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Assessment of relationship on excess arsenic intake from drinking water and cognitive impairment in adults and elders in arsenicosis areas

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ABSTRACT

In this study, the relationships between high water arsenic exposure and cognitive impairment were investigated. A total of 483 residents aged 40 or older were randomly recruited and were divided into four groups according to the concentrations of arsenic in their water. Consumption levels ($-\bar{x} \pm s_d$) of drinking water arsenic for normal, mild, moderate, and high exposure groups were 4 ± 2 μg/L, 25 ± 11 μg/L, 73 ± 15 μg/L, and 183 ± 88 μg/L, respectively. The average scores ($-\bar{x} \pm s_d$) of the Chinese version Mini-Mental State Examination (MMSE) for females in each group were 21.49 ± 3.14, 19.04 ± 5.87, 16.18 ± 8.14, and 15.82 ± 7.78, and the average scores ($-\bar{x} \pm s_d$) for males were 24.50 ± 3.97, 23.16 ± 4.45, 21.00 ± 6.57, and 18.92 ± 7.99, respectively. Significant differences among the average scores of MMSE for males or females in the four groups were found ($p < 0.05$). The prevalence of cognitive impairment for females in each group was 10.86%, 29.63%, 53.48%, and 55.29%, and the prevalence of cognitive impairment for males was 10.71%, 12.00%, 35.71%, and 50.89%, respectively. Significant differences between all groups were observed ($p < 0.05$). In the multivariable regress model, high water was closely associated with the MMSE score (Standardized Coefficient = −0.021) and cognitive impairment (arsenic □100 μg/L $PR_{4/1} = 4.01$). The findings of our research suggested a significant positive relationship between arsenic exposure from drinking water and cognitive impairment.

1. Introduction

The transitional stage between normal aging and Alzheimer's disease cognitive impairment was described as "The Silent Epidemic" in the early 1980s (Petersen, 2004). With the arrival of the era of an aging population around the world, cognitive impairment has become a clarion call for public health experts worldwide. Studies have shown that the prevalence of cognitive impairment is above 30% among those 65 years of age or older (Winter Holz et al., 2013; Woo et al., 1994; Lee et al., 2014). Clarifying the contributing factors is especially important for public health and the development of prevention strategies; moreover, prevention is the key to stopping epidemics (Apostolo et al., 2016; Zhou, 2015). Studies have shown that many elements are neurovirulent to people, including arsenic (Zhou et al., 2010; Gupta et al., 2007; Negahdar et al., 2015). Arsenic (As), which is a toxic metalloid element, is widely distributed in nature, and long-term exposure to arsenic can result in a chronic systemic disease called arsenicosis. The main source of exposure to arsenic for humans in the arsenic-endemic area is through ingestion of high-arsenic drinking water (Bhattacharya et al., 2011; Jadhav et al., 2007). Arsenicosis has been an emerging epidemic in the world since last century; more than 100 million people are exposed to underground water with high concentrations of arsenic. Moreover, excessive arsenic intake has been found to be associated with hypertension, diabetes mellitus, coronary artery disease, blackfoot disease, and cancer. Because the nerve injury caused by environmental toxins is difficult to find, we called it a "silent pandemic" and did not pay enough attentions to this harm for a long time (Tyler and Allan, 2014). However, in recent years, public concern has been raised about arsenic neurotoxicity all over the world. Epidemiological studies in Bangladesh and the United States have determined that arsenic exposure may injure

Abbreviations: PR, prevalence ratio; CI, confidence interval; WAs, water arsenic concentration.

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cognitive function during childhood (Sun et al., 2015; Cordeiro et al., 2016). In a more recent cross-sectional study in Maine in the United States, the results showed that compared with school children regarding water arsenic on concentration ≤5 μg/L, the school children exposed to water arsenic on concentration ≥5 μg/L showed significant reductions in full-scale IQ scores (WISC-IV), resulting in losses of 5–6 points in most indices (Wang et al., 2016).

Most epidemiological studies have focused on the impact of arsenic exposure on children's intelligence; and research on the effect of arsenic exposure on adult cognition is limited. A key study in the U.S. has recently revealed a significant correlation between arsenic exposure and altered adult cognition, especially for symptoms associated with Alzheimer's disease (O'Bryant et al., 2011). I think it important to characterize the American study as 'limited' for generalizing to Chinese population, thus the important differences between the U.S. and China. First, the key limitation to this American study is a lack of both the direct measurement of the actual water arsenic level at participants' homes and a biomarker of arsenic exposure (O'Bryant et al., 2011). Second, the assessments of adult cognition in the U.S. are not precisely the same tests that were administered in China (Chua et al., 2005). Third, their nutritional status, as well as their habits of living and drinking water arsenic concentrations, differs greatly from Chinese rural adults (Popkin, 2014). Meanwhile, the population mobility in the U.S. is large, and the types of daily drinking water in the U.S. are different. Instead, the population mobility in Chinese rural areas is low. In addition, for the inhabitants of the area without running water during their lifetime, their own wells are the only source of the domestic water in China (Muthumani and Prabu, 2014; Moon et al., 2013; Gusman et al., 2013). This situation exists widely in rural endemic arsenicosis areas in the Shanxi and Jilin provinces in China. Therefore, in China, we can examine the association between the stable long-term arsenic exposure from drinking water and the cognitive function of Chinese rural adults. More importantly, the various arsenic concentrations of drinking water in Chinese rural endemic arsenicosis areas were in a wide range, so we could have paid more attention to the impact of stable, long-term, and lower-level exposure to arsenic on neuropsychological functioning.

2. Methods

2.1. Study area and population

Our ongoing research project is being conducted in Shanyin county of the Shanxi province and Tongyu county of the Jilin province in China. Shanyin county is approximately 112° east longitude and 39° north latitude, and Tongyu county is approximately 122° east longitude and 44° north latitude. Both of the two counties are serious arsenic-endemic areas identified in China in the 1980s (Muthumani and Prabu, 2014). The main reasons why they were chosen as our study sites are as follows. First, both Shanyin and Tongyu counties are in the region that has variable concentrations of arsenic in groundwater, which ranges from 0 to 650 μg/L according to the report of the local public health organization. Second, household wells constructed by the residents themselves were the only option as life's drinking water source. In addition, Shanyin and Tongyu are typical eco-agricultural counties in China, without industrial pollution and excessive residues of other heavy metals in soil and water. Third, most of local rural residents engaged in farm production, so their labor strength, habits, and customs are similar. In accordance with the principles of matching natural and social factors, five villages in Shanyin and four villages in Tongyu were selected as the study sites. By building on our own investigation, both the dietary habits and the yearly incomes (6000–7000 yuan) of residents in the nine villages are similar.

After investigating the basic information (sex, age, and marital status) for all residents who were living in the selected villages, residents were selected for this study based on the following criteria: adults over 40 years old; residents living in the selected village for at least 10 years who drank the water from their own household wells; inhabitants with accurate records of drinking and living history and Han nationality (to decrease the potential effects of gene polymorphism of the susceptibility to the toxicity of arsenic). Adults with any of the following circumstances were excluded: a past history of stroke, suffering from depression, and mental disease or using an antidepressant. To avoid bias from the inclusion of unexposed subjects with historic arsenic exposure, we excluded the subjects who were from the other endemic arsenic areas in China. The subjects were divided into the following four categories according to the arsenic concentration in their drinking water: normal exposure group (<10 μg/L), mild exposure group (10–50 μg/L), moderate exposure group (50–100 μg/L), and high exposure group (≥100 μg/L). To limit the analysis to the stable subjects exposed, we also excluded those who changed their concentration of arsenic in drinking water by more than one category.

2.2. Procedures

The procedures were approved by the Institutional Review Board of Harbin Medical University and had plenty of respective local government support. All of the procedures were carried out in accordance with the second Helsinki Declaration. All selected subjects received a written consent form that had to be signed by themselves or their spouses. And participants were given the results of all examinations and information on mitigation procedures (if appropriate).

2.2.1. Questionnaire

A standardized personal interview of selected subjects based on a structured questionnaire was carried out by well-trained researchers with several doctors. Before the survey was executed, all staffs were trained according to the need of this study. Information obtained from the field survey included demographic characteristics, alcohol consumption and smoking habits, dietary consumption frequency, residential and drinking water history, and health information. Different variables had different grading standards according to the statistical standards for this study. Similar for the smoking habit, subjects were divided into three categories: no smoking, less than 10 cigarettes/day, and more than 10 cigarettes/day in the past 6 months or longer. Regarding alcohol consumption, subjects were divided into three categories: no drinking, less than 3 times/week, and more than 3 times/week in the past 6 months or longer.

The detailed information of residential history (including villages of residence and duration of residence) and a history of water consumption (including water source and duration of drinking) were obtained through the questionnaire interview and were confirmed with the local public health organization. Therefore, all of the previously discussed information was considered as reliable in this study.

2.2.2. Physical examination and laboratory examinations

Anthropometric characteristics, such as standing height, and weight were measured according to a standard protocol. The water samples in the household wells at each participant's home were obtained in 60 ml acid-cleaned polyethylene during the field investigation. Water samples were shipped to Harbin Medical University for analysis. Arsenic concentration in water obtained from household wells was determined by using atomic fluorescence spectrometry (AFS) according to the national standardized method in China (Schmitt et al., 2005). Further details on the laboratory