%CI=1.7-6.2) or men who quit smoking not long enough (OR=5.3, 95%CI=1.9-14.7), reflecting smoking as the main source of current cadmium exposure.

In conclusion this study suggests that age had a stronger association with the level of urine cadmium than with the level of blood cadmium. Data also show that cigarette smoke inhalation is a more important exposure source of cadmium than occupational exposure, and the intake of alcohol and fish/shell fish.

Table 4. Odds ratios (OR) and 95% confidence intervals (CI) for subjects with blood cadmium ≥ 0.84 ug/L and urine cadmium ≥ 1.73 ug Cd/ g creatinine by associated factors obtained from multivariate logistic regression

Factor	Blood cadmium OR (95%CI)	Urine cadmium OR (95%CI)
Age (years)		
50-59	1.0	1.0
60-69	1.2 (0.7-2.3)	2.0 (1.0-4.0)
70+	2.0 (0.9-4.8)	3.4 (1.3-8.8)
Occupation		
White collar	1.0	1.0
Blue collar	1.2 (0.6-2.3)	1.0 (0.5-2.2)
Others	0.9 (0.4-1.8)	0.9 (0.4-2.1)
Smoking		
No	1.0	1.0
Quit > 5 years	1.0 (0.5-2.2)	0.5 (0.2-1.5)
Quit ≦ 5 years	5.3 (1.9-14.7)	1.5 (0.5-4.2)
Yes	3.2 (1.7-6.2)	2.5 (1.2-5.1)
Alcohol		
No	1.0	1.0
Quit	1.3 (0.5-3.5)	0.7 (0.2-2.1)
Yes	1.0 (0.6-1.9)	1.1 (0.5-1.9)
Calcium in blood (mg/dL)		
≦9.0	1.0	1.0
>9.0	1.1 (0.7-1.9)	2.0 (1.1-3.6)
Iron in blood (mg/dL)		
≦110	1.0	1.0
>110	0.9 (0.5-1.5)	1.1 (0.6-2.1)
Fish and Shellfish (dish/ week)		
<1	1.0	1.0
1-6	0.7 (0.3-1.6)	1.1 (0.4-2.9)
≧7	1.6 (0.6-4.2)	2.3 (0.8-7.2)

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