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Arsenic drinking water exposure and urinary excretion among adults in the Yaqui Valley, Sonora, Mexico

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Abstract

The objective of this study was to determine arsenic exposure via drinking water and to characterize urinary arsenic excretion among adults in the Yaqui Valley, Sonora, Mexico. A cross-sectional study was conducted from July 2001 to May 2002. Study subjects were from the Yaqui Valley, Sonora, Mexico, residents of four towns with different arsenic concentrations in their drinking water. Arsenic exposure was estimated through water intake over 24 h. Arsenic excretion was assessed in the first morning void urine. Total arsenic concentrations and their species arsenate (As V), arsenite (As III), monomethyl arsenic (MMA), and dimethyl arsenic (DMA) were determined by HPLC/ICP-MS. The town of Esperanza with the highest arsenic concentration in water had the highest daily mean intake of arsenic through drinking water, the mean value was 65.5 μg/day. Positive correlation between total arsenic intake by drinking water/day and the total arsenic concentration in urine ($r = 0.50$, $P < 0.001$) was found. Arsenic excreted in urine ranged from 18.9 to 93.8 μg/L. The people from Esperanza had the highest geometric mean value of arsenic in urine, 65.1 μg/L, and it was statistically significantly different from those of the other towns ($P < 0.005$). DMA was the major arsenic species in urine (47.7–67.1%), followed by inorganic arsenic (16.4–25.4%), and MMA (7.5–15%). In comparison with other reports the DMA and MMA distribution was low, 47.7–55.6% and 7.5–9.7%, respectively, in the urine from the Yaqui Valley population (except the town of Cocorit). The difference in the proportion of urinary arsenic metabolites in those towns may be due to genetic polymorphisms in the As methylating enzymes of these populations.

Keywords: Arsenic; Urinary arsenic; Arsenic drinking water; Sonora; Yaqui Valley

1. Introduction

Arsenic is a naturally occurring element present in the environment in both inorganic and organic forms. Inorganic arsenic is considered to be the principal form of arsenic in groundwater, surface water, soil, and many foods (NCR, 2001). Arsenic in well water usually originates from natural geological sources (Kurttio et al., 1998). Arsenic is classified as a human carcinogen (NCR, 1999). In several countries, including India, China, Taiwan, Mexico, Argentina, and Chile, the people are exposed to high arsenic concentrations through their drinking water. A wide variety of adverse health effects including skin, bladder, and internal cancers have been associated with chronic arsenic exposure (Hopenhayn-Rich et al., 1996a; Guo et al., 1997, 1998), with the toxic effects most evident in regions where the groundwater contains high arsenic concentrations. There are limited studies about arsenic metabolism in humans, and more research is needed, especially involving low and moderate arsenic levels.

The detailed mechanisms of arsenic carcinogenicity and related susceptibility of humans are poorly understood (Abernathy et al., 1999; Aposhian and Zakharyan, 1999). Arsenic is methylated in the body via alternating reduction of pentavalent to trivalent arsenic and oxidative methylation to methyl arsenic (MMA) and dimethyl arsenic (DMA). The arsenic pentavalent compounds, monomethylarsonic acid (MMA V) and dimethylarsinic acid (DMA V), are less reactive with tissue constituents and more readily excreted in urine than inorganic arsenic (Aposhian, 1997; Petrick et al.,

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2000; Styblo et al., 2002). However, recent studies (Aposhian et al., 2000; Mandal et al., 2001) have shown the presence of trivalent methylated forms of arsenic, monomethyarsonous acid (MMA III) and dimethylarsionous acid (DMA III), in human urine that are more toxic than arsenite, specially MMA III (NCR, 2001). Because the methylation of arsenic seems to influence its toxicity, it is essential to assess the methylation on an individual level (Concha et al., 2002; Vather, 2002).

Although most studies on arsenic-exposed people have shown average values of 10–30% inorganic arsenic, 10–20% MMA, and 60–70% DMA in urine, there are major differences between population groups and individuals reported. There seems to be variation in the susceptibility to arsenic, which may be related to variation in arsenic biotransformation. Few data that link methylation patterns to arsenic-induced disease exist, although it has been suggested that genetic polymorphisms cause variations in arsenic-methylation. Therefore, the same arsenic exposure may result in different health outcomes in different ethnic groups, thus it is important that the metabolism of arsenic is evaluated among different exposed populations (Vather, 2000; Loffredo et al., 2003).

The US drinking water standard for As has been set at 10 ppb based primarily on epidemiological studies in Taiwan (Chiou et al., 1995, 2001; Hsueh et al., 1998; Tseng et al., 2000) whose people exposed chronically to high concentrations of arsenic in their drinking water. These studies demonstrated an association between arsenic exposure and development of skin, bladder, and lung cancers. The current Mexican drinking water standard for As is at 35 ppb. Because almost all epidemiological studies have been done at higher endemic arsenic concentrations, further research in ethnic populations exposed to low levels of arsenic is needed.

In the southwest United States and northern Mexico, drinking water arsenic exposure is primarily restricted to Hispanic populations and there are few reports about chronic exposure of Hispanics at low arsenic levels. In Sonora, situated in northern Mexico, high arsenic levels have been reported in the drinking water from Magdalena, Caborca, Etchojoa, and Hermosillo, with total arsenic concentrations of 117, 67, 51, and 305 μg/L, respectively (Wyatt et al., 1998a). In addition in Hermosillo, arsenic in drinking water was correlated to the appearance of arsenic in the urine of the children, but there was no information about the possible risk in the health of this adult population, who have been exposed chronically to low arsenic levels.

The purpose of this study was to determine arsenic exposure through drinking water and to characterize urinary arsenic excretion in a Mexican population from the Yaqui Valley, Sonora, Mexico.

2. Materials and methods

2.1. Sampling sites and procedures

Our experimental protocol was approved by the Human Subject Committee of the University of Arizona and the by Public Health Department of Sonora State.

Thirty-five water wells were sampled in August 2001 in 25 towns in the Yaqui Valley, an agricultural region in southwestern Sonora, Mexico (Table 1). Water samples were obtained directly from the water pump heads and stored in polypropylene bottles. The samples were preserved with 200 μL of concentrated nitric acid and were kept at −20°C until the analysis of total arsenic was performed.

Four towns that had different arsenic concentrations (range 3.3–49.3 ppb) were selected to carry out the study: Esperanza and Cocorit in the north of the Yaqui Valley, Pueblo Yaqui in the center, and Col. Allende in the south (Fig. 1). In all these towns the only supply of

Table 1
Distribution of total arsenic in well water from the major towns in the Yaqui Valley, Sonora, Mexico

Town	ppb	Town	ppb
Esperanza	43.33[a]	SJ Bacum	10.11
Well 1	37.40		
Well 2	49.26	Pueblo Yaqui	9.65[a]
		Well 1	9.81
		Well 2	9.48
Villa Juarez	31.06[a]		
Well 1	34.26		
Well 2	24.44	Bacum	8.62
Well 3	34.50		
		Alameda	7.80
Tobarito	25.10[a]		
Well 1	21.38	Pascual Ayon	4.71
Well 2	28.82		
Campo 5	19.58	S. Giron and Providencia	4.49
Cocorit	19.33	Campo 77	3.93
MR Gomez	14.65	Col. Allende	5.51
Morelos 1	14.61	Altos de Jecopaco	5.51
Morelos 2	13.11	Campo 47	3.30
Ejido Teras	13.11	Potabilizadora N[b]	14.04
		Tank 1	13.73
		Tank 2	5.74
Quetchehueca	11.48		
El Porton	10.56	Potabilizadora S[b]	9.31
		Tank 3	8.92
Ej. Independencia	10.12		
Navojoa	14.53[a]		
Well 1	16.33		
Well 2	9.37		
Well 3	17.89		

NOM-127-SSA1, 35 ppb; US-EPA, MCL, 10 ppb. Thirty-five samples were collected with all analyses performed in duplicate.

[a] Average of total arsenic (μg/L) in the existing wells. These wells were working while sampling was done. In all other towns there is only one well which was the only source of drinking water.

[b] Located in Cd. Obregon, Sonora.

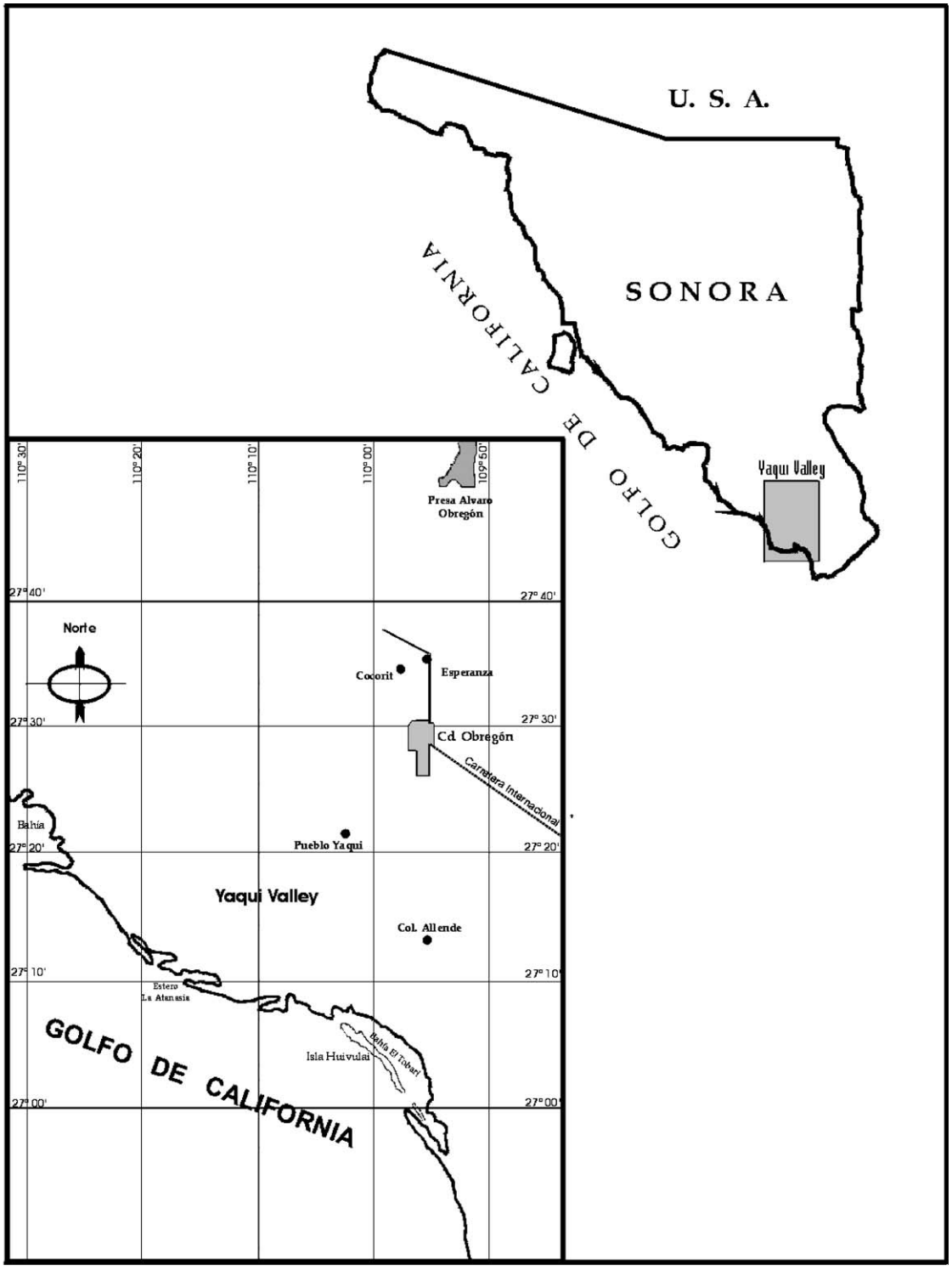

Fig. 1. Location of the Yaqui Valley and the study towns in Sonora, Mexico.

drinking water was from the wells. The total number of wells that supplied drinking water was one in Cocorit and Col. Allende and two in Pueblo Yaqui and Esperanza (Table 2).

The study was conducted using 43 volunteer adults, selected at random in at least 10 households in each town. In each of the households 1 adult was invited to participate in the study with the inclusion criteria being consumption of local well drinking water for at least 1 year and being between the ages of 18 and 75 years.

Participants were asked to exclude seafood from their diet for the preceding 3 days. Each participant was

Table 2
Demographic details of the study group in the Yaqui Valley, Sonora, Mexico

Locality	Esperanza	Cocorit	Pueblo Yaqui	Col. Allende
Population	30,600	15,300	30,600	2000
No. subjects (male/female)	3/14	0/10	3/9	0/10
Mean age years (range)	40.2 (19–59)	36.8 (18–53)	29.9 (18–58)	37.1 (22–73)
Mean residence years (range)	27.2 (5–50)	30.2 (1–51)	16.7 (2–34)	17.5 (6–27)
No. of wells in each town	2	1	2	1
Total arsenic (average) (μg/L)/well	43.3±8.4	19.33±0.8	9.65±0.23	5.5±0.20
Tap water (average)[a] (μg/L)/household	36±4.7	13.7±2.4	6.12±0.65	3.91±0.20
As from drinking water (μg/day)	65.5 (18–108)	23 (6.9–41.2)	11.9 (3.1–24.5)	14.9 (3.9–27.4)

[a] Tap water samples: Esperanza ($n = 14$), Cocorit ($n = 10$), Pueblo Yaqui ($n = 9$), and Col. Allende ($n = 10$).

familiarized with the protocol and signed a consent form. Data on health status, length of exposure to arsenic, alcohol consumption, cigarette smoking, dietary habits, and other variables were obtained by questionnaire and physical examination. Potential confounding factors, such as exposure to fertilizers and pesticides were also noted.

2.2. Urine collection

First morning void urine samples were obtained in 100-mL polypropylene bottles and kept on ice. Approximately 6 h after collection cooled samples were taken to the Institute Technological of Sonora and kept frozen at −40°C. After 2 months the samples were shipped on dry ice to the University of Arizona (Tucson, AZ, USA) where the samples were stored at −80°C until the analysis was performed.

2.3. Analysis of total arsenic

Duplicate water samples were digested according to US EPA Method 3015 (EPA, 1995), except that the sample volume was modified to 3.0 mL and the nitric acid concentration was changed to 25% w/v. For quality control purposes, the Standard Reference Water, SMR 1640 (NIST, Gaithersburg, MD) was used. The average recovery was 106.5% and the percentage CV was below 3.8%.

Urine samples were digested with nitric acid using a microwave oven, according to Francesconi et al. (2002). Freeze-dried Urine Reference Material for trace elements (Clinchek-control; RECIPE, Munich, Germany), containing normal level (68 μg/L of As), was used for quality control and to validate the assay. Analysis of this material ($n = 8$) by ICP-MS yielded 64.6±0.6 ppb with a 94.9% recovery.

2.4. Analysis of arsenic species

Frozen samples were diluted two-fold using Milli-Q water and filtered with a Millex-HV filter (0.45-μm-syringe-driven filter unit; Millipore) prior to injection (Mandal et al., 2001). The HPLC systems consisted of an Agilent 1100 HPLC with a reverse-phase C18 column (Prodigy 3 μm ODS (3), 150 × 4.60 mm^2, Phenomenex, Torrance, CA), with an Agilent 7500 ICP-MS used as a detector for the analysis of four arsenic species (As III, As V, MMA V, and DMA V). The detection limits, quality control, precision, and accuracy of this analytical method were assessed. It was found that the detection limits were 0.42–1.08 μg/L for arsenic compounds. The precision was estimated 10 times with a solution containing approximately 10 times the detection limit concentrations, yielding percentages of relative standard deviation (RSD%) of 1.14–4.0. Accuracy values were calculated by spiking standard compounds of all the species that were studied (10 μg/L of As III, As V, and MMA V, and 20 μg/L of DMA V) in urine samples. The recovery of added compounds was 96–108%.

Due to difficulties in collecting, storing, and transporting samples across the US/Mexican border, analysis of unstable MMA III and DMA III metabolites was not possible because these trivalent species are quickly oxidized to pentavalent arsenic compounds (MMA V and DMA V). MMA and DMA are generic terms that include the trivalent and pentavalent species (MMA III + MMA V and DMA III + DMA V, respectively) so urinary analysis detected only inorganic arsenic and MMA and DMA arsenic metabolites that were traditionally measured in past arsenic studies.

2.5. Arsenic daily intake

The average daily intake of arsenic was calculated using daily volume of water consumed, the arsenic concentration in the tap water (supply from the well) for each study subject's household, and the weight of each study subject.

2.6. Statistical analysis

The concentrations of total arsenic and arsenic species in urine were transformed to a log scale to calculate geometric means and confidence intervals. The signifi-

cance of the differences between means for each town was analyzed using ANOVA with Bonferroni correction. (After the log transformation of the data the assumptions of normality and equality of variances were met. In addition using a Kruskal–Wallis test, similar results were obtained.) The association between the total arsenic values in water and those in urine was analyzed by Pearson correlation coefficient. All statistical analyses were computed using Stata 7.0 (2002) software (College Station, TX, USA).

3. Results

3.1. Well water

The range of total arsenic concentration in the well water from some major towns in the Yaqui Valley was from 3.30 to 49.26 μg/L with an average of 12.70 ± 9.3 μg/L (Table 1). Forty-four percent of the sampled towns (Esperanza, Villa Juarez, Tobarito, Campo 5, Cocorit, MR Gomez, Morelos1 and 2, Ej. Teras, Quetchehueca including Cd. Obregon) had arsenic levels greater than 10 ppb, the current EPA drinking water standard (Smith et al., 2002). Esperanza, Villa Juarez, and Tobarito had the highest average total arsenic levels at 43.33, 31.1, and 25.1 μg/L, respectively. Porton, Ej. Independencia, and SJ Bacum had concentrations slightly above those of the US guideline (10.3 ± 0.26 μg/L).

Four towns were selected for the epidemiological studies with arsenic in well water ranging from 5.5 to 43.3 μg/L.

3.2. Study subjects

Forty-three study subjects were selected in the Yaqui Valley, 14 from Esperanza, and 10 from Pueblo Yaqui, Cocorit, and Col. Allende. General characteristics of the subjects are shown in Table 2. One subject from pueblo Yaqui was excluded because of incomplete participation (no first morning void urine sample).

The majority of the study subjects were women, with only three men participating from Esperanza and three from Pueblo Yaqui. Participants from Esperanza had the highest average age (40.2 years), while study subjects from Cocorit had the longest residence time, 30.2 years.

3.3. Arsenic uptake

Average water consumption was 1.86 L/day (range 0.5–4.0 L/day), and there were no statistical differences in water intake by town ($P > 0.05$). Using water consumption, total arsenic intake was greatest in Esperanza, 65.5 μg As/day, and lowest in Pueblo Yaqui, 11.9 μg As/day ($P < 0.05$), and this was reflected in urinary excretion, because Esperanza had the highest values, with 64.5 μg As/L in urine.

3.4. Urinary arsenic

Total and arsenic species distribution in urine of the study subjects by town of residence are shown in Table 3. There was a good agreement between the values obtained for total arsenic and the sum of species, indicating that in this study the latter was not influenced by seafood arsenic ($r = 0.994$, $P < 0.0001$).

Table 3
Levels and relative distributions of urinary arsenic species in people chronically exposed to low arsenic concentrations through drinking water Geometric mean (95% Confidence Interval)

Measure	Esperanza ($n = 14$)		Cocorit ($n = 10$)		Pueblo Yaqui ($n = 9$)		Col. Allende ($n = 10$)		P value[a]
	Mean	Range	Mean	Range	Mean	Range	Mean	Range	
Total arsenic (μg/L)	64.5[b]	(46–90.6)	29.5	(20.8–41.9)	38.4	(26–56.7)	36.2	(23.6–55.3)	0.0064
AsIII	14.0[c]	(7.2–27.1)	3.3	(2.5–4.4)	6.3	(2.7–14.3)	5.8	(2–17)	0.0070
As V	1.7	(1.3–2.3)	1.3	(0.1–1.6)	1.6	(1.1–2.3)	1.2	(1.0–1.4)	0.1499
MMA V	6.3[c]	(4.5–8.8)	4.2	(3.0–5.8)	2.9	(2.1–3.9)	2.3	(1.7–3.3)	0.0001
DMA V	34.6[c]	(26–46)	18.8	(12.5–28.1)	17.3	(11.3–26.5)	14.7	(11.2–19.3)	0.0021
Sum As species (μg/L)	65.1[b]	(42.2–93.8)	28.0	(19.6–39.8)	31.1	(19.2–50.4)	30.8	(18.9–50)	0.0045
Relative proportions[d]									
%As	24.1	(13.1–45.2)	16.4	(12.3–21.4)	25.4	(12.2–53.4)	22.9	(9.7–59.7)	0.2429
%MMA	9.7	(6.9–13.5)	15.0	(10.7–20.7)	9.3	(6.7–12.5)	7.5	(5.5–10.7)	0.2301
%DMA	53.1	(40–70.7)	67.1	(44.6–100)	55.6	(36.3–85.2)	47.7	(36.4–62.7)	0.5095
MMA/DMA[e]	0.18	(0.13–0.30)	0.22	(0.16–0.31)	0.17	(0.12–0.22)	0.16	(0.12–0.22)	0.2124

Sum As species, inorganic arsenic + MMA + DMA; inorganic arsenic ($As^{3+} + As^{5+}$); MMA, monomethylarsonate; DMA, dimethylarsinate.
[a] ANOVA test.
[b] Statistically significantly different from the other three towns; Bonferroni $P < 0.05$.
[c] Statistically significantly different from Cocorit; Bonferroni $P < 0.05$.
[d] Percentage of given arsenic concentration in the given arsenic species from Sum As species in urine.
[e] Ratio of the first to the second methylation step for inorganic arsenic.

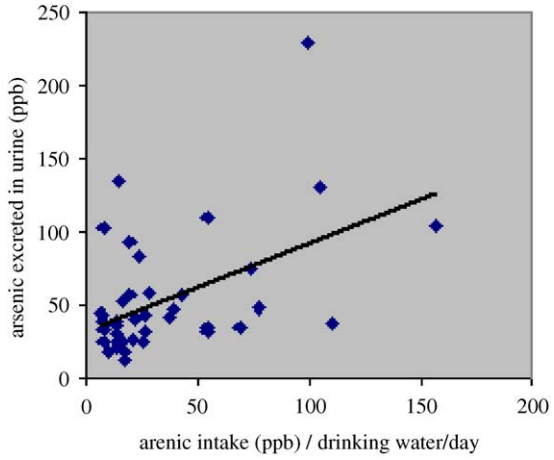

Fig. 2. Relationship between total arsenic intake by drinking water/day and urine and its excretion in residents from the Yaqui Valley, Sonora, Mexico. ($r = 0.496$, $P = 0.0007$).

Compared to the other towns, Esperanza had the highest arsenic concentrations in urine ($P = 0.0045$). The average arsenic level for Esperanza was 64.5 (46–90.6) μg As/L compared to 29.5 (20.8–41.9), 38.4 (26–56.7), and 36.2 (23.6–55.3) μg/L, for Cocorit, Pueblo Yaqui, and Col. Allende, respectively.

There was a positive weak correlation between the total arsenic concentration in water and the total arsenic concentration excreted in urine ($r = 0.35$, $P = 0.02$), but this correlation was increased ($r = 0.50$, $P < 0.001$) when the total arsenic intake by drinking water/day was correlated with the total arsenic concentration in urine (Fig. 2).

3.5. Urinary arsenic species

DMA was the major arsenic species, followed by inorganic arsenic and MMA. The majority of the inorganic arsenic was in the trivalent form As III (mean 82.1%, min–max 77–89%). The proportion of AsV was notably lower (mean 19.6%, min–max 11–30%).

The proportion of inorganic arsenic in urine was significantly higher in Esperanza than Cocorit ($P = 0.007$) with values 24.1% and 16.4%, respectively. The relative excretion of DMA and MMA was statistically lower in Esperanza than in Cocorit ($P = 0.007$), with proportions of 9.7% versus 15% for MMA and 53.1% versus 67.1% for DMA.

The MMA/DMA ratio was highest in Cocorit (0.22), but this difference was not statistically significant ($P = 0.21$) compared with 0.18, 0.17, and 0.16 for Esperanza, Pueblo Yaqui, and Col. Allende, respectively.

4. Discussion

We have identified a Mexican population that has been chronically exposed to arsenic in their drinking water at concentration ranges where national and international standards have been set. The population is stable (resulting in long-term exposure) and alternative water sources (e.g., bottled water) are not utilized. Thus, this population offers the opportunity to examine the health effects of long-term, low-level arsenic in an ethnic population often exposed to arsenic in drinking water (i.e., southwestern United States and northern Mexico).

Analysis of drinking water from these towns showed that sections of this population are exposed to arsenic concentrations above permissible levels. The arsenic concentrations in Esperanza, Villa Juarez, and Tobarito were 4.3, 3.1, and 2.5 times above the US EPA drinking water standard of 10 ppb. Relative to the Official Mexican Norm of arsenic in drinking water (NOM-127-SSA1-1994), which was modified in 2001 by the Mexican government to 35 μg/L, the town of Esperanza had concentrations 1.23 time above this new Mexican Norm. Arsenic exposure in this population represents a particular concern due to possible health effects from their long-term exposure at these levels.

In our population the average daily water consumption volume was 1.86 L. Using this value the daily arsenic intake in Esperanza was 0.98 μg/kg, whereas intakes in Cocorit, Pueblo Yaqui, and Col. Allende were in the range 0.17–0.31 μg/kg/day. Considering that the oral reference dose (RfD) or daily intake for ingested arsenic from all sources is 0.30 μg/kg/day (EPA-IRIS, 1998), and taking into account only arsenic from water, Esperanza exceeded 3.3 times the recommended dose and Cocorit was slightly above this guideline.

Only a limited correlation between arsenic exposure and urinary arsenic excretion was observed. Esperanza, with the highest level of arsenic in drinking water, was associated with the highest level of arsenic excretion in urine (Table 3). Cocorit, Pueblo Yaqui, and Col. Allende, with a range of arsenic levels in drinking water (19.33, 9.65, and 5.5 μg/L, respectively) had similar levels of arsenic appearing in the urine (Table 3). Individually, though, there was a moderate correlation ($r = 0.496$, $P = 0.0007$) between the arsenic intake in drinking water and the total arsenic appearing in urine (Fig. 2).

There is considerable variability between the urinary excretion of arsenic and the level of exposure by drinking water. In some instances the level of exposure versus urinary excretion has a moderate correlation. For example Wyatt et al. (1998b) and Kurttio et al. (1998) observed positive trends between daily intake of arsenic and excretion in children and adults, respectively, similar to our observation. However Mandal et al. (2001), reported that people exposed to 33 ± 7 ppb of arsenic in drinking water excreted urinary arsenic at concentration of 50 ± 3.4 μg/L, while Hopenhayn-Rich et al. (1996b), observed a group that was exposed at

total arsenic concentrations of 15 μg/L but excreted 61 μg/L. These results are similar to the variability observed in our population in Cocorit, Pueblo Yaqui, and Col. Allende.

In our population the percentages of methylated arsenic metabolites were typically lower than those reported in the literature. Many studies report the percentage DMA as 60–80% (Hopenhayn-Rich et al., 1996a, b; Mandal et al., 2001; Chiou et al., 1997), while in our groups (except Cocorit) only 47–56% was excreted. Similary, MMA typically constitutes 10–20% of the urinary arsenic, although some exceptions have been reported for some indigenous groups from Argentina and Chile which excreted very low percentages (Vather et al., 1995; Hopenhayn-Rich et al., 1996a, b; Concha et al., 1998). In our study all groups (except Cocorit) excreted low MMA percentages (7.5–9.7%).

Our study groups were normalized for socioeconomic status, alcohol/tobacco use, water consumption, and sex. One factor that may affect the handling of arsenic by an individual could be their proportion of native Yaqui Indian in their genetic composition. Cocorit has the highest percentage of native Yaqui Indians, approximately 1.3% compared to the other towns with percentages less than 0.6% (INEGI, 2002), and the difference seen in how these populations excreted and metabolized arsenic could be attributed to these additional ethnic differences. The mixture of Spanish, Mexican, and native Yaqui Indian in our population could result in genetic polymorphisms which would affect the excretion and metabolism of arsenic. For example Weinshilboum et al. (1999) has reported polymorphisms of human methyltransferases and there is the possibility that there are polymorphisms in arsenic methylation enzymes. Cocorit with a high native Yaqui Indian population had a higher percentage of methylated arsenic metabolites and a lower percentage of inorganic arsenic than the other groups. This may be attributed to differences in arsenic-metabolizing enzymes in the groups.

In summary, there was a moderate correlation between arsenic exposure and urinary excretion of arsenic. There was considerable variation in metabolism of arsenic in the groups. These variations in metabolism could be attributed to polymorphisms of the methylation enzymes. This is an important population for studying the processing and health effects of arsenic because it is exposed to relevant low-level arsenic in drinking water and it represents an important ethnic population of the southwestern United States and northwestern Mexico.

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