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Inorganic arsenic exposure and type 2 diabetes mellitus in Mexico

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Abstract

Inorganic arsenic exposure in drinking water has been recently related to diabetes mellitus. To evaluate this relationship the authors conducted in 2003, a case-control study in an arseniasis-endemic region from Coahuila, a northern state of Mexico with a high incidence of diabetes. The present analysis includes 200 cases and 200 controls. Cases were obtained from a previous cross-sectional study conducted in that region. Diagnosis of diabetes was established following the American Diabetes Association criteria, with two fasting glucose values $\geqslant 126$ mg/100 ml ($\geqslant 7.0$ mmol/l) or a history of diabetes treated with insulin or oral hypoglycemic agents. The next subject studied, subsequent to the identification of a case in the cross-sectional study was taken as control. Inorganic arsenic exposure was measured through total arsenic concentrations in urine, measured by hydride-generation atomic absorption spectrophotometry. Subjects with intermediate total arsenic concentration in urine (63.5–104 μg/g creatinine) had two-fold higher risk of having diabetes (odds ratio = 2.16; 95% confidence interval: 1.23, 3.79), but the risk was almost three times greater in subjects with higher concentrations of total arsenic in urine (odds ratio = 2.84; 95% confidence interval: 1.64, 4.92). This data provides additional evidence that inorganic arsenic exposure may be diabetogenic.

Keywords: Arsenic; Case-Control Studies; Diabetes mellitus; Type 2; Risk factors; Water pollutants; Chemical

1. Introduction

Mexico has a high occurrence of type 2 diabetes mellitus. It is estimated that by the year 2025 it will rank seventh among the countries with the largest number of cases worldwide (King et al., 1998). In the year 2000, 7.5% of the adult population (20 years and older) had type 2 diabetes (Olaiz et al., 2003). Diabetes is the main cause of death in Mexico (Secretaría de Salud, 2005) and is an important economic burden for the country's health services (Arredondo and Zúñiga, 2004). Different risk factors for diabetes have been identified in Mexico, such as high blood pressure, body fat distribution and a family history of diabetes (Escobedo-de la Peña et al., 1998; Posadas-Romero et al., 1994). However, other risk factors associated to the environment have not been sufficiently studied in Mexico.

Inorganic arsenic exposure is one of the disease–environment interactions that have recently been related to the occurrence of type 2 diabetes mellitus (Navas-Acien et al., 2006). In Taiwan and Bangladesh, countries with high arsenic contamination levels in human drinking water, a significant link has been documented between exposure levels and incidence (Tseng et al., 2000), prevalence (Lai et al., 1994; Rahman et al., 1998) and mortality due to diabetes (Tsai et al., 1999). No studies have evaluated the association of arsenic exposure and diabetes in endemic areas with high arsenic concentrations in drinking water outside of Taiwan and Bangladesh (Navas-Acien et al., 2006). At low and intermediate levels of exposure, moreover, few studies addressing the association of arsenic and diabetes are available (Navas-Acien et al., 2006). Because of study limitations in arsenic exposure and diabetes

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assessment in most available studies, the association of arsenic exposure with diabetes development is still uncertain (Longnecker and Daniels, 2001; Zierold and Knobeloch, 2004; Navas-Acien et al., 2006).

In Mexico there are several geographic areas with high arsenic levels in water supplies for human consumption (Cebrian et al., 1994; Rosas et al., 1999). The Lagunera region, located in the north-central part of the country in the states of Coahuila and Durango, is an important producer of dairy, cotton and metal mineral products and is the most studied area as regards arsenic exposure in Mexico. Excessive arsenic in water of the Lagunera region is due to the dissolution of metal mineral and other ores, mainly arsenopyrite, transported to water sources through limestone fractures. This region has been identified as an endemic area for arsenicism since 1965. While Coahuila is among the states with the greatest occurrence and highest mortality rate due to diabetes in Mexico (Olaiz et al., 2003), the contribution to of arsenic exposure to diabetes development in this region is unknown.

In view of the fact that current evidence is still insufficient and inadequate to establish a causal link, and given the recommendation of the United States of America's National Research Council Subcommittee on Arsenic in Drinking Water from the need to conduct epidemiological studies so as to establish the dose–response relationship for arsenic-associated diseases other than cancer, especially at low dosages (National Research Council (US), 1999), a decision was reached to evaluate the association between inorganic arsenic exposure and the occurrence of type 2 diabetes mellitus in a population exposed to high levels of arsenic in drinking water.

2. Materials and methods

2.1. Study design and population

A case control study with 400 participants was conducted on the population of nine locations from the municipalities of Matamoros, Francisco I. Madero and San Pedro, in the state of Coahuila, Mexico. These locations were selected because prior studies have identified high inorganic arsenic levels in sources of water (20–400 μg/l) for human consumption (Cebrian et al., 1994). The study was approved by the Institutional Committee on Research and Ethics and an informed consent was obtained from all participants.

In the months of March–July 2003 a cross-sectional study with 1314 participants was conducted in the selected locations in order to identify cases for the case-control study and to estimate the prevalence of type 2 diabetes. According to the population census of the year 2000, there were 4069 inhabitants in this area from which 2038 had not Social Security (target population). All subjects aged $\geqslant$30 years old who did not have Social Security, were invited to the study by personnel of the medical units of the IMSS-Solidarity system.

2.2. Type 2 diabetes mellitus case identification

Fasting glucose, cholesterol and triglyceride concentrations were measured in all participants. If the subject had a glucose concentration equal or greater than 126 mg/100 ml ($\geqslant$7.0 mmol/l) under fasting conditions, a second fasting glucose test was performed within 1 week and if the results were confirmed a diagnosis of type 2 diabetes mellitus was established. Subjects with previous diagnosis of diabetes who at the time of the interview were taking insulin or oral hypoglycemic drugs were also considered to be diabetics, regardless of their fasting glucose values.

Three hundred and two subjects were identified with type 2 diabetes, 227 (75.2%) had been previously diagnosed and 75 (24.8%) were newly diagnosed. This proportion is similar to what has been found at the recent National Health Survey (Olaiz, et al., 2003).

The prevalence of diabetes was 23% (95% confidence intervals 20.7–25.3%). Two hundred cases were randomly selected from 302 of the subjects with a diagnosis of diabetes and were included in the case-control study.

2.3. Controls

For the selection of the 200 controls, the next subject studied during the cross-sectional study immediately after the identification of a selected case (and who had no diabetes) was included, irrespective of their gender or age. In the event the next subject had diabetes, the following subject was selected.

2.4. Data collection

All subjects were measured for serum concentrations of glucose, cholesterol and triglycerides under at least 8 h of fasting conditions. A semi-structured questionnaire was applied to all of them in order to measure socio-demographic variables as well as other risk factors. Height was measured in meters to the nearest centimeter; weight was measured in kilograms, with the minimum of clothing, to the nearest 50 g. Body mass index was estimated as a measurement of obesity, dividing their weight in kilograms by their height in meters raised to the second power. Blood pressure was measured in all subjects with the usual techniques, with subjects sitting down, after 5 min of rest, with an empty bladder and without having smoked or drank coffee that morning. The first phase was recorded as systolic pressure, and the fifth, as diastolic pressure. All subjects with a systolic pressure equal or greater than 140 mmHg or a diastolic pressure equal or greater than 90 mmHg were considered to be hypertensive. Likewise, those subjects with prior diagnosis of hypertension who at the time of the interview were taking anti-hypertensive drugs were considered to suffer hypertension, irrespective of the arterial blood pressure numbers.

2.5. Urine arsenic assessment

In order to evaluate inorganic arsenic exposure, total arsenic concentrations in urine were measured. All identified cases and controls were asked for a 10–100 ml urine spot sample in a wide-mouth jar previously washed with 10% nitric acid and rinsed with bidestilled and deionized water. Spot urine samples were collected and stored in stoppered polyethylene bottles at $-15\,^{\circ}C$ until they were analyzed (no more than 6 months after collection). To determine the concentration of total arsenic in urine, an aliquot of the sample (1–10 ml) was digested with a mixture of nitric, sulfuric and perchloric acids according to Del Razo et al. (1997). Since total arsenic in urine may be highly influenced by ingestion of seafood arsenic, participants were asked to exclude seafood from the diet for the preceding 5 days before urine donation. Nevertheless, in the rural area studied in this work, marine food is seldom included in diet.

Total arsenic concentration was determined by means of hydride-generation atomic absorption spectrophotometry, using the standard reference material (SRM 2670) from the National Institute of Standards and Technology (NIST®) as a control to evaluate the precision and accuracy of total arsenic concentration in urine resulting in a variation coefficient of $\pm$11.2% and an accuracy of 108.1%. To control the possible dilution or arsenic concentration present in the urine sample, the arsenic concentration was adjusted as a function of urinary creatinine