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Urinary Arsenic Concentrations and their Associated Factors in Korean Adults

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Arsenic (As) is a well-known human carcinogen and its dietary exposure has been found to be the major route of entry into general population. This study was performed to assess the body levels of As and their associated factors in Korean adults by analyzing total As in urine. Urine and blood samples were collected from 580 adults aged 20 years and older, who had not been exposed to As occupationally. Demographic information was collected with the help of a standard questionnaire, including age, smoking, alcohol intake, job profiles, and diet consumed in the last 24 hrs of the study. Total As, sum of As(III), As(V), monomethylarsonic acid (MMA), dimethylarsinic acid (DMA), in urine was determined using atomic absorption spectrometer involving hydride generation method. The geometric mean concentration of total As in urine was 7.10 μg/L. Urine As was significantly higher in men (7.63 μg/L) than in women (6.75 μg/L). Age, smoking, alcohol consumption, and job profiles of study subjects did not significantly affect the concentration of As in urine. No significant relationship was observed between body mass index (BMI), Fe, and total cholesterol in serum and urinary As. Urine As level was positively correlated with seaweeds, fishes & shellfishes, and grain intake. A negative correlation between urinary As level and HDL-cholesterol in serum and meat intake was observed. Overall, these results suggest that urinary As concentration could be affected by seafood consumption. Therefore, people who frequently consume seafood and grain need to be monitored for chronic dietary As exposure.

***Key words*:** Arsenic, Korean adult, Life style, Seafood, Urine

INTRODUCTION

Various arsenic (As) compounds widely exist in the natural environment with soil, minerals and volcanic eruptions. Toxicity of As depends on chemical forms of As compounds (1). Inorganic As has been known as a human carcinogen in the lung, skin, bladder, kidney, and liver as well as non-carcinogenic adverse health effects such as skin disease, diabetes, cardiovascular disease and neurotoxicity. Inorganic arsenics, arsenite and arsenate, are metabolized to the less toxic forms, monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA), through methylation process in the body which are more toxic than organoarsenics. Organoarsenics, arsenocholine, arsenobetaine and arsenosugars, essentially are harmless and easily excreted in urine without metabolism. And the trivalent forms are more toxic than the pentavalent arsenics.

Anthropogenically produced As compounds are primarily arsenic trioxide (As_2O_3) and arsenic pentoxide (As_2O_5), those are used to the various industrial processes such as non-ferrous metal smelteries, semiconductor and wood preservatives. About 90% of all produced As is copper chromated arsenic (CCA) as a wood preservative, and others are used in pesticides, alloys, optical glass and medicines (2). Uses of inorganic As compounds in CCA and pesticides are prohibited or suggested to transit by the eco-friendly products because of their risk on the living environment. However, previous uses of inorganic As contained products before the regulation may act as exposure sources of As in the living environment.

Human body can be exposed to the As by inhalation and oral ingestion. Workers generally are exposed to inorganic As through inhalation in industry, otherwise general popula-

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tion are exposed to inorganic As through a drinking water contaminated by arsenic, and organic As through food particularly seafood (2). Arsenicosis was reported from several countries such as Bangladesh, China, India, and Taiwan (3-6). Arsenic-induced adverse health effect has not been established yet in the general population of Korea, but several studies reported that some As compounds are found in seafood, fishes & shellfishes and seaweeds, which are favorite foods of Korean (7,8). Those marine foods contain As compounds naturally from < 1 up to 25 mg/kg or more, the most of As compounds is organic forms (2,7,8). However, recently it was reported that increased seafood consumption elevates internal exposure to inorganic As and its metabolites, MMA and DMA (9,10). Therefore, Korean diet patterns preferred consumption of seafood may increase the risk of As exposure. Also, it was demonstrated that individual iron (Fe) and zinc (Zn) level might affect the absorption and excretion of As, and cholesterol level could be changed by exposure to As (11,12). Currently, As intake from diet was reported by several studies in Korea (7,13), however, which is limited to perform a health risk assessment of As exposure in Korean. This study was performed to assess internal exposure level to As and their associated factors by analyzing total As in urine.

MATERIALS AND METHODS

Study subjects and sample collection. Study subjects of 580 adults (242 males and 338 females) with 20 years of age and older were recruited from randomly selected 6 districts (two districts of urban, rural and costal, respectively) in Korea. They had not been exposed to As occupationally. Study subjects were informed about study aim and details and a written consent was obtained from each individual who are willing to participate in this study. We conducted an individual personal interview to get information about demographic characteristics, life-styles such as drinking and smoking habits, jobs, and diets during the last 24 hrs, followed a physical measurement. Whole blood and spot urine were sampled from each subject. Serum was separated by centrifugation at 3,000 rpm for 10 min. All samples stored at −80°C until analysis.

Determination of As concentration in urine. Total As in urine was analyzed by the hydride generation method with an atomic absorption spectrometer (Perkin-Elmer model 5100) coupled with the hydride generation system (Perkin-Elmer FIAS 400). In this study, total As is defined as the sum of inorganic As (arsenite and arsenate) and their metabolites such as monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA), because organic arsenics such as arsenocholine, arsenobetaibe and arsenosugars, could not measure by the hydride generation method (14). Briefly, 1 ml of urine sample mixed with 1 ml of HCl (36%, w/v), 0.5 ml of potassium iodide (5%, w/v), and 0.5 ml of ascorbic acid (5%, w/v) and diluted with 10% HCl after 1 hr incubation. Then the mixture reacted with 0.2% sodium borohydride and 0.05% sodium hydroxide to produce the hydride arsine gas. Generally, organoarsenics, arsenocholine, arsenobetaibe and arsenosugars, do not produce an arsine gas by reacting with the reductants. The limit of detection of As in this method was 0.05 μg/L.

Physical measurement and serum analyses. Height and weight in the study subjects were measured according to the standard protocol, and body mass index (BMI) was calculated from weight (kg)/height^2 (m^2) (15). Total cholesterol and high density lipoprotein- (HDL-) cholesterol in serum were measured by an auto-analyzer (ADVIA 1650/2400, Hitachi 7180, Japan). Fe and unsaturated iron binding capacity (UIBC) in serum were measured using the FE-750 reagent (Shin-yang Co., Korea) which reacts with Fe^{2+} specific Nitroso-PSAP reagent. Total iron binding capacity (TIBC) was calculated from the sum of Fe and UIBC. Ferritin in serum was measured using the Accu-Bind ELISA kit (Monobind Imc., USA) according to the manufacturers' instruction.

Statistical analysis. All statistical analyses were performed using SPSS version 17.0. The concentration of As in urine was presented as geometric mean (GM) and geometric standard deviation (GSD), and the others are shown as the arithmetic means ± standard deviations. Statistical evaluation for means was performed by unpaired t-test or analysis of variance (ANOVA) following multiple comparison tests with Duncan's method. The relations between As concentration in urine and other variables were examined by Pearson's correlation analysis. The level of statistical significance was set at $p < 0.05$.

RESULTS

The geometric mean concentration of total As in urine was 7.10 μg/L with ranged from 0.36 μg/L to 36.79 μg/L. Concentration of total As in urine was significantly higher in males (7.63 μg/L) than in females (6.75 μg/L) ($p < 0.05$, Table 1). No significant differences in urinary As levels were observed among age groups. The levels of As in urine were not different by smoking status and drinking habit. The highest As concentration in urine was observed in fisherman (8.27 μg/L), however the As levels in urine were not significant statistically among jobs in this study subjects (Table 2).

BMI, cholesterol and body Fe levels in serum of study subjects are shown in Table 3. The means of height and weight were higher in males than in females, but BMI was similar between two groups. Total cholesterol and HDL-cholesterol were higher in females than in males. Fe and

Table 1. Geometric mean concentrations of arsenic in urine of study subjects (μg/L)

	Male	Female	Total	Statistics
N	242	338	580	
GM (GSD)	7.63 (1.82)	6.75 (2.04)	7.10 (1.96)	t=2.24*
(Min-Max)	(0.36-27.72)	(0.47-36.79)	(0.36-36.79)	

GM: geometric mean, GSD: geometric standard deviation, *: $p < 0.05$.

Table 2. Geometric mean concentrations of arsenic in urine by demographic factors in study subjects (μg/L)

		Male		Female		Total		Statistics
		N	GM (GSD) (Min-Max)	N	GM (GSD) (Min-Max)	N	GM (GSD) (Min-Max)	
Age	~39	22	8.38 (1.48) (2.79-15.37)	44	6.81 (2.13) (0.47-33.42)	66	7.30 (1.94) (0.47-33.42)	F = 1.02
	40~59	107	7.36 (1.88) (0.36-25.72)	148	6.40 (2.04) (0.49-36.79)	255	6.79 (1.98) (0.36-36.79)	
	60-	113	7.74 (1.83) (1.31-27.72)	146	7.09 (2.02) (0.91-33.80)	259	7.37 (1.94) (0.91-33.80)	
Smoking	Current	99	7.21 (1.81) (0.36-26.25)	7	4.45 (1.89) (2.01-10.23)	106	6.99 (1.83) (0.36-26.25)	F = 0.96
	Ex-Smoker	78	7.65 (1.89) (1.27-27.72)	7	9.50 (1.69) (4.81-22.71)	85	7.78 (1.87) (1.27-27.72)	
	None	65	8.27 (1.76) (2.11-25.72)	321	6.74 (2.05) (0.47-36.79)	386	6.98 (2.01) (0.47-36.79)	
Drinking	Yes	185	7.53 (1.80) (1.27-27.72)	125	5.89 (2.11) (0.47-32.00)	310	6.82 (1.95) (0.47-32.00)	t = 1.50
	No	57	7.95 (1.88) (0.36-23.72)	210	7.28 (1.99) (0.49-36.79)	267	7.42 (1.96) (0.36-36.79)	
Job	Business	43	8.60 (1.60) (2.91-20.84)	33	5.50 (2.38) (0.47-20.50)	76	7.08 (2.02) (0.47-20.84)	F = 1.84
	Farmer	82	7.39(2.00) (0.36-25.72)	56	5.96(2.24) (0.75-33.80)	138	6.77(2.11) (0.36-33.80)	
	Fisherman	48	8.04 (1.69) (1.62-19.11)	47	8.51 (1.93) (1.50-32.00)	95	8.27 (1.80) (1.50-32.00)	
	Service	23	6.33 (1.82) (1.27-16.78)	41	6.37 (1.92) (1.27-29.89)	64	6.36 (1.87) (1.27-29.89)	
	Labor & housekeeper	46	7.49 (1.81) (2.11-27.72)	158	6.93 (1.95) (1.16-36.79)	204	7.05 (1.92) (1.16-36.79)	

GM: geometric mean, GSD: geometric standard deviation.

Table 3. Physical characteristics and the levels of cholesterol and iron in serum of study subjects

	Male	Female	Total	Statistics
Height (cm)	166.2 ± 6.6	153.1 ± 6.6	158.6 ± 9.2	t = 23.1**
Weight (kg)	66.5 ± 10.1	57.4 ± 8.7	61.3 ± 10.4	t = 11.12**
BMI (kg/m^2)	24.1 ± 3.2	24.5 ± 3.3	24.3 ± 3.3	t = −1.30
h-cholesterol (mg/dl)	41.6 ± 10.7	45.7 ± 11.7	44.0 ± 11.5	t = −4.32**
t-cholesterol (mg/dl)	177.6 ± 35.1	188.1 ± 36.4	183.7 ± 36.2	t = −3.46**
sFe (μg/dl)	132.5 ± 48.7	104.7 ± 39.0	116.2 ± 45.4	t = 7.26**
UIBC (μg/dl)	175.0 ± 55.7	208.4 ± 56.2	194.6 ± 58.3	t = −6.99*
TIBC (μg/dl)	307.5 ± 49.8	313.0 ± 49.7	310.8 ± 49.8	t = −1.30
Ferritin (μg/dl)	105.9 ± 104.3	51.8 ± 58.8	74.2 ± 84.9	t = 7.15**

* $p < 0.05$, ** $p < 0.01$.

Table 4. Pearson's correlation coefficients of BMI, serum cholesterols and serum irons with arsenic concentration in urine

Subjects	Correlation coefficient
BMI (kg/m^2)	−0.008
h-cholesterol (mg/dl)	−0.098*
t-cholesterol (mg/dl)	0.012
sFe (μg/dl)	−0.014
UIBC (μg/dl)	−0.020
TIBC (μg/dl)	−0.036
Ferritin (μg/dl)	−0.040

* $p < 0.05$.

ferritin in serum were higher in males than in females and UIBC was higher in females than in males. Therefore, TIBC was similar level between males and females. Correlation analysis was performed between total As in urine with BMI, cholesterols, and Fe levels (Table 4). No relation was observed between urine As and BMI. Arsenic concentration in urine was not significant with total cholesterol in serum, while was significantly correlated negatively with HDL-cholesterol in serum. Total As in urine was not associated with body Fe status, such as serum Fe, UIBC, TIBC and ferritin.

In the previous study, we estimated daily As intakes from diet at 56.46 μg/day in the same study subjects with this study (13). In this study, we performed a correlation analysis to evaluate whether As intakes through diet affect on the As level in urine. Daily As intake was estimated with the 24-hr recall method. There was shown a significantly positive relation between As intakes from diet and As concentrations in urine (r = 0.096, $p < 0.05$). This finding suggests that dietary As intake may affect on the total As level in urine. However, As concentration in urine was not statistically correlated with total diet intake or calorie daily. Further analysis was performed to evaluate the relation between urine As and specific food group consumption (Table 5). Total As in urine was positively correlated with specific food groups consumptions such as seaweeds (r = 0.114, $p < 0.01$), fishes & shellfishes (r = 0.087, $p < 0.05$) and grains (r = 0.083, $p < 0.05$), while was negatively correlated with meats consumption ($p < 0.05$).

Table 5. Relations between the dietary intake in each food group with the arsenic concentration in urine

Food group	Correlation coefficient
Energy (kcal)	−0.015
Total food intakes	−0.051
Daily As intake	0.096*
Grains	0.083*
Potatoes	−0.051
Sugars	−0.031
Pulse	−0.013
Seeds	−0.022
Vegetables	−0.071
Fruits	−0.051
Meats	−0.107*
Fishes & shellfishes	0.087*
Seaweeds	0.114**
Oils	0.048
Milks	0.005
Beverages	−0.035
Flavors	−0.039
Eggs	−0.008
Others	0.019

* $p < 0.05$, ** $p < 0.01$.

DISCUSSION

In this study, we analyzed total As in urine for 580 adults, who had not been exposed to As occupationally, and evaluated associated factors, such as age, gender, lifestyles, nutritional status and diet habit, with urinary As concentration.

The geometric mean concentration of As in urine was determined at 7.10 μg/L (male 7.63 μg/L, female 6.75 μg/L) in Korean adults. The urine As level observed in Korean adults was lower than those reported in other Asian countries [Bangladesh, 20.77 μg/L (16); China, 28.30 μg/L (17); Taiwan 20.71 μg/g creatinine (18)], but was similar or higher than western countries [Spain, 1.14 μg/L (19); Italy, 7.8 μg/L (20)]. However, urine As from this study was similar level with previous report by the same method in Korea [8.47 μg/g creatinine (21)]. The wide variations of urine As among countries might be attributed by various geographical contaminations sourced from natural, such as volcanic eruption and weathering, and anthropogenic activities such as mines and metal industries. Also, it could be influenced by race, life-style, nutrition and diet habits (3,22-24).

In generally, the human exposure to various metals has been observed a tendency of gender differences and age-dependent patterns (25). At present study, As concentration in urine was higher in males than in females, but was not different among the age groups. Arsenic has much short biological half-life in the body compared to other metals which could be explained partially for the independence of age (2). Several studies reported that lifestyles such as smoking and drinking habits may affect the metabolism of inorganic As (18,22). In particularly, smoking may act competitively with enzymes and co-factors in the methylation process of inorganic As (26). Aguilera *et al*. (19) reported that alcohol intake is associated with As concentration in urine. In this study, urine As levels were not statistically different by smoking and drinking habits which were consistent with previous reports (27,28). The As concentration in urine was the highest in fisherman, but was not significant among jobs.

Cholesterol is a well known risk factor for atherosclero-

sis and cardiovascular disease. Previous studies reported that chronic exposure to As could increase the risk of cardiovascular disease as well as diabetes mellitus (29,30). These findings suggest that As could affect to the lipid metabolism or regulation. However, Nabi *et al*. (12) reported that chronic As exposure subjects, arsenicosis patients, had significantly lower levels of cholesterol, HLD- and LDL-cholesterols, compared to unexposed subjects. At present study, no relation was observed between total cholesterol in serum and urine As, while HDL-cholesterol was associated negatively with As concentration in urine ($p < 0.05$). No relation was shown between BMI and urinary As concentration in this study. There is suggested that some essential metals, such as iron and zinc, interact with toxic metals in absorption in the gastrointestinal tract and in deposit in the tissues (31). Paul *et al*. (11) reported that As accumulation in the tissues was higher in Fe-deficient rats than in Fe-supplemented rats. However, we could not find any significant relation between body Fe level and As level in urine. This finding might be attributed to the body iron levels with normal range in the most of study subjects.

In our previous study, we estimated daily As intake at 56.46 μg/day, 0.93 μg/kg/day (male: 56.60 μg/day, female: 56.36 μg/day) using 24-hr recall method for the same population with this study (13). In this study, we analyzed a relation between daily As intake from diet and As concentration in urine individually. There was shown a significantly positive relation between As intakes from diet and As concentrations in urine ($r = 0.096$, $p < 0.05$), which suggests that dietary As intake may affect on the total As level in urine. In analysis for the relation between urine As and specific food group consumption, urine As was positively correlated with the consumptions of seaweeds ($r = 0.114$, $p < 0.01$), fishes & shellfishes ($r = 0.087$, $p < 0.05$) and grains ($r = 0.083$, $p < 0.05$). Approximately 75% of daily As intakes by diet were sourced from the consumptions of fishes & shellfishes and seaweeds (13). Those findings suggest that seafood and grain consumption may increase internal exposure to the As.

Most of arsenics in fishes & shellfishes and seaweeds are organic forms, such as arsenobetaine, arsenocholine, arsenosugar, and also contain trace of inorganic As and their metabolites. Although, organoarsenics are essentially harmless to human health, overconsumption of seafood could increase body exposure to the inorganic As as well as organic As. Meanwhile, several studies reported the increase of DMA excretion in urine after the seafood consumption (8,32), which is more toxic than organoarsenics. Accordingly, long-tem effects of seafood consumption frequently might be interested in public health, particularly races including Korean who have diet habit favorable to seafood. Therefore, people who frequently consume seafood and grain may need to be monitored for chronic low-level As exposure through diet.

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