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Low-level arsenic exposure: Nutritional and dietary predictors in first-grade Uruguayan children

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ABSTRACT

Arsenic exposure in children is a public health concern but is understudied in relation to the predictors, and effects of low-level exposure. We examined the extent and dietary predictors of exposure to inorganic arsenic in 5–8 year old children from Montevideo, Uruguay. Children were recruited at school; 357 were enrolled, 328 collected morning urine samples, and 317 had two 24-h dietary recalls. Urinary arsenic metabolites, i.e. inorganic arsenic (iAs), methylarsonic acid (MMA), and dimethylarsinic acid (DMA), were measured using high-performance liquid chromatography with hydride generation and inductively coupled plasma mass spectrometry (HPLC-HG-ICP-MS), and the sum concentration (U-As) used for exposure assessment. Proportions of arsenic metabolites (%iAs, %MMA and %DMA) in urine were modelled in OLS regressions as functions of food groups, dietary patterns, nutrient intake, and nutritional status. Exposure to arsenic was low (median U-As: 9.9 μg/L) and household water (water As: median 0.45 μg/L) was not a major contributor to exposure. Children with higher consumption of rice had higher U-As but lower %iAs, %MMA, and higher %DMA. Children with higher meat consumption had lower %iAs and higher %DMA. Higher scores on "nutrient dense" dietary pattern were related to lower %iAs and %MMA, and higher %DMA. Higher intake of dietary folate was associated with lower %MMA and higher %DMA. Overweight children had lower %MMA and higher %DMA than normal-weight children. In summary, rice was an important predictor of exposure to inorganic arsenic and DMA. Higher meat and folate consumption, diet rich in green leafy and red-orange vegetables and eggs, and higher BMI contributed to higher arsenic methylation capacity.

1. Introduction

The health effects of exposure to inorganic arsenic, a highly toxic and carcinogenic element, are well documented in adults (ATSDR, 2007), whereas children's exposure is less well studied. Nevertheless, arsenic exposure in children is a public health concern because of its potential negative effects on growth and development (ATSDR 2007; Naujokas et al., 2013), with both preschool (Hamadani et al., 2011; Hsieh et al., 2014) and school (Wasserman et al. 2004; Rosado et al., 2007) children experiencing cognitive deficits.

Arsenic exposure is common, from sources such as contaminated drinking water and industrial activities (Tolins et al., 2014), and an estimated 200 million people worldwide are affected from drinking water alone. Based on its abundance, toxicity and potential for exposure, arsenic poses significant threat to human health (ATSDR, 2011). Certain food may also contribute to inorganic arsenic exposure. In Europe, processed grain products, rice, milk and dairy are the main contributors of inorganic arsenic in food (EFSA, 2014), including baby foods (Meharg et al., 2008; Ljung et al., 2011; Rintala et al., 2014). Furthermore, higher consumption of fish, fruits, grains, legumes, meat and rice was associated with higher concentrations of urinary arsenic in the NHANES study (Rey deCastro et al., 2014). Among US children (6–17 years of age), urinary arsenic increased significantly with each cup of rice consumed (Davis et al., 2012).

The role of nutrients in arsenic metabolism has also been

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studied, focusing on folate and other B-vitamins (Gamble et al., 2006, 2007; Hall et al., 2009; Argos et al., 2010; Peters et al., 2015), but many of these studies were carried out in adults with elevated arsenic exposure through drinking water and there is limited understanding of these relationships in children, especially with different exposure situations and dietary preferences.

The objectives of this study were to: 1) determine the extent of exposure to inorganic arsenic, 2) clarify whether drinking water is an important source of exposure, and 3) investigate the influence of nutritional status, nutrient intake, and diet on urinary arsenic concentrations in a group of 5–8 year old children in Montevideo, Uruguay.

2. Methods

2.1. Study setting

The study was conducted in Montevideo, the capital of Uruguay. Children in Montevideo are exposed to multiple toxic metals including lead, arsenic, cadmium, and manganese (Mañay et al., 2008; Kordas et al., 2010). Still, the problem of metal exposure in children (perhaps with the exception of lead) has received limited attention. Arsenic is emitted from municipal and hazardous waste incineration, metal smelting, glass manufacturing and mining, as well as agricultural chemical production and application (EPA, 2000). Although some of these industries are present in Montevideo, the specific sources of arsenic contamination are not well characterized. Water, an important source of exposure, is generally delivered to households via the state provider, and arsenic concentrations are closely monitored.

2.2. Participant recruitment

The study was carried out in private elementary schools in several Montevideo neighbourhoods, between November 2009 and August 2013, with recruitment methodology described elsewhere (Roy et al., 2015). In addition to media advertising, private elementary schools in the selected neighbourhoods were contacted to gauge interest in participation, and when agreed, informational meetings were scheduled for parents. All first grade children regularly attending the participating schools were eligible. The sole exclusion criterion was a blood lead level >45 μg/dL, based on parental report of any previous assessments carried out by paediatricians or specialist clinics; none of the children were excluded.

Of the 673 eligible children from 11 participating schools, 357 children (53%) and their mothers were enrolled upon providing written consent. Of those, 332 provided urine samples, and arsenic species could be determined in 328 samples.

The study was approved by the Ethics Committee for Research Involving Human Participants at the Catholic University of Uruguay and the Office of Research Protections at the Pennsylvania State University.

2.3. Assessments

Caregivers completed questionnaires about family socio-demographic characteristics, child's medical history and home environment, including questions on crowding at home and family possessions of household items like TV, video, telephone, refrigerator, etc.

Two 24-h dietary recalls were conducted by trained nutritionists with the mother or another caregiver familiar with the child's diet. The child was present at the time and contributed to the recall. One recall took place at the school and the second over the phone without prior appointment, at least 2 weeks later, either on a weekday or a weekend. Neutral probing questions were asked and photographs and models of foods, plates and serving/eating utensils were presented to aid in the estimation of serving sizes. All foods were assigned a unique code and entered, along with amounts consumed, into a database containing the nutrient composition of typical Uruguayan foods and preparations, and considering current mineral fortification laws in Uruguay.

Children's height was measured in triplicate to the nearest of 0.1 cm, using a portable stadiometer (Seca 214, Shorr Productions, Colombia, MD). They were weighed without shoes in light clothing, in triplicate to the nearest 0.1 kg using a digital scale (Seca 872, Shorr Productions, Colombia, MD). BMI for age z-scores (BAZ) were derived using the WHO AnthroPlus (http://www.who.int/growthref/tools/en/).

Approximately 3 ml of fasting blood was collected by a phlebotomy nurse at the school (8–11 am), using a 25-gauge safety butterfly blood collection set (Vacutainer, Becton Dickinson, Franklin Lakes, NJ) into a serum tube with clot activator and separator gel (Becton Dickinson, Franklin Lakes, NJ). Samples were left to stand for 45 min, centrifuged 10 min at 3000 rpm, and later stored at -20 °C at the Research Center, Catholic University of Uruguay.

Hemoglobin (Hb) was measured at the time of the blood draw using a portable hemoglobinometer (HemoCue Inc, Lake Forest, CA). Serum ferritin (SF) concentrations were determined in duplicate using one of two methods, according to manufacturer instructions: 1) an immunoradiometric assay (Coat-A-Count Ferritin IRMA; SIEMENS Diagnostic Products, USA) and 2) an enzyme immunoassay (Spectro Ferritin, RAMCO Laboratories, Texas, USA). The ELISA assay was used when the laboratory no longer had the capability to handle radioactive materials. Intra- and inter-assay coefficients (CV) were 4.2% and 9.5% respectively for the IRMA method and 1.7% and 7.6% for the ELISA method. The use of different assays was addressed by deriving a correction factor, with the IRMA method serving as gold standard, and both values being log-transformed prior to the derivation step, and back-transformed for the main analysis.

Children provided first void urine samples on the morning of the clinic in screw-top cups previously rinsed with 10% HNO_3 and deionized water. The samples were transported on ice to the Center for Research, Catholic University of Uruguay, and stored at -20 °C in 10 mL plastic tubes also rinsed as above.

Individual arsenic exposure was assessed based on the concentration of inorganic arsenic (iAs) and its methylated metabolites in urine (MMA and DMA). The sum of arsenic species (iAs, MMA and DMA), hereinafter referred to as U-As, reflects exposure to inorganic arsenic from all sources. The concentrations of arsenic species were measured using HPLC-HG-ICP-MS (HG, hydride generation, selects inorganic arsenic and its methylated metabolites into the ICP-MS, Inductively Coupled Plasma Mass Spectrometry). Briefly, the separation of the metabolites of inorganic arsenic (i.e. arsenite As(III) and arsenate As(V)), methylarsonic acid (MMA(V)) and dimethylarsinic acid (DMA(V)) was performed by Agilent 1100 series HPLC system (Agilent Technologies, Waldbronn, Germany), with an anion exchange column (Hamilton PRP X-100, 10 μm, 250 × 4.6 mm) and 10 μL injection volume. The LC separation was online with HG and ICP-MS (Agilent 7500ce, Agilent Technologies, Tokyo, Japan) and operated as described previously (Li et al., 2008; Gardner et al., 2011). Standard solutions of the four arsenic species were prepared from sodium arsenite (Purum p.a., $\geq 99.0\%$; Fluka Chemika, Switzerland), sodium hydrogenarsenate hepahydrate (98+%, A.C.S. reagent, Aldrich Chemical Company, WI, USA), sodium dimethylarsinate trihydate (Merck, Schuchardt, Germany), and disodium methylarsenate hexahydrate ($>97.5\%$, Supelco, Bellefonte, PA, USA). The working