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Nutritional status and diet as predictors of children's lead concentrations in blood and urine☆

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ABSTRACT

Lead exposure remains an important public health problem. Contaminated foods may act as a source of lead exposure, while certain nutrients may reduce lead absorption. We examined the cross-sectional associations of dietary patterns and the intake of several nutrients and foods with blood (Pb-B) and urinary (Pb-U) lead concentrations in children (5–8 y) from Montevideo, Uruguay. From two 24-hour recalls completed by caregivers, we derived the mean daily intake of select nutrients and food groups (dairy, milk, fruit, root vegetables, foods rich in heme and non-heme iron), as well as "nutrient dense" and "processed" food patterns. Pb-B (n = 315) was measured using atomic absorption spectrometry; Pb-U (n = 321) using ICP-MS. Pb-U was adjusted for specific gravity and log-transformed to approximate a normal distribution. Iron deficiency (ID) and dietary variables were tested as predictors of Pb-B and log-Pb-U in covariate-adjusted regressions. Median [5%, 95%] Pb-B and Pb-U were 3.8 [0.8–7.8] μg/dL and 1.9 [0.6–5.1] μg/L, respectively; ~25% of Pb-B above current U.S. CDC reference concentration of 5 μg/dL. ID was associated with 0.75 μg/dL higher Pb-B, compared to non-ID ($p < 0.05$). Consumption of root vegetables was not associated with Pb-B or log-Pb-U. Higher scores on the nutrient-dense pattern were related with higher Pb-Bs, possibly due to consumption of green leafy vegetables. Dietary intake of iron or iron-rich foods was not associated with biomarkers of lead. Conversely, children consuming more calcium, dairy, milk and yogurt had lower Pb-B and log-Pb-U. Our findings appear consistent with existing recommendations on including calcium-rich, but not iron- or vitamin-C-rich foods in the diets of lead-exposed children, especially where the consumption of these foods is low.

1. Introduction

Childhood exposure to lead, a ubiquitous neurotoxicant, is a significant concern globally (Attina and Trasande, 2013; Hanna-Attisha et al., 2016; Laborde et al., 2015; Mitra et al., 2009). Foods are an important source of lead exposure (CONTAM, 2010). At the same time, nutritional factors and diet as a whole may modify the gastrointestinal absorption, and possibly, the toxic effects of lead (Kwong et al., 2004; Wright, 1999). Yet, the relationship between diet and lead toxicity is not entirely clear. With few exceptions, this research has mostly focused on single nutrients.

Among the most thoroughly studied single nutrients, the deficiency of iron (ID) is associated with higher blood lead concentrations (Pb-Bs) in children, in large part due to increased absorption of lead via the Divalent Metal Transporter 1 (DMT1) (Kordas, 2010; Wright et al., 2003). On the other hand, higher dietary iron intake is associated with lower Pb-Bs (Hammad et al., 1996; Schell et al., 2004). Iron fortification appears to hold promise for lowering children's Pb-B (Bouhouch et al., 2016; Zimmermann et al., 2006), but important questions remain regarding this strategy (Kordas, 2017). For calcium, while higher dietary intake was associated with lower Pb-Bs in some observational studies

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(Lacasaña et al., 2000; Mahaffey et al., 1986; Schell et al., 2004), the efficacy of calcium supplementation in lowering children's Pb-Bs has been questioned (Ballew and Bowman, 2001; Kordas, 2017). Evidence for other nutrients, including vitamin C and zinc, is mixed (Rosado et al., 2006; Schell et al., 2004; Simon, 1998).

In contrast to individual nutrients, some of which have been found to impair the intestinal absorption of lead, little evidence is available on which foods, food groups or dietary patterns could effectively prevent lead exposure or lower children's Pb-Bs. This is despite recommendations from the U.S. CDC on the nutritional management of children with elevated Pb-Bs, which includes the daily provision of one serving of red meat, as well as of calcium- and vitamin C-rich foods (CDC, 2002b). In one study, the consumption of hamburgers, doughnuts, and peanut butter and jelly sandwiches, was associated with higher Pb-B in 13–24 months-old (Freeman et al., 1997). In the same study, 13–24 and 25–36 months-old who consumed yogurt had lower Pb-Bs (Freeman et al., 1997). In a randomized controlled trial, ground fish consumption had no benefit in reducing Pb-Bs in young children compared to placebo (Keating et al., 2011). A further complication in the lead-diet relationship is that foods, including candy (CDC, 2002a; Tamayo y Ortiz et al., 2016), and vegetables and cereals (Callan et al., 2014; Chen et al., 2011; Jin et al., 2014), may be an important source of lead exposure.

Given the gaps in understanding of how nutrients and foods impact the exposure to, excretion, and accumulation of lead in children's bodies, particularly at low or very-low level of lead exposure, our objective was to assess the associations between the intake of several nutrients and foods, as well as dietary patterns, with Pb-B and Pb-U in Uruguayan children. We have shown previously that children in this setting are exposed to metals, including lead (Kordas et al., 2010; Queirolo et al., 2010).

2. Methods

2.1. Study setting and participant recruitment

This cross-sectional study was conducted in Montevideo, the capital of Uruguay, from July 2009 to August 2013. Children who participated in the study attended 11 private elementary schools in several municipal areas where lead exposure was suspected based on clinical experience of one of the co-authors (EIQ) or previously reported in the literature (Queirolo et al., 2010). Leaded gasoline was a major source of lead exposure until it was phased out in 2004; however, lead contamination of dust and soil likely persists and contributes to exposure among children. Additionally, informal battery recycling and occupational exposures of the parents have become more prominent sources.

Participant recruitment has been described in detail previously (Roy et al., 2015). All 673 first-grade children attending the participating schools were eligible, 357 were enrolled. The sole exclusion criterion for the study was a previous diagnosis of Pb-B > 45 μg/dL, a level which would have necessitated medical intervention. None of the children were excluded based on this criterion. The study was approved by ethics committees at the Pennsylvania State University, the Catholic University of Uruguay, and the Faculty of Chemistry at the University of the Republic of Uruguay.

2.2. Socio-demographic information

Parents/caregivers who agreed to participate completed a questionnaire about socio-demographic characteristics of the family, the child's medical history and the home environment. They reported their age, education, occupation, smoking history, and family structure. To assess socio-economic status (SES), caregivers provided information on home ownership, number of rooms, number of persons living in the house, and family possession of 12 common household items (ex., TV, washer, cellular phone, and car). An SES index was computed from a factor analysis of household assets. A single factor consisting of 5 items was retained. The resultant score (0–5) was split at the median for use in statistical analysis. Household occupant density was calculated based on the number of people living in the house divided by the number of rooms. Crowding was defined as occupant density > 2 persons/room.

2.3. Sample collection and lead analysis

Lead concentrations for this study were analyzed in blood and urine. Urinary Pb concentrations (Pb-Us) were included as an indicator of lead excretion. As opposed to Pb-B, which has a half-life of months, Pb-U has a half-life of days. Venous blood was collected in the morning (between 8 and 11 am), after an overnight fast by a phlebotomy nurse. Lithium heparin coated trace-metal free tubes (Becton Dickinson) were used for data collection. Samples were transported on ice to the Toxicology Laboratory in the Faculty of Chemistry at the University of the Republic of Uruguay. Blood lead concentrations were measured by Atomic Absorption Spectrometry (AAS, VARIAN SpectrAA-55B) using flame or graphite furnace ionization techniques, depending on the volume of whole blood available. The detection limit was 1.8 μg/dL for flame AAS and 0.7 μg/dL for graphite furnace AAS, respectively. There were no values below the limit of detection. The analytical method was taken into account in statistical analysis. Analytical conditions were validated with standard quality assurance/quality control procedures (Parsons and Chisolm, 1997). The laboratory participates in CDC's Lead and Multi-Element Proficiency Program (LAMP) and the Interlaboratory Program of Quality Control for Lead in Blood, Spain (PICC Pb-S).

Children collected first void urine samples and brought them to school on the same morning as the blood draw. Samples were collected in polyethylene cups that had previously been rinsed repeatedly with 10% HNO_3 and deionized water to avoid contamination. Parents received instructions for urine collection at home, including capturing urine mid-stream. The urine samples were transported on ice to the Toxicology Laboratory of the University of the Republic, Montevideo. Specific gravity of each sample was measured using a portable specific gravity refractometer (PAL 10S, Atago Inc., USA) on the day of the collection. Lead concentrations in urine were analyzed in two batches at the Karolinska Institutet, Sweden. Urine was diluted 1:10 with 1% nitric acid (65% w/w, Scharlau, Scharlab S.L., Sentmenat, Spain) and the measurement was performed on an Agilent 7700 × ICP-MS (Agilent Technologies, Tokyo, Japan), equipped with collision/reaction cell technology. The limit of detection was 0.005 ng/g in batch 1 and 0.0009 ng/g in batch 2. No batch differences in (Pb-U) were detected. There was one value below the limit of detection and the actual reported value was used in statistical analysis.

We analyzed two reference urine samples (Seronorm Urine 1011644 L1 and Seronorm Urine 1011645 L2) with recommended concentrations of 0.66 and 90.7 μg/L. The obtained average concentrations were 0.51 ± 0.01 and 80.43 ± 0.71 μg/L, respectively (n = 4). To compensate for the variation in dilution of the urine samples, Pb-Us were adjusted the average specific gravity (SG, Mean [range]: 1.024 [1.003–1.045]). Adjustment by SG is less affected by body size, muscle mass and diet (particularly meat intake), than creatinine adjustment (Nermell et al., 2008).

2.4. Nutritional status assessment

Fasting venous blood was also drawn into a serum tube with clot activator and separator gel (Vacutainer SST Tube, Becton Dickinson). Immediately following the draw, a drop of blood was removed from this tube to measure the child's hemoglobin concentration using a portable hemoglobinometer (HemoCue, Lake Forest, CA). Quality control checks were performed daily using standard HemoCue controls (low, medium, high) provided by the manufacturer. Approximately 45 min after the blood draw, serum was separated by centrifuging for 10 min at 3000 rpm.

Serum samples were shipped on dry ice to the Department of