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Hypertension among adults exposed to drinking water arsenic in Northern Chile

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ABSTRACT

Background: A growing number of studies have identified an association between exposure to inorganic arsenic and hypertension. However, results have not been consistent across studies. Additional studies are warranted, given the global prevalence of both arsenic exposure and morbidity attributable to hypertension.
Methods: We analyzed data collected from October 2007-December 2010 for a population-based cancer case-control study in northern Chile. Data included lifetime individual arsenic exposure estimates and information on potential confounders for a total of 1266 subjects. Those self-reporting either a physician diagnosis of hypertension or use of an anti-hypertensive medication were classified as having hypertension (n=612). The association between hypertension and drinking water arsenic exposure was analyzed using logistic regression models.
Results: Compared to those in the lowest category for lifetime highest 5-year average arsenic exposure (< 60 μg/L), those in the middle (60–623 μg/L) and upper (> 623 μg/L) exposure categories had adjusted hypertension ORs of 1.49 (95% CI: 1.09, 2.05) and 1.65 (95% CI: 1.18, 2.32), respectively. Similar results were observed in analyses of lifetime cumulative exposures and analyses restricted to exposures from the distant past.
Conclusions: We identified evidence of increased odds of hypertension with exposure to arsenic in drinking water among study participants. Our findings add to the growing body of research supporting this association, which could have important public health implications.

1. Introduction

Hypertension, or elevated blood pressure, is a well-known risk factor for cardiovascular disease (CVD), the leading cause of morbidity and mortality worldwide (World Health Organization, 2009). With a global prevalence of approximately 40%, the World Health Organization (WHO) estimates that 12.8% (7.5 million) of all deaths are attributable to hypertension each year (Alwan, 2011). There is growing evidence that drinking water arsenic exposure is associated with hypertension and a number of cardiovascular diseases (National Research Council, 2014).

Arsenic-induced damage to the vascular system is hypothesized to be associated with oxidative stress and inflammation, but is not fully understood (Lantz and Hays, 2006).

A small number of epidemiologic studies have assessed the relationship between arsenic exposure and hypertension, and several, though not all, have identified positive associations (Chen et al., 1995; Rahman et al., 1999; Huang et al., 2007; Abhyankar et al., 2012; Wang et al., 2011, 2007; Guo et al., 2007; Kwok et al., 2007). One recent prospective study found significantly greater year-to-year increases in blood pressure (BP) among participants with higher drinking water arsenic exposure compared to those in the lowest exposure group (Jiang et al., 2015).

While several studies have identified associations between drinking water arsenic exposure and hypertension, study limitations impede characterization of the dose-response relationship (Abhyankar et al., 2012; Navas-Acien et al., 2005). The majority have been cross-sectional. Individual lifetime arsenic exposure data have not been available, and some have depended on ecological estimates of exposure. Furthermore, many studies have taken place in Taiwan, Bangladesh

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and the United States (Abhyankar et al., 2012); results may not be generalizable to all potentially-exposed populations due to possible differences in nutrition, genetics, baseline hypertension rates, co-exposures, or other susceptibility factors (Chen et al., 1996; Lan et al., 2011).

Each year, millions are at risk of drinking water arsenic exposure in excess of the WHO-recommended limit of 10 μg/L, and it is estimated that over 100 million individuals might consume water containing arsenic concentrations greater than 50 μg/L (Alwan, 2011; van Halem et al., 2009). Considering the sizable population exposed to arsenic, and the high global prevalence of morbidity and mortality attributable to high blood pressure, any arsenic-associated increase in hypertension could result in hundreds of thousands of additional deaths (Alwan, 2011). Therefore, further investigation is needed to confirm and further elucidate the characteristics of this association.

The cities and towns in Regions I and II in northern Chile have had a wide range of arsenic concentrations in their drinking water sources (Ferreccio et al., 2000). In the largest city in the area, Antofagasta, hundreds of thousands of residents were exposed to high levels of drinking water arsenic beginning in 1958, when arsenic-contaminated rivers were diverted to supply water to the area's growing population. Residents of Antofagasta and neighboring Mejillones ingested water containing 860 μg/L or greater of arsenic until these concentrations were drastically decreased between 1970 and 1978 with the installation and improvement of a new water treatment plant (Yuan et al., 2007; Steinmaus et al., 2013; Ferreccio et al., 2013; Ferreccio and Sancha, 2006). Other cities in Regions I and II, which are demographically comparable to Antofagasta, vary widely in drinking water arsenic concentrations, from 1 μg/L to >600 μg/L (Ferreccio et al., 2013).

Northern Chile is the driest habitable place on earth, and there are relatively few individual water sources. Almost all inhabitants receive water from one of a limited number of public water utilities, which have robust historical records of water arsenic concentrations over a period of many decades in the past. Until recently, consumption of bottled water was uncommon. Because of the limited water sources and availability of good historical arsenic records, individual lifetime drinking water arsenic exposure can be estimated with a high level of accuracy (Steinmaus et al., 2013; Ferreccio et al., 2013).

Previous studies conducted in northern Chile have found increased lung, bladder, skin, and kidney cancer risk, as well as cardiovascular disease mortality among exposed populations (Yuan et al., 2007; Steinmaus et al., 2013; Smith et al., 2012). This is the first study of the relationship between drinking water arsenic and hypertension in this population.

2. Methods

2.1. Study setting

To assess the relationship between historical drinking water arsenic exposure and hypertension later in life among adults in northern Chile, we conducted a secondary analysis of data collected from a cancer case-control study in this area. Details of the original case-control study are described elsewhere (Steinmaus et al., 2013; Ferreccio et al., 2013). In summary, participants were selected from Regions I and II in northern Chile. Lung, bladder, and kidney cases newly diagnosed between October 2007 and December 2010 were identified from all local pathologists, radiologists, and hospitals in the Regions. Cancer cases over 25 years of age, residing in the study area at diagnosis, and who were available for interview or had a close relative who was, were included in the study. Lung, bladder, and kidney cancer-free controls residing in the study area from 2007 to 2009 were randomly selected from the Chilean Voter Registry, and frequency matched to cases by sex and 5-year age range. Because of this matching, the study participants represent the age and sex distribution of bladder, lung, and kidney cancer cases in the study area. The registry is estimated to include over 90% of Chilean adults ages 40 years and older. A total of 665 cancer cases and 640 cancer-free controls (or their proxy respondents) were eligible, gave informed consent, and participated in standardized interviews. Proxies responded for 121 (19.8%) of those with hypertension and 130 (19.9%) of those without hypertension.

2.2. Outcome assessment

All participants were interviewed using a standard structured questionnaire by trained personnel during a single study visit. During interviews, all participants were asked if they had ever been told by a physician that they had high blood pressure or hypertension. Additionally, they were asked to report all medications taken in the calendar year prior to the time of interview. All study participants who answered either of these questions were eligible for inclusion in the current analysis. Those self-reporting either a physician diagnosis of hypertension or use of an anti-hypertensive medication were classified as hypertension cases (n=612), while the remainder (n=654) comprised the hypertension-free controls. Among those with hypertension, 224 (36.6%) reported physician diagnosis alone, 20 (3.3%) reported anti-hypertensive medication use alone, and the remaining 368 (60.1%) reported both. Because analyses showed no major effect modification by cancer status, cancer cases and non-cancer controls were combined in some analyses. Thirty-nine individuals with missing outcome or predictor variable data were excluded. The remaining 1266 participants ranged in age from 32 to 98 years.

Subjects who reported physician-diagnosed diabetes or use of an oral hypoglycemic medication were defined as having diabetes. Current height and weight were also measured in all subjects by study nurses using standard study protocols. Information on diet was collected using a food frequency questionnaire that asked about intake of all foods within the year preceding interview and any major changes from 20 years previously. Socioeconomic status (SES) scores were calculated on a 12-point scale based on self-reported ownership of several household appliances, electronics (e.g. computer, television), car, or employment of domestic help.

2.3. Exposure estimation

A detailed lifetime residential history was collected for each participant during interview. Annual drinking water arsenic concentrations for each year of every participant's life were then estimated by linking each residence with arsenic water records for that residence. Arsenic water concentration records were available for approximately 95% of municipal water sources in the study area and for all larger Chilean cities outside of the study area (Ferreccio et al., 2000). These annual estimates were then used to calculate arsenic exposure metrics. Because it is unknown whether exposure intensity or cumulative exposure has a greater impact on the risk of arsenic-associated hypertension, results for several different metrics are reported. Cumulative arsenic exposure was calculated by summing the annual arsenic concentrations estimated for each year of each subject's life. Each subject's peak exposure was defined as the highest arsenic concentration estimated for any single year, while the highest 5-year average exposure was calculated as the highest annual concentration averaged over any contiguous 5-year period. Because high exposures in Antofagasta ended in 1970, and to evaluate possible latency effects, some analyses were limited to exposures before 1971 and excluded 11 individuals born in 1971 or later. For 23 individuals born between 1966 and 1970, highest average exposures prior to 1971 were calculated for time periods less than 5 years. These individuals were included in analyses, as their exclusion did not impact results.

Participants were categorized by tertile values for each metric among all participants. For several exposure metrics, the value dividing the lowest and middle tertiles was 60 μg/L, which corresponded to water arsenic concentrations in Iquique, one of the largest cities in the