Environ Health Prev Med (2016) 21:327–333
DOI 10.1007/s12199-016-0533-3

REGULAR ARTICLE

Association of beer consumption with arsenic concentration in urine: a result from a cross-sectional study of the general Japanese population

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Received: 23 January 2016 / Accepted: 10 April 2016 / Published online: 22 April 2016

Abstract
Objectives The first aim of this study was to evaluate the association between time spent living near a contaminated area and concentration of arsenic (As) compounds in the urine among study subjects. The second aim is to assess the association between consumption of various foods or beverages and As concentration in urine among them.
Methods Urine sampling was performed on 177 persons who voluntarily participated in the survey in May 2014. The median value of the sum of inorganic As (iAs) and total As (tAs) compounds was used for us to divide into two groups, such as the high and low iAs and high and low tAs groups. We analyzed data separately in two-age strata of age group A (the subjects <18 years old), and age group B (the subjects ≥18 years old). A multivariate analysis was performed with the logistic regression model to adjust for potential confounding variables.
Results No link between time spent living near a contaminated area and urinary As concentration was observed in our study. For age group B, frequently drinking beer was significantly associated with risk of being in the high tAs group ($p = 0.008$). Compared to not drinking beer, odds ratios (95 % confidence intervals) of drinking beer <1 or 2 times per week, and drinking beer ≥3 or 4 times per week were 3.09 (1.32–7.24) and 3.00 (1.02–8.80), respectively, after adjusting for age, sex, and smoking index.
Conclusion Frequent consumption of beer may be associated with high tAs in age group B

Keywords Arsenic · Inorganic arsenic · Urine · Beer · Cross-sectional studies

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Introduction

Major sources of human exposure to arsenic (As) are dusts in air, contaminated water or soil, or the food chain [1]. Exposure to As occurs via ingestion, inhalation, dermal contact, and vertical transmission from the mother [1]. The Toroku area in the Kyushu island of Japan was previously reported to be contaminated with arsenic while refining ores [2]. Not only the workers at the workplace, but also the residents living near the mine or refinery were affected by the As [2].

Most cases of human toxicity from As have been associated with exposure to inorganic As [1]. However, organic As have also been shown to have a toxic effect [3]. Epidemiological studies indicate that exposure to As increases risk of cancer in the bladder [1] and lung [4]. Furthermore, exposure to As has been shown to be associated with risk of cardiovascular disease [5].

In Japan, houses were sometimes built on land where As-using industries were previously sited, or where industries disused As compounds, especially, before the law (the Law Against Disposal of Waste Matter, Japan, 1970) inhibited to disuse arsenic compounds. Areas must now register, by law, as chemically polluted, if the concentration is more than 150 mg As/kg of soil in Japan (the Law Against Contamination of Soil, Japan, 2003).

In 2013, a survey conducted in Japan revealed that the soils of the surveyed area were polluted with As compounds. The arsenic-contaminated area surveyed is located in a city notorious for industry in the center of Hokkaido. To evaluate the health effect by the As contamination, the city bureau recruited inhabitants near the contaminated area to conduct their health check-up survey in April of 2014. Urine sampling was conducted, because the accuracy of urinary As analysis has been established [6, 7]. However, there has been no report in Japan about the effect of living near an As contaminated area on urinary As concentration, to our knowledge. Accordingly, the first aim of this study was to evaluate the association between time spent living near a contaminated area and concentration of As compounds in the urine of study subjects.

Rice, fish, seaweed, shellfish, and others have been shown to be foods abundant in arsenic compounds [8]. Beer and wine have been shown to be beverages abundant in arsenic compounds [9]. Moreover, intake of foods rich in As compounds has been shown to elevate urinary arsenic concentrations in humans [7]. However, there has been no report about the effect of drinking beer or wine on urinary As concentration among Japanese, to our knowledge. Consequently, the second aim is to assess the association between consumption of various foods or beverages and inorganic or total As concentration in urine and among them.

Materials and methods

Participants/Subjects

Participants were recruited by the city bureau from the residents living near the area contaminated with As compounds in the center of Hokkaido in April, 2014. Eventually, 177 persons (78 males, 99 females) participated in the survey with a written informed consent in May 2014. The group of subjects younger than 18 years old and the group of subjects 18 years old or older were designated as age group A and age group B, respectively.

Measurements of As compounds

Urine sampling was performed at a room in an adjacent elementary school in May 2014. Five components of As compounds, such as arsenite (AsIII), arsenate (AsV), monomethylarsonate (MMA), dimethylarsinate (DMA), and arsenobetaine (AsBe), were measured with HPLC-ICP-MS [6, 10–12] (Chuo-Rodosaigai-Boshikyokai, Tokyo).

Questionnaire

Each adult subject or person responsible for a child subject completed a structured questionnaire, which consisted of inquiries about personal characteristics such as age, sex, body height, body weight, BMI (body mass index), and duration of living near the contaminated area. Foods abundant in arsenic compounds have been shown to be rice, fish, octopus and squid, shellfish, and seaweed [8]. Beverages abundant in arsenic compounds have been also shown to be beer and wine [9]. Accordingly, frequencies consuming these foods and beverages were inquired. In addition, smoking habits were surveyed, and smoking

Table 1 Comparison of urinary concentration of arsenic compounds between the group younger than 18 years old (age group A) and the group 18 years old or older (age group B)

Items	Age group A ($N = 51$)		Age group B ($N = 126$)		p value[#]
	Mean (SD)	Median (min–max)	Mean (SD)	Median (min–max)	
AsIII (μg/L)	5.64 (6.51)	3.9 (1.5–41.4)	6.00 (7.75)	3.5 (1.5–54.7)	0.749
AsV (μg/L)	1.54 (0.23)	1.5 (1.5–3.1)	1.77 (1.70)	1.5 (1.5–14.9)	0.137
MMA (μg/L)	2.31 (1.26)	2.1 (1.5–9.5)	2.11 (1.00)	1.6 (1.5–8.7)	0.317
DMA (μg/L)	31.12 (19.28)	26.9 (1.5–94.3)	33.60 (27.16)	25.2 (1.8–140.3)	0.495
AsBe (μg/L)	143.7 (579.9)	32.1 (1.5–4136.2)	69.29 (78.41)	44.3 (1.5–458.1)	0.365
Inorganic As (AsV + AsIII) (μg/L)	7.17 (6.49)	5.4 (3.0–42.9)	7.77 (8.10)	5.2 (3.0–65.2)	0.608
Total As (μg/L)	184.3 (578.5)	77.4 (13.6–4158.0)	112.8 (97.28)	85.8 (8.0–529.7)	0.384

AsV (μg/L) arsenate, *AsIII* arsenite, *MMA* monomethyl arsonate, *DMA* dimethyl arsinate, *AsBe* arsenobetaine, *SD* standard deviation

[#] Welch's test for comparison between the two age groups

Table 2 Comparison of personal characteristics and consumption of foods between the high and low inorganic arsenic (iAs) groups as well as between the high and low total arsenic (tAs) groups in urine of the subjects younger than 18 years old (age group A)

Items	Contents	The high iAs group (≧5.4 µg/L)		The low iAs group (<5.4 µg/L)		p value[#]	The high tAs group (≧77.4 µg/L)		The low tAs group (<77.4 µg/L)		p value[#]
		No.		No.			No.		No.		
Age (years)	Mean (SD)	26	9.4 (3.7)	25	8.6 (5.1)	0.554	26	9.6 (4.6)	25	8.4 (4.2)	0.329
Sex	Male (%)	13	50.0 (%)	12	48.0 (%)	0.886[$]	10	38.5 (%)	16	64.0 (%)	0.068[$]
Body height (cm)	Mean (SD)	26	135.3 (22.2)	25	127.4 (28.5)	0.275	26	133.9 (25.1)	25	128.9 (26.2)	0.490
Body weight (Kg)	Mean (SD)	26	34.5 (14.3)	25	30.6 (16.3)	0.367	26	35.4 (16.3)	25	29.6 (13.9)	0.181
BMI (Kg/m^2)	Mean (SD)	26	17.9 (2.3)	25	17.4 (2.9)	0.538	26	18.4 (2.6)	25	16.9 (2.4)	0.031
Residency (years)[a]	Mean (SD)	26	7.9 (4.4)	25	6.3 (4.6)	0.219	26	7.8 (5.2)	25	6.4 (3.7)	0.267
Rice	Less than everyday	0	0.0 (%)	0	0.0 (%)	1.000[$]	0	0.0 (%)	0	0.0 (%)	1.000[$]
	Almost everyday	26	100.0 (%)	25	100.0 (%)		26	100.0 (%)	25	100.0 (%)	
Bread	<1–2 times per week	9	34.6 (%)	7	28.0 (%)	0.719	11	42.3 (%)	5	20.0 (%)	0.177
	3–4 times per week	6	23.1 (%)	11	44.0 (%)		7	26.9 (%)	10	40.0 (%)	
	Almost everyday	11	42.3 (%)	7	28.0 (%)		8	30.8 (%)	10	40.0 (%)	
Fish	<1–2 times per month	7	38.1 (%)	23	36.5 (%)	0.909	6	23.1 (%)	12	48.0 (%)	0.208
	1–2 times per week	18	44.4 (%)	26	41.3 (%)		17	65.4 (%)	9	36.0 (%)	
	≧3–4 times per week	1	17.5 (%)	14	22.2 (%)		3	11.5 (%)	4	16.0 (%)	
Octopus and squid	None	5	19.2 (%)	6	24.0 (%)	0.861	7	26.9 (%)	4	16.0 (%)	0.557
	1–2 times per month	14	53.9 (%)	12	48.0 (%)		12	46.2 (%)	14	56.0 (%)	
	≧1–2 times per week	7	26.9 (%)	7	28.0 (%)		7	26.9 (%)	7	28.0 (%)	
Shellfish	None	6	23.1 (%)	10	40.0 (%)	0.430	8	30.8 (%)	8	32.0 (%)	0.817
	1–2 times per month	17	65.4 (%)	11	44.0 (%)		14	53.9 (%)	14	56.0 (%)	
	≧1–2 times per week	3	11.5 (%)	4	16.0 (%)		4	15.4 (%)	3	12.0 (%)	
Seaweed	<1–2 times per month	8	30.8 (%)	2	8.0 (%)	0.320	8	30.8 (%)	2	8.0 (%)	0.892
	1–2 times per week	11	42.3 (%)	17	68.0 (%)		9	34.6 (%)	19	76.0 (%)	
	≧3–4 times per week	7	26.9 (%)	6	24.0 (%)		9	34.6 (%)	4	16.0 (%)	

SD standard deviation

[#] Welch's test or Mann–Whitney *U* test for comparison between the high and low iAs groups as well as between the high and low tAs groups

[$] Chi square test

[a] Duration of time living near arsenic-contaminated area (year)

Table 3 Comparison of personal characteristics and consumption of foods and beverages between the high and low inorganic arsenic (iAs) groups as well as between the high and low total arsenic (tAs) groups in urine of the subjects 18 years old or older (age group B)

Items	Contents	The high iAs group (≧5.2 μg/L)		The low iAs group (<5.2 μg/L)		p value[#]	The high tAs group (≧85.8 μg/L)		The low tAs group (<85.8 μg/L)		p value[#]
		No.		No.			No.		No.		
Age (years)	Mean (SD)	63	50.9 (15.5)	63	52.8 (17.4)	0.517	63	52.1 (15.5)	63	51.6 (17.4)	0.880
Sex	Male (%)	30	47.6 (%)	22	34.9 (%)	0.148[$]	28	44.4 (%)	24	38.1 (%)	0.469[$]
Body height (cm)	Mean (SD)	63	161.4 (8.4)	63	159.9 (8.0)	0.304	63	161.3 (7.9)	63	159.9 (8.5)	0.350
Body weight (kg)	Mean (SD)	63	62.0 (15.1)	63	58.6 (9.8)	0.147	63	61.5 (15.2)	63	59.1 (9.8)	0.296
BMI (kg/m^2)	Mean (SD)	63	23.6 (4.1)	63	22.9 (3.3)	0.307	63	23.4 (4.1)	63	23.1 (3.4)	0.634
Residency (years)[a]	Mean (SD)	63	14.8 (7.3)	63	16.1 (6.1)	0.262	63	15.1 (7.4)	63	15.8 (6.0)	0.554
Smoking index	Mean (SD)	63	205.4 (257.4)	63	218.2 (295.1)	0.795	63	234.0 (304.6)	63	189.6 (244.2)	0.369
Rice	Less than everyday	4	6.4 (%)	3	4.8 (%)	0.699[$]	5	7.9 (%)	2	3.2 (%)	0.245[$]
	Almost everyday	59	93.6 (%)	60	95.2 (%)		58	92.1 (%)	61	96.8 (%)	
Bread	<1–2 times per week	19	30.2 (%)	25	39.7 (%)	0.325	19	30.2 (%)	25	39.7 (%)	0.581
	3–4 times per week	14	22.2 (%)	12	19.0 (%)		16	25.4 (%)	10	15.9 (%)	
	Almost everyday	30	47.6 (%)	26	41.3 (%)		28	44.4 (%)	28	44.4 (%)	
Fish	<1–2 times per month	24	38.1 (%)	23	36.5 (%)	0.657	20	31.8 (%)	27	42.9 (%)	0.302
	1–2 times per week	28	44.4 (%)	26	41.3 (%)		30	47.6 (%)	24	38.1 (%)	
	≧3–4 times per week	11	17.5 (%)	14	22.2 (%)		13	20.6 (%)	12	19.0 (%)	
Octopus and squid	None	7	11.1 (%)	4	6.4 (%)	0.852	7	11.1 (%)	4	6.4 (%)	0.262
	1–2 times per month	26	41.3 (%)	32	50.8 (%)		23	36.5 (%)	35	55.6 (%)	
	≧1–2 times per week	30	47.6 (%)	27	42.9 (%)		33	52.4 (%)	24	38.1 (%)	
Shellfish	None	12	19.1 (%)	9	14.3 (%)	0.202	9	14.3 (%)	12	19.1 (%)	0.689
	1–2 times per month	39	61.9 (%)	36	57.1 (%)		39	61.9 (%)	36	57.1 (%)	
	≧1–2 times per week	12	19.1 (%)	18	28.6 (%)		15	23.8 (%)	15	23.8 (%)	
Seaweed	<1–2 times per month	13	20.6 (%)	9	14.3 (%)	0.477	10	15.9 (%)	12	19.1 (%)	0.828
	1–2 times per week	29	46.0 (%)	31	49.2 (%)		31	49.2 (%)	29	46.0 (%)	
	≧3–4 times per week	21	33.3 (%)	23	365 (%)		22	34.9 (%)	22	34.9 (%)	
Beer	None	29	46.0 (%)	37	58.7 (%)	0.090	25	39.7 (%)	41	65.1 (%)	0.008
	<1–2 times per week	20	31.8 (%)	19	30.2 (%)		25	39.7 (%)	14	22.2 (%)	
	≧3–4 times per week	14	22.2 (%)	7	11.1 (%)		13	20.6 (%)	8	12.7 (%)	
Sake	None	51	81.0 (%)	55	87.3 (%)	0.282	51	80.9 (%)	55	87.3 (%)	0.318
	1–2 times per month	7	11.1 (%)	7	11.1 (%)		8	12.7 (%)	6	9.5 (%)	
	≧1–2 times per week	5	7.9 (%)	1	1.6 (%)		4	6.4 (%)	2	3.2 (%)	
Shochu	None	42	66.7 (%)	47	74.6 (%)	0.309	43	68.2 (%)	46	73.0 (%)	0.556
	1–2 times per month	8	12.7 (%)	7	11.1 (%)		8	12.7 (%)	7	11.1 (%)	
	≧1–2 times per week	13	20.6 (%)	9	14.3 (%)		12	19.1 (%)	10	15.9 (%)	

index was calculated as duration of smoking in years multiplied by number of cigarettes per day.

Statistical analysis

The median value of the sum of AsIII and AsV in urine was used for the division of the two groups, such as the high and low inorganic As (iAs) groups. Furthermore, the median value of the sum of all As components in the urine was used for the division of the two groups, such as the high and low total As (tAs) groups. Welch's test, Mann–Whitney *U* test, and Chi square test were used for the univariate analysis, and the multivariate analysis of the logistic regression model was performed to calculate an odds ratio (OR), and its 95 % confidence interval (95 % CI), adjusting for age and sex as the potential confounding factors. SAS version 9.4 was utilized for these analyses. Significance level was set at 5 %. This study was approved by the Ethics Committee of Sapporo Medical University.

Results

Mean (standard deviation, or, SD), median, and range of age of the 177 subjects were 39.5 (24.0), 40.0, and 0–86 years, respectively. Table 1 shows the mean, standard deviation, median, and range of AsIII, AsV, MMA, DMA and AsBe concentrations in the urine among the total subjects, age group A and age group B. None of these As compounds were significantly different between age group A and age group B.

Table 2 shows the results of the comparison of the personal characteristics and consumption of foods between the high and low iAs groups, as well as, between the high and low tAs groups, in age group A. BMI in the high tAs group was significantly higher than that in the low tAs group ($p = 0.031$). However, if age and sex were adjusted by the multivariate analysis, high BMI was not associated with risk of being in the high tAs group (OR = 1.30, 95 % CI 0.98–1.72, $p = 0.067$). (Data were not shown in a Table). No other items were significantly different between the groups.

Table 3 shows the results of the comparison of the personal characteristics and consumption of foods and beverages between the high and low iAs groups, as well as, between the high and low tAs groups in age group B. Frequency of drinking beer in the high tAs group was significantly higher than that in the low tAs group ($p = 0.008$). Few study subjects reported to drink wine. None of the other items were significantly different between the groups.

Table 4 shows ORs and the 95 % CI of being the high iAs and tAs groups for frequency of beer consumption in

Table 3 continued

Items	Contents	The high iAs group (≧5.2 μg/L)		The low iAs group (<5.2 μg/L)		*p* value[#]	The high tAs group (≧85.8 μg/L)		The low tAs group (<85.8 μg/L)		*p* value[#]
		No.		No.			No.		No.		
Other kinds of alcohol beverage	None	51	81.0 (%)	50	79.4 (%)	0.712	49	77.8 (%)	52	82.5 (%)	0.686
	1–2 times per month	6	9.5 (%)	3	4.8 (%)		8	12.7 (%)	1	1.6 (%)	
	≧1–2 times per week	6	9.5 (%)	10	15.9 (%)		6	9.5 (%)	10	15.9 (%)	

SD standard deviation

[#] Welch's test or Mann–Whitney *U* test for comparison between the high and low iAs groups as well as between the high and low tAs groups

[$] Chi square test

[a] Duration of time living near arsenic-contaminated area (year)

Table 4 Odds ratios (ORs) and their 95 % confidence intervals (95 % CIs) of being the high inorganic As (iAs) or total As (tAs) groups for beer consumption in the subjects 18 years old or older (age group B), after adjusting for age, sex, and smoking index

Items	Contents	iAs			tAs		
		OR	95 % CI	*p* value	OR	95 % CI	*p* value
Beer	None	1.00			1.00		
	<1–2 times per week	1.26	0.56–2.85	0.579	3.09	1.32–7.24	0.009
	≧3–4 times per week	2.26	0.77–6.64	0.137	3.00	1.02–8.80	0.045
			P for trend	0.150		P for trend	0.012

age group B, adjusting for age, sex and smoking index. Compared to not drinking beer, drinking beer less than 1 or 2 times per week (OR = 3.09, 95 % CI 1.32–7.24, $p = 0.009$), as well as, more than or equal to 3 or 4 times per week (OR = 3.00, 95 % CI 1.02–8.80 $p = 0.045$) were significantly associated with increased risk of being in the high tAs group. A significant positive trend was observed between frequency of drinking beer and risk of being in the high tAs group ($p = 0.012$).

Discussion

To our knowledge, there were two previous reports to show the distribution of As in urine among the Japanese population [6, 7]. The concentrations of As components in our study were not so different from the results of these two reports. No link between duration of living near the contaminated area and urinary As concentration was observed in our study, and similar results as ours were reported in France [13, 14] as well as in Denmark [15]. Geometric means of urinary As levels (iAs + MMA + DMA) were reported to be 3.5 μg/L among persons 18 years old or older living near contaminated areas in France, and 4.7 μg/L in frequent beer drinkers among them [14]. These values seemed to be much lower than our results shown in Table 1. This difference may arise from dietary dissimilarity between French and Japanese people, because Japanese generally eat more rice and seafood than French people.

Frequency of drinking beer was significantly associated with increased risk of being in the high-level total As group in the adult subjects. Fillol et al. [13, 14] also showed that consumption of beer was significantly positively associated with urinary As concentration. Furthermore, Cottingham et al. [16] showed that consumption of beer was significantly positively associated with toenail As concentration. There are several reports showing high As concentration in beer samples from Europe [9, 17–19], but there have been no reports from Japan, to our knowledge. The Food and Drug Administration in USA has warranted that some beers has arsenic levels topping drinking water limits [20]. Accordingly, As concentration is required to be measured for Japanese beer.

Consumption of foods such as rice [21–26], fish [8, 10, 11, 16, 26–29], and, crustacea [26, 29, 30], shellfish [28, 30], and seaweed [21, 28–30] have been indicated as an elevated risk of urinary arsenic concentration. However, we did not find any difference in frequency consumption of these foods.

There were some limitations in this study. First, the design was a cross-sectional study, and accordingly, we could not infer a causal relationship of higher urinary As with the measured variables. Second, the study participants were not randomly selected, but voluntarily participated in the study. Therefore, an unknown selection bias might exist in the study. Third, because information on amount of foods or beverages per opportunity was not collected, a dose–response relationship was not evaluated between food or beverage consumption and high urinary As. In particular, inquiries about consumption of rice and hijiki (seaweeds), both of which are known as major sources of arsenic in Japanese, were insufficient.

In conclusion, although a causal inference was not be allowed because of the results from the cross-sectional study, frequent consumption of beer may be associated with the high total As in the adult subjects.

Acknowledgments The authors thank Dr. Shuji Dohi, MD & PhD, General Administrator of Muroran City General Hospital. Without his help, this research could not be executed.

Compliance with ethical standards

Conflict of interest No conflict of interest was declared by any author.

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