



Biomarkers for the evaluation of population health status 16 years after the intervention of arsenic-contaminated groundwater in Xinjiang, China



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HIGHLIGHTS

- We examined arsenic and two biomarkers in subjects post the water intervention.
- Urinary arsenic levels were significantly higher in villagers from the endemic area.
- Urinary porphyrins and malondialdehyde were elevated when arsenic was high.
- Skin lesions were observed in 51 out of 178 surveyed people in the As-endemic area.
- Four out of nine young villagers born after the intervention exhibited As-related skin lesions.

ARTICLE INFO

Article history:

Received 19 December 2012
Received in revised form 3 March 2013
Accepted 27 March 2013
Available online 2 April 2013

Keywords:

Arsenic
Biomarker
Water intervention
Porphyrin
Malondialdehyde

ABSTRACT

The arsenicosis endemic area in the region of Kuitun and Chepaizi, Dzungaria district, Xinjiang, People Republic of China was the first identified arsenic endemic area in China where arsenic concentration of up to 850 µg/L in the groundwater was reported. An intervention was put in place in 1985 by government to provide an alternative water source at a centralized community level. Sixteen years on since the intervention, we evaluated the health status of 178 villagers from endemic and 179 villagers from control sites. Biomarkers in their urine, included arsenic, porphyrins and malondialdehyde (MDA) were measured and the prevalence of skin lesions was also assessed. The average urinary arsenic (117 ± 8.3 µg/g of creatinine) from the endemic-villages was significantly higher ($p < 0.001$) than that of the controls (73.6 ± 3.2 µg/g of creatinine) while no significant difference was found in urinary porphyrins and malondialdehyde concentrations in the overall studies subjects from these two areas. However when the urinary arsenic was higher than 150 µg/g of creatinine, MDA and porphyrins were higher in the endemic-villagers compared to the controls. Fifty-one out of 178 people from the arsenic endemic area showed skin lesions related to arsenicosis but these were absent among villagers from the control site. Of particular concern, skin lesions related to arsenicosis were observed in 4 out of 9 subjects 16 years of age or younger who were from different villages and born after the completion of water intervention. Although sporadic exposure and/or voluntary drinking contaminated water were thought to be a contributor of arsenicosis after the water intervention, the contribution from other dietary arsenic intakes remain unclear.

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Abbreviations: ECA, Endemic chronic arsenicosis; MDA, Malondialdehyde; HPLC, High performance liquid chromatography; GC-MS, Gas chromatograph-mass spectrometry; HBT-MDA, 2-(Pyrazol-1'-yl)-benzothiazole; HBT, Hydrazinobenzothiazole; HBT-AA, 2-(3',5'-Dimethylpyrazol-1'-yl)-benzothiazole; CAT, Catalase; SOD, Superoxide dismutase; GST, Glutathione S-transferase; ROS, Reactive oxygen species.

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1. Introduction

Arsenic contamination in drinking water causing global health problems has been known for decades. Ground water is a major source of drinking water in many parts of the world, especially the South East Asia countries. Typical arsenic endemic areas extend to geo-chemical origins in Taiwan, West Bengal, Bangladesh, Vietnam, PR China, the States of California, Utah, Nevada, Washington and

Alaska, Argentina, Chile and southwestern Finland. It has been estimated that tens of millions of people are being exposed to excessive levels of arsenic from a natural source in the drinking water [1].

Drinking water containing elevated inorganic arsenic can cause multi-site cancers in the human body, and the risk of it can be as high as 1% when the arsenic level is greater than 50 $\mu\text{g/L}$ [2]. Non-cancerous effects of arsenicosis include skin pigmentation changes, keratosis, hyperkeratosis, peripheral vascular disease, hypertension, cardiovascular disease, cerebrovascular disease and long-term neurological effects [3] and diabetes [4,5]. The current WHO recommended guideline value for arsenic in the drinking water is 10 $\mu\text{g/L}$. The WHO/FAO Joint Expert Committee on Food Additives (JECFA) recently conducted a review on arsenic and decided to withdraw its previously set provisional tolerable weekly intake (PTWI) [6]. The implication of this withdrawal on future setting of regulatory standards for arsenic remains to be realized.

The region of Kuitun and Chepaizi in Xinjiang province of China (Fig. 1) is a settlement area where influx of habitation commenced in early 1960s. At that time, many peasants from inland China immigrated and settled in the northwest of China including Xinjiang, where until then it was a minority area with a sporadic population. A number of farms were established in areas of a desert or semi desert. Owing to the poor quality of the surface water, the residents used deep groundwater from over 100 m in depth for drinking without the knowledge that they were at risk of chronic arsenic poisoning by drinking arsenic-contaminated water.

The arsenicosis endemic area in Dzungaria Xinjiang, China (Fig. 1), with a population of 100,000, was the first identified arsenic endemic area in mainland China especially in Kuitun with arsenic concentration of up to 880 $\mu\text{g/L}$ was reported [7]. The first case of endemic arsenicosis in China was reported in Xinjiang autonomous regiment in 1980 [8]. The affected area is about 1200 km^2 and there were about 50,760 people out of a population of 100,000 drinking elevated arsenic containing well water in Kuitun. A water improvement intervention program by providing an alternative water supply from shallow aquifer and surface water was implemented in 1984 and completed in 1985. This water supply is a centralized community facility where improved quality water is pumped to individual households. The tap-water connection is available at a cost. Unfortunately, not all households had taken up this alternative water supply and some arsenic-contaminated old wells were still being used as drinking water by personal choice. These old wells were kept at a community/village level and meant to be for washing clothes and bathing purposes.

A five-year follow-up of 119 villagers with endemic chronic arsenicosis (ECA) carried out in 1982 (2 years before water intervention) and in 1987 [9], showed an arsenic level in drinking water in Kuitun, Xinjiang decreased from 600 to 850 $\mu\text{g/L}$ to below 45 $\mu\text{g/L}$. Three years after the water intervention, 74% patients had either relieved symptoms or were recovered from ECA, a few cases of arsenic keratosis had become less severe [9]. However, arsenic-related cardiovascular symptoms were found to be worse than before, and paroxysmal numbness of hands and feet was common; Raynaud's syndrome, hyperpigmentation of hands and feet, and abnormal ECG were also common [9]. Four cases of skin cancer were reported by these same authors [9]. In another study, the development of malignant tumors was continuing ten years after the completion of water improvement [10]. The death rate of cardiovascular disease was 92 per 10,000 in the endemic district compared to 39 per 10,000 in the control area, and the death rate from malignant tumors was 46 per 10,000 compared to 31 per 10,000 in the control area [10].

This study aimed to survey the health status of a local population in order to gain an insight of the effectiveness of the water intervention over a longer time period upon chronic arsenic exposure in Xinjiang, PR China, through analysis of biomarkers including

Table 1

Urine samples obtained from participants from arsenic-endemic (regiment 123) and control (regiment 125) sites in the region of Kuitun–Chepaizi of Dzungaria, Xinjiang province, PR China.

Age group (years)	Endemic-site		Control-site	
	Male	Female	Male	Female
(0–20)	27	28	31	30
(20–40)	28	33	28	28
>40	34	28	30	28
Total	89	89	89	86

urinary arsenic, porphyrins and malondialdehyde, and arsenic-related skin lesions. We are also interested in the younger population who were born or new immigrants since the water intervention implementation program.

2. Materials and methods

2.1. Study site and sampling

Xinjiang is the most north western province in China. To its west are countries of Kazakhstan and Kyrgyzstan. The surveyed area, namely Division 7, Xinjiang Production and Construction Corps, consists of 8 regiments located within the Xinjiang Uygur autonomous province. Regiment 123 is the endemic area in this study. It is located about 100 km north of Kuitun central city area where arsenicosis is prevalent. Regiment 125 was the control area. It is about 60 km east of regiment 123, where there is little or no arsenic contamination in the drinking water, and arsenicosis is absent (Fig. 1). Groups of villagers are referred to as regiments in Xinjiang, China.

Of the 360 people surveyed, 180 were from the endemic regiment and 180 from the control regiment.

The majority of people from the endemic area surveyed come from families of early settlers in the 1960s. Although young people often have had secondary education, their parents are very poor peasants and generally have had little or no education. These families are impoverished, and can rarely afford seafood. People from the control area surveyed generally have had a slightly better education and their living standard marginally higher. However, being inlanders, their access to seafood is also limited.

Out of the 180 residents surveyed from each regiment (regiments 123 and 125) 353 urine samples were collected in accordance with protocols as described in other studies [11–14]. These samples were divided into 3 categories and are shown in Table 1. About 4% of the surveyed subjects reported consumption of seafood prior to the urinary collection and their urinary results were excluded from this study. Demographic data including education standard and occupation were also collected but details of which are not shown here.

The sampling month of May is a dry season, there might not have been sufficient drinking water from the shallow aquifer and surface water to supply to all villagers. The local tap water is supplied via the aid of electrical-powered water pump. In the event of power shortage, villagers may have to revert to the use of arsenic-contaminated well water. In addition, some individuals prefer the taste of the deep-well water compared to tap water from a community supply [15] that was also evident during our field work.

Urine sample jars were handed to the participants on the collection point with a questionnaire form which have included demographic information and dietary intake information from the past 3 days. Other confounding factors such as smoking, alcohol consumption and diet (data not shown) that could influence the arsenic methylation profile were surveyed by a questionnaire. Water sample (500 mL) was collected from all of the accessible

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