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Arsenic in drinking water and prostate cancer in Illinois counties: An ecologic study

Catherine M. Bulka [a,*], Rachael M. Jones [b], Mary E. Turyk [a], Leslie T. Stayner [a], Maria Argos [a,*]

[a] University of Illinois at Chicago, School of Public Health, Epidemiology and Biostatistics Division, 1603 W. Taylor Street, Chicago, IL 60612, United States

[b] University of Illinois at Chicago, School of Public Health, Environmental and Occupational Health Sciences Division, 2121W. Taylor Street, Chicago, IL 60612, United States

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ABSTRACT

Background: Inorganic arsenic is a lung, bladder, and skin carcinogen. One of the major sources of exposure to arsenic is through naturally contaminated drinking water. While positive associations have been observed between arsenic in drinking water and prostate cancer, few studies have explored this association in the United States.

Objectives: To evaluate the association between inorganic arsenic concentrations in community water systems and prostate cancer incidence in Illinois using an ecologic study design.

Methods: Illinois Environmental Protection Agency data on arsenic concentrations in drinking water from community water systems throughout the state were linked with county-level prostate cancer incidence data from 2007 to 2011 from the Illinois State Cancer Registry. Incidence rates were indirectly standardized by age to calculate standardized incidence ratios (SIRs) for each county. A Poisson regression model was used to model the association between county-level SIRs and mean arsenic tertile (0.33–0.72, 0.73–1.60, and 1.61–16.23 ppb), adjusting for potential confounders.

Results: For counties with mean arsenic levels in the second tertile, the SIR was 1.05 (95% CI: 0.96–1.16). For counties with mean arsenic levels in the third tertile, the SIR was 1.10 (95% CI: 1.03–1.19). There was a significant linear dose-response relationship observed between mean arsenic levels and prostate cancer incidence (p for trend = 0.003).

Conclusions: In this ecologic study, counties with higher mean arsenic levels in community water systems had significantly higher prostate cancer incidence. Individual-level studies of prostate cancer incidence and low-level arsenic exposure are needed.

1. Introduction

Arsenic is ubiquitous in nature, and is the 20th most common element in the earth's crust (International Agency for Research on Cancer, 2012) Arsenic is emitted from volcanic activity and industrial activities, in addition to being historically used as a pesticide. For humans, the major source of exposure is through food and drinking water (Agency for Toxic Substances Control and Disease Registry, 2007). In the United States, arsenic is distributed in surface and groundwater at varying concentrations, but arsenic in public/community water supplies is not to exceed 10 parts per billion (ppb) based on the current standard from the Environmental Protection Agency (EPA) (United States Environmental Protection Agency). However, concerns remain regarding the carcinogenicity of arsenic in drinking water at levels at or below the current guideline (Smith). In Illinois, the majority of community water supplies have arsenic levels below 10 ppb, while private wells are not regulated for arsenic concentrations in groundwater (Warner et al., 2003).

The International Agency for Research on Cancer (IARC) has categorized arsenic as a "Group 1 Carcinogen," meaning there is sufficient evidence of carcinogenicity in humans. However, the majority of epidemiologic studies focused on the carcinogenicity of arsenic have been limited to skin, urinary bladder, and lung cancers (Smith et al., 1992). There is some evidence of an association between arsenic exposure and prostate cancer, the second leading cause of cancer death in males in the United States, but this association is not well established for low-level arsenic exposure. The majority of existing epidemiologic studies evaluating arsenic in relation to prostate cancer have been conducted outside of the United States where exposure levels were in excess of

* Correspondence to: University of Illinois at Chicago, School of Public Health, Epidemiology and Biostatistics Division, 1603 W. Taylor St., MC923 Chicago, IL 60612, United States.

E-mail addresses: cbulka2@uic.edu (C.M. Bulka), rjones25@uic.edu (R.M. Jones), mturyk1@uic.edu (M.E. Turyk), lstayner@uic.edu (L.T. Stayner), argos@uic.edu (M. Argos).

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10 ppb (Yang et al., 2008; Chen and Wang, 1990; Wu et al., 1989; Hsu et al., 2013; Hinwood et al., 1999; Chen et al., 1988; Tsai et al., 1999; Rivara et al., 1997). To date, only two studies on arsenic and prostate cancer have been conducted in the United States (Table 1) (García-Esquinas et al., 2013; Lewis et al., 1999). Garcia-Esquinas et al. (2013) found a 4-fold increase in the hazard of prostate cancer mortality (hazard ratio: 4.58, 95% CI: 1.31–16.6) when comparing those in the highest tertile of total urinary arsenic (> 13.32 μg/g creatinine) to those in the lowest tertile (< 6.91 μg/g creatinine) among American Indians in Arizona, Oklahoma, North Dakota, and South Dakota, in what is to date the only prospective cohort study of low-dose arsenic exposure in the United States. Lewis et al. (1999) found elevated mortality from prostate cancer among men exposed to medium (1000–4999 ppb-years) and high levels (≥ 5000 ppb-years) of cumulative arsenic exposure based on ecologic measurements of arsenic in community water supplies in Utah. It has been suggested that arsenic can impact prostate cancer cell progression through androgen-independence, which is often associated with advanced and lethal prostate cancers that are difficult to treat (Benbrahim-Tallaa and Waalkes, 2008; Arsenic, 2005). Other research has suggested that arsenic exposure through drinking water inhibits DNA repair processes as part of its carcinogenic mechanism of action (Andrew et al., 2006).

Given the limited existing epidemiologic studies examining the association between low-level arsenic exposure and prostate cancer, we sought to examine the association between inorganic arsenic concentration in community water supplies and prostate cancer incidence in Illinois using an ecologic study design.

2. Methods

The county-level concentration of arsenic in finished drinking water (water that has been treated and is ready for distribution and consumption by the public), provided by community water systems (CWSs) between 2000 and 2006, was the main exposure of interest. Prostate cancer incidence data from the Illinois State Cancer Registry for 2007–2011 aggregated at the county-level were merged with county-level population and demographic data from the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) program. As such, an ecological analysis was conducted at the county-level. This study was approved by the University of Illinois at Chicago Institutional Review Board.

2.1. Water data

Arsenic levels in finished drinking water provided by community water systems (CWSs) were obtained from Illinois Safe Drinking Water Information System (SDWIS) for the period January 1, 2000 to December 31, 2006. CWSs are public water systems that supply water for human consumption to the same population-year round through at least 15 service connections or to at least 25 people (United States Environmental Protection Agency). The Arsenic and Clarifications to Compliance and New Source Monitoring Rule 66 FR 6976, which was finalized in January 2001, required CWSs using groundwater to take one sample between 1999 and 2001, 2002–2004, and 2005–2006; annual measurements were required for CWSs using surface water.

The most frequently reported limits of detection (for samples identified below the detection limit) were 0.5 ppb (n = 1509 samples) and 1 ppb (n = 1401 samples), and ranged from 0 to 50 ppb. For samples below the limit of detection, the value imputed was ½ the limit of detection. If the limit of detection was reported as zero, then 0.25 ppb was imputed (n = 6 samples). Overall, 50.9% of samples were indicated to be below the limit of detection.

Table 1
Epidemiologic studies of arsenic exposure and prostate cancer.

Study	Country	Study design	Sample size	Exposure	Result summary
Chen and Wang (1990)	Taiwan	Ecologic	314 precincts and townships	Arsenic in drinking water (range = 50 ppb to ≥ 350 ppb)	Increased prostate cancer mortality
Chen et al. (1988)	Taiwan	Ecologic	313 townships	Arsenic in drinking water (range = ≤ 300 ppb to ≥ 600 ppb)	Increased prostate cancer mortality
García-Esquinas et al. (2013)	U.S.	Prospective	18 deaths, 3932 total cohort	Inorganic arsenic levels in urine (interquartile range = 5.8–15.6 μg/g creatinine)	Increased prostate cancer mortality
Hinwood et al. (1999)	Australia	Ecologic	22 geographic areas	Arsenic in surface soil and drinking water (< 10 to > 200 ppb)	Increased prostate cancer incidence
Hsu et al. (2013)	Taiwan	Prospective	9 cases, 1231 total cohort	Arsenic skin lesions (present vs. absent)	Increased prostate cancer incidence
Lewis et al. (1999)	U.S.	Ecologic	7 communities	Arsenic in drinking water (range = 3.5–620 ppb)	Increased prostate cancer mortality
Rivara et al. (1997)	Chile	Ecologic	2 regions	Arsenic in drinking water (range = 10 ppb to 860 ppb)	No association with prostate cancer mortality
Tsai et al. (1999)	Taiwan	Ecologic	4 townships	Arsenic in drinking water (range = 250 ppb to 1140 ppb)	Increased prostate cancer mortality
Wu et al. (1989)	Taiwan	Ecologic	42 villages	Arsenic in drinking water (range = 10 ppb to 1752 ppb)	Increased prostate cancer mortality
Yang et al. (2008)	Taiwan	Ecologic time series	4 townships	Arsenic in drinking water (range = < 10 to 2500 ppb)	Reduced prostate cancer mortality associated with elimination of arsenic from well water