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Dietary micronutrient intake and its relationship with arsenic metabolism in Mexican women

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ABSTRACT

Introduction: Concentrations of inorganic arsenic (iAs) metabolites in urine present intra- and inter-individual variations, which are determined not only by the magnitude of exposure to iAs, but also by differences in genetic, environmental and dietary factors.
Objective: To evaluate whether differences in dietary intake of selected micronutrients are associated with the metabolism of iAs.
Methods: The intake of 21 micronutrients was estimated for 1027 women living in northern Mexico using a food frequency questionnaire. Concentration of urinary metabolites of iAs was determined by high performance liquid chromatography inductively coupled plasma mass spectrometry (HPLC-ICP-MS) and the proportion of iAs metabolites was calculated (%iAs, monomethylarsonic acid [%MMA] and dimethylarsinic acid [%DMA]), as well as ratios corresponding to the first (MMA/iAs), second (DMA/MMA) and total methylation (DMA/iAs).
Results: After adjustment for covariates, it was found that methionine, choline, folate, vitamin B12, Zn, Se and vitamin C favor elimination of iAs mainly by decreasing the %MMA and/or increasing %DMA in urine.
Conclusions: Our results confirm that diet contributes to the efficiency of iAs elimination. Further studies are needed to assess the feasibility of dietary interventions that modulate the metabolism of iAs and the consequent risk of diseases related to its exposure.

1. Introduction

Inorganic arsenic (iAs) is metabolized and excreted in urine in its monomethylated (15–25%) and di-methylated forms (40–75%) and as iAs (20–25%) (Agency for Toxic Substances and Disease Registry, 2007). A greater proportion of monomethylarsonic acid (MMA), and a lower of dimethylarsinic acid (DMA) increase the risk of various cancers, skin lesions and diseases of the circulatory system among others (Steinmaus et al., 2010).

The concentrations of iAs metabolites in urine present intra- and interindividual variations, determined not only by the amount of iAs exposure but also by differences in genetic, environmental and dietary factors, such as the intake of several nutrients involved in one carbon metabolism, a series of oxidation-reduction reactions that provide methyl groups needed for arsenic methylation (Tseng, 2009).

Several studies undertaken in different human populations exposed to iAs, have consistently shown a negative association between urinary %MMA and dietary intake and/or plasma levels of some micronutrients (selenium [Se], zinc [Zn], calcium [Ca], folate, methionine, vitamin C and B6). In some studies, an increase in % DMA has been observed in relation to the consumption of these

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nutrients (Basu et al., 2011; Gamble et al., 2006, 2005; Hall et al., 2009; Heck et al., 2007; Steinmaus et al., 2005a). Likewise, the intake of certain pro-vitamins and vitamins (β-carotene, B2, B6, B12, A, C, E and folic acid) have been associated with a reduced risk of diseases linked to iAs exposure (skin cancer, hyperkeratosis diseases, melanosis and changes in blood pressure) (Chen et al., 2007; Hsueh et al., 1997; Zablotska et al., 2008).

In north Mexico, iAs is naturally found in drinking water in concentrations exceeding the limit (10 μg/L) recommended by the World Health Organization (Camacho et al., 2011). Recently, our research group reported an increased risk of breast cancer in women living in the area, who had reduced ability to metabolize iAs, expressed by higher %MMA and lower %DMA in urine (López-Carrillo et al., 2014). The aim of the present study is to evaluate whether differences in the dietary intake of micronutrients related to one carbon metabolism, as well as other selected nutrients, could explain variations in iAs metabolism among clinically healthy control women participating in the above mentioned study.

2. Materials and methods

2.1. Study population

A cross-sectional study was undertaken among 1027 healthy Mexican women aged at least 20 years and resident for at least one year in any of the following states: Chihuahua, Coahuila, Durango, Nuevo Leon and Sonora, during the period 2007–2011 (López-Carrillo et al., 2014). The women were identified with the Master Sampling System for National Health Surveys in Mexico, which provides a list of homes located in both urban and rural areas, grouped into city blocks and also into basic geostatistical areas (BGA). A certain number of BGAs and city blocks were randomly selected, where homes were systematically visited in order to identify an eligible woman. In homes where no eligible woman was found, or if she did not consent, we proceeded to locate a new home; when there was more than one eligible woman, we randomly selected one. The response rate was 99.6% (1027/1031). The project was approved by the Research, Biosecurity and Bioethics Committees at the National Institute of Public Health (Mexico).

2.2. Interviews

Pending informed consent, participants were interviewed face to face in one occasion, at their homes by trained interviewers about sociodemographic characteristics, diet, alcohol, and tobacco consumption. Anthropometric measurements for calculating the body mass index were also obtained [BMI=body weight (kg)/height (m^2)]. All interviews were made in the period of 2007–2009.

2.3. Urinary arsenic determination

Participants donated a first morning void urine sample, not necessarily the same day of interview. Samples were collected in a sterile disposable polypropylene urine collection cup, stored in a fridge and maintained at least for two years at −70 °C until analysis. Concentrations (μg/L) of urinary species for arsenite (As^{3+}), arsenate (As^{5+}), monomethylarsonic acid (MMA^{5+}), dimethylarsinic acid (DMA^{5+}) and arsenobetaine (AsB) were determined by high performance liquid chromatography coupled with mass spectrometry (HPLC-ICP-MS), according to methodology previously described (Gilbert-Diamond et al., 2011). Measurements below the limit of detection (LOD) (AsB: 24.25%; As^{3+}: 19.28%; As^{5+}: 56.28%; MMA^{5+}: 1.95%; DMA^{5+}: 0.49%) were given the corresponding LOD: AsB: 0.08; As^{3+}: 0.15; As^{5+}: 0.41; MMA^{5+}: 0.12 and DMA^{5+}: 0.12, divided by two (LOD/2), as suggested by Barr et al. (2006). The urinary concentration of creatinine (mg/dL) was measured using an enzymatic method kit (Randox, Antrim County, UK). Coefficients of variation were: MMA^{5+}=8%, DMA^{5+}=9%, As^{3+}=8% and creatinine=2.76%.

In order to evaluate iAs metabolism, we calculated: 1) iAs concentration from the sum of As^{3+} and As^{5+}; 2) Total As (TAs) as a result of the sum of iAs, MMA^{5+} (MMA), DMA^{5+} (DMA) and AsB; 3) proportions of iAs, MMA and DMA based on the total sum of these; 4) methylation ratios: first=MMA/iAs; second=DMA/MMA; and total=DMA/iAs.

2.4. Micronutrient intake evaluation

Daily consumption over the last year of 119 foods and 14 dishes was estimated using a validated semi-quantitative food frequency questionnaire, which included predetermined portions for each food, with 10 response options from "never" to "six or more times per day" (Galván-Portillo et al., 2011). Fruits and vegetables frequency of consumption was adjusted according to their availability throughout the year; for example, half the reported plum consumption was assumed because they are only available six months of the year.

Previously, our work group identified the specific foods contained in our questionnaire, with those in the reference tables for nutrient composition No. 20 of the United States Department of Agriculture (USDA). Based on the frequency of food consumption reported by participants, the daily intake of total energy was estimated, as well as that of the following micronutrients: retinol, vitamin C, α-tocopherol, thiamine, riboflavin, niacin, vitamin B6, folate, vitamin B12, choline, methionine, betaine, phosphorus (P), magnesium (Mg), iron (Fe), copper (Cu), sodium (Na), potassium (K), Ca, Zn and Se.

2.5. Statistical analysis

Sociodemographic characteristics, proportions and methylation ratios of iAs metabolites, as well as nutrient intakes in the study population were described using measures of central tendency and dispersion. The percentage of women with consumption below the Daily Recommended Intake (DRI) was calculated using the values reported for Mexican women of 19–70 years (Bourges et al., 2009), and when the corresponding information was not available, that suggested for American women was taken as reference (Institute of Medicine, 2006).

The associations between each nutrient of interest with each urinary As metabolite were determined by multiple linear regression models. The proportions and iAs methylation ratios were transformed to log scale to improve their normality. Nutrient intakes of interest were adjusted for total energy intake, according to the residual method proposed by Willett et al. (1997). We included as covariates those that first: correlated significantly with any of the proportions or methylation ratios of iAs; second: correlated significantly with energy-adjusted nutrients of interest; third: were not significantly correlated with each other. Those covariates were: age (years), total energy intake (kcal/day) and TAs-AsB (μg/l). BMI was not included because it was highly correlated with total energy intake.

3. Results

On average, participants in the study were 54 years old, with 6 years of education, a BMI on the margin of obesity (30 kg/m^2) and 48 years of residence in the selected states (Table 1). Most women did not smoke (85%) or consume alcohol (89%) (Data not