AJKD
Original Investigation

Arsenic Exposure From Drinking Water and the Incidence of CKD in Low to Moderate Exposed Areas of Taiwan: A 14-Year Prospective Study

Ling-I Hsu, PhD,[1,2] Fang-I Hsieh, PhD,[3] Yuan-Hung Wang, PhD,[4,5] Tai-Shuan Lai, MD, PhD,[6] Meei-Maan Wu, PhD,[3] Chien-Jen Chen, ScD,[7] Hung-Yi Chiou, PhD,[3] and Kuang-Hung Hsu, PhD[1,2,8]

Background: Arsenic exposure is associated with decreased kidney function. The association between low to moderate arsenic exposure and kidney disease has not been fully clarified.

Study Design: The association between arsenic exposure from drinking water and chronic kidney disease (CKD) was examined in a long-term prospective observational study.

Setting & Participants: 6,093 participants 40 years and older were recruited from arseniasis-endemic areas in northeastern Taiwan. Arsenic levels were 28.0, 92.8, and 295.7 μg/L at the 50th, 75th, and 90th percentiles, respectively.

Predictor: Well-water arsenic and urinary total arsenic (inorganic plus methylated arsenic species) concentrations, adjusted for urinary creatinine concentration.

Outcomes: Kidney diseases (*ICD-9* codes: 250.4, 274.1, 283.11, 403.*1, 404.*2, 404.*3, 440.1, 442.1, 447.3, or 580-589) and CKD (*ICD-9* code: 585) ascertained using Taiwan's National Health Insurance database 1998 to 2011.

Measurements: HRs contrasting CKD risk across arsenic exposure levels were estimated using Cox regression. Prevalence ORs for proteinuria (protein excretion ≥ 200 mg/g) comparing quartiles of total urinary arsenic concentrations were estimated using logistic regression.

Results: We identified 1,104 incident kidney disease cases, including 447 CKD cases (incidence rates, 166.5 and 67.4 per 10^4 person-years, respectively). A dose-dependent association between well-water arsenic concentrations and kidney diseases was observed after adjusting for age, sex, education, body mass index, cigarette smoking, alcohol consumption, and analgesic use. Using arsenic concentration ≤ 10.0 μg/L as reference, multivariable-adjusted HRs for incident CKD were 1.12 (95% CI, 0.88-1.42), 1.33 (95% CI, 1.03-1.72), and 1.33 (95% CI, 1.00-1.77) for arsenic concentrations of 10.1 to 49.9, 50.0 to 149.9, and ≥150.0 μg/L, respectively (*P* for trend = 0.02). The association between arsenic concentration and kidney diseases was stronger for women (*P* for interaction = 0.06). Arsenic values in the range of 50th to 75th and 75th to 100th percentiles of total urinary arsenic concentrations were associated with 50% and 67% higher prevalences, respectively, of proteinuria.

Limitations: Kidney diseases and CKD outcomes were based on diagnostic codes. Glomerular filtration rates were not available. Other heavy metals were not measured.

Conclusions: This study describes the temporal relationship between arsenic concentrations ≥ 10 μg/L in drinking water and CKD. A dose-dependent association between well-water arsenic concentration and kidney diseases was observed. Higher creatinine-adjusted urinary total arsenic concentrations were associated with a higher prevalence of proteinuria.

Am J Kidney Dis. 70(6):787-797. *© 2017 by the National Kidney Foundation, Inc.*

INDEX WORDS: Arsenic; chronic kidney disease (CKD); arsenic toxicity; gender; sex differences; drinking water; well water contamination; environmental exposure; modifiable risk factor; proteinuria; renal disease; Taiwan; prospective study.

Arsenic exposure is an important public health issue worldwide, with more than 100 million people exposed to arsenic-contaminated water supplies (arsenic concentrations above the internationally accepted standard of 10 μg/L).[1] Long-term arsenic ingestion may have adverse health effects, including diabetes, hypertension, cataracts, vascular diseases, and various cancers.[1] Acute arsenic poisoning may

From the [1]Laboratory for Epidemiology, Department of Health Care Management, and [2]Healthy Aging Research Center, Chang-Gung University, Taoyuan City; [3]Department of Public Health, School of Medicine, and [4]Graduate Institute of Clinical Medicine, College of Medicine, Taipei Medical University, Taipei; [5]Department of Medical Research, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan; [6]Division of Nephrology, National Taiwan University Hospital Bei-Hu Branch; [7]Genomics Research Center, Academia Sinica, Taipei; and [8]Department of Urology, Chang Gung Memorial Hospital, Taoyuan City, Taiwan.

Received November 30, 2016. Accepted in revised form June 2, 2017. Originally published online August 23, 2017.

Address correspondence to Kuang-Hung Hsu, PhD, Laboratory for Epidemiology, Department of Health Care Management, and Healthy Aging Research Center, Chang-Gung University, No. 259, Wenhua 1st Rd, Guishan District, Taoyuan City, 333, Taiwan (e-mail: khsu@mail.cgu.edu.tw) or Hung-Yi Chiou, PhD, School of Public Health, College of Public Health and Nutrition, Taipei Medical University, 250 Wu-Xin Street, Taipei 110, Taiwan (e-mail: hychiou@tmu.edu.tw).

© 2017 by the National Kidney Foundation, Inc.

0272-6386
http://dx.doi.org/10.1053/j.ajkd.2017.06.012

cause kidney damage, including acute kidney injury.[2,3]

Recent epidemiologic studies have provided evidence for an association between long-term arsenic exposure and decreased kidney function. A previous study from arseniasis-endemic areas in southwestern Taiwan indicated an association between high-level arsenic exposure from drinking water (>300 μg/L) and several microvascular diseases, including kidney disease.[4] Two Taiwanese population studies have shown that elevated total urinary inorganic arsenic metabolite concentrations are associated with reduced glomerular filtration rate and/or increased risk for abnormal β_2-microglobulinuria.[5,6] A positive association between concentrations of urinary arsenic and urinary *N*-acetyl-β-D-glucosaminidase, an indicator of decreased kidney function, has been observed in Korea and in an endemic area of China.[7,8] Similarly, a positive association between external/internal arsenic levels and the prevalence of proteinuria/albuminuria has also been observed in Bangladesh and among American Indians.[9,10] Prenatal or early childhood exposure to high arsenic concentrations (870 μg/L) has been shown to be associated with increased kidney disease mortality among young adults in Chile.[11]

Based on these observations, there is strong evidence to suggest an association between arsenic exposure and nephrotoxicity. However, most studies that have evaluated this association are cross-sectional or case-control studies. Studies exploring the temporal relationship between ingested arsenic and kidney disease remain limited.[12] Furthermore, the pattern of the association between low-level exposure and adverse kidney outcomes needs to be explored.

We investigated the dose-response relationship between low to moderate arsenic exposure from drinking water and chronic kidney disease (CKD) via a prospective study in northeastern Taiwan. In addition, we evaluated the disease modification effects of risk factors, including diabetes and hypertension.

METHODS

Study Population

The cohort was recruited from 18 villages in the Lanyang Basin of northeastern Taiwan during 1991 to 1994, and 6,093 residents 40 years or older were recruited.[13] Residents in this area had consumed well water since the 1940s and had stopped well-water consumption in the 1990s. Water in the wells had arsenic levels ranging from undetectable to 3,590 μg/L. Sociodemographic characteristics, occupational history, and lifestyle variables of the study population were obtained at baseline using a structured questionnaire. Although the analysis was performed using a prospective method, the nature and protocol of this study were reviewed and approved by the Institutional Review Board of Chang Gung Memorial Hospital, which provided an exemption certificate for this review (201600153B0). Therefore, written or verbal informed consent was not required from study participants. All research methods in this study were performed in accordance with the approved guidelines.

Arsenic Exposure Assessment

All study participants were interviewed at baseline and detailed histories of residency and duration of well-water consumption were obtained. Altogether, 3,901 well-water samples (1 sample from each household) were collected. Well-water arsenic concentrations were determined by hydride generation plus flame atomic absorption spectrometry.[13] Cumulative arsenic exposure was defined as (household well-water arsenic concentration) × (duration of well-water consumption). If a study participant moved and the arsenic level of the previous residence was unknown, the individual's arsenic exposure was considered to be missing. Overall, 14% of participants had unknown exposures.

Identification of Kidney Diseases, Diabetes, Hypertension, and Hyperlipidemia

Cohort participants who died before 1998, those who had no well arsenic concentrations available, and those with prevalent kidney diseases (diagnosed before March 1, 1998) were excluded. Overall, 6,093 participants underwent further analysis (Fig 1). Each participant's disease status was obtained by retrieving his or her comprehensive health care information, including diagnoses and prescriptions, from Taiwan's National Health Insurance (NHI) database covering 1998 to 2011. Approximately 96.1% of the 23 million population of Taiwan had NHI coverage at the end of 1999, and this had increased to 98.0% at the end of 2004.[14] *International Classification of Diseases, Ninth Revision* (*ICD-9*) codes were used to ascertain disease status.

Participants with 3 or more outpatient visits or 1 or more hospitalized record or 1 or more catastrophic illness record for kidney diseases (*ICD-9* codes: 250.4, 274.1, 283.11, 403.*1, 404.*2, 404.*3, 440.1, 442.1, 447.3, and 580-589) and CKD (*ICD-9* code: 585) were identified as the 2 primary outcomes in this study. Diabetic patients were defined as those with 3 or more outpatient visits within 365 calendar days or with at least 1 hospitalization and having an *ICD-9* diagnosis code of 250, 357.2, 362.0, or 366.41 at a discharge.[15] Hypertension was diagnosed if the participant had an *ICD-9* code of 362.11, 401 to 405, or 437.2 and had received 3 or more monthly packs of antihypertensive agents over 365 calendar days. Participants were identified as having dyslipidemia if they had an *ICD-9* code of 272 and had received 3 or more monthly packs of antihyperlipidemia agents over 365 calendar days. To ensure that ascertainment bias based on test ordering did not occur, we also examined each individual's urine or blood examination records, and >90% of participants had at least 1 examination during follow-up.

Urinary Arsenic Metabolites

First-morning spot urine samples were collected in 1991 to 1994, frozen within 2 to 3 hours of collection, and stored at −20°C. Participants were asked not to consume seafood for the 3 days before urine collection. These samples were transported to the laboratory at Chang-Gung University for measurement of arsenic metabolites. Urinary arsenic speciation was performed by high-performance liquid chromatography for separation of arsenic species, followed by inductively coupled plasma mass spectrophotometry (NexION300; PerkinElmer) for determining concentrations of arsenic species. Limits of detection were 0.4, 1.4, 1.4, and 1.0 μg/L for inorganic arsenic As^{3+} and As^{5+} and for monomethylarsonate (MMA) and dimethylarsinate (DMA), respectively. Percentages of participants with concentrations less than the limit of detection were 0.07%, 0.06%, and 0.00% for inorganic arsenic, MMA, and DMA, respectively. A spiking analysis yielded an average recovery rate of 95.18% to 100.03%. SRM 2670a, a standard reference material, was used for validation

Download English Version:

https://daneshyari.com/en/article/8770039

Download Persian Version:

https://daneshyari.com/article/8770039

Daneshyari.com