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Predictors of urinary bisphenol A and phthalate metabolite concentrations in Mexican children

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HIGHLIGHTS

- We studied urinary BPA and phthalate metabolite concentrations in Mexican children.
- Urinary concentrations at third trimester and 8–13 years were not correlated.
- Personal care product use was associated with exposure to several phthalates.
- Reduced or delayed use of certain personal care products in children may be warranted.

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ABSTRACT

Exposure to endocrine disrupting chemicals such as bisphenol A (BPA) and phthalates is prevalent among children and adolescents, but little is known regarding important sources of exposure at these sensitive life stages. In this study, we measured urinary concentrations of BPA and nine phthalate metabolites in 108 Mexican children aged 8–13 years. Associations of age, time of day, and questionnaire items on external environment, water use, and food container use with specific gravity-corrected urinary concentrations were assessed, as were questionnaire items concerning the use of 17 personal care products in the past 48-h. As a secondary aim, third trimester urinary concentrations were measured in 99 mothers of these children, and the relationship between specific gravity-corrected urinary concentrations at these two time points was explored. After adjusting for potential confounding by other personal care product use in the past 48-h, there were statistically significant ($p < 0.05$) positive associations in boys for cologne/perfume use and monoethyl phthalate (MEP), mono(3-carboxypropyl) phthalate (MCPP), mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), and mono(2-ethyl-5-oxohexyl) phthalate (MEOHP), and in girls for colored cosmetics use and mono-*n*-butyl phthalate (MBP), mono(2-ethylhexyl) phthalate (MEHP), MEHHP, MEOHP, and mono(2-ethyl-5-carboxypentyl) phthalate (MECPP), conditioner use and MEP, deodorant use and MEP, and other hair products use and MBP. There was a statistically significant positive trend for the number of personal care products used in the past 48-h and log-MEP in girls. However, there were no statistically significant associations between the analytes and the other questionnaire items and there were no strong correlations between the analytes measured during the third trimester

Abbreviations: BPA, bisphenol A; ELEMENT, Early Life Exposure in Mexico to ENvironmental Toxicants; CDC, Centers for Disease Control and Prevention; BBZP, butylbenzyl phthalate; DBP, di-*n*-butyl phthalate; DEHP, di(2-ethylhexyl) phthalate; DEP, diethyl phthalate; DIBP, di-isobutyl-phthalate; DOP, di-*n*-octyl phthalate; FDA, Food and Drug Administration; FSRA, forward stepwise regression analysis; GM, geometric mean; ID–LC–MS/MS, isotope dilution–liquid chromatography–tandem mass spectrometry; LOQ, limit of quantitation; MBP, mono-*n*-butyl phthalate; MBZP, monobenzyl phthalate; MCPP, mono(3-carboxypropyl) phthalate; MECPP, mono(2-ethyl-5-carboxypentyl) phthalate; MEHP, mono(2-ethylhexyl) phthalate; MEHHP, mono(2-ethyl-5-hydroxyhexyl) phthalate; MEOHP, mono(2-ethyl-5-oxohexyl) phthalate; MEP, monoethyl phthalate; MIBP, mono-isobutyl phthalate; NHANES, National Health and Nutrition Examination Survey; SG, specific gravity.

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and at 8–13 years of age. We demonstrated that personal care product use is associated with exposure to multiple phthalates in children. Due to rapid development, children may be susceptible to impacts from exposure to endocrine disrupting chemicals; thus, reduced or delayed use of certain personal care products among children may be warranted.

1. Introduction

Bisphenol A (BPA) and phthalates are synthetic chemicals used in the production of a wide variety of consumer and medical products, and exposure to these chemicals has been documented worldwide (Hauser and Calafat, 2005; Vandenberg et al., 2007). In particular, urinary BPA and multiple phthalate metabolites have been measured in children across a variety of ages and in pregnant women where BPA and phthalates can cross the maternal-fetal placental barrier (Vandenberg et al., 2007; Buckley et al., 2012). Because exposure to these endocrine-disrupting chemicals is ubiquitous in children at various stages of development and trends for rates of endocrine-related diseases and disorders among children have increased, there is growing concern among scientists, physicians, governments, and the public that these chemicals may influence child development (Meeker, 2012).

The animal evidence suggests that BPA and phthalate exposures may influence development through the disruption of hormonally-mediated pathways (vom Saal et al., 2007; Lyche et al., 2009). These findings are supported by human epidemiology studies reporting associations between biomarkers of exposures to BPA and phthalates and endocrine-related outcomes, including shorter gestation (Latini et al., 2003; Meeker et al., 2009; Whyatt et al., 2009; Cantonwine et al., 2010), low birth weight (Zhang et al., 2009; Chou et al., 2011), and changes in breast and pubic hair development (Wolff et al., 2010; Frederiksen et al., 2012), brain development (Braun et al., 2009; Cho et al., 2010; Engel et al., 2009, 2010; Kim et al., 2009), body mass index (Wolff et al., 2007; Hatch et al., 2008; Teitelbaum et al., 2012; Trasande et al., 2012), and reproductive and thyroid hormone levels (Main et al., 2006; Boas et al., 2010; Chevrier et al., 2013) during various stages in childhood and adolescence. However, epidemiology studies conducted in children beyond infancy have largely been cross-sectional in design, relying on data concerning current exposures. If current exposures to BPA or phthalates in children are associated with exposures occurring in the prenatal environment, cross-sectional epidemiology studies that report associations with health outcomes may reflect effects related to exposures occurring during childhood/adolescence or in utero or both (i.e. exposures at one time point could be a surrogate for exposures at the other time point). This is a topic yet to be reported in the literature, but is important for understanding the results of such studies and in the design of future studies.

Numerous studies concerning predictors of exposure to BPA and phthalates in adult men and women, including pregnant women have been conducted (Duty et al., 2005; Kwapniewski et al., 2008; Mahalingaiah et al., 2008; Berman et al., 2009; Carwile et al., 2009; He et al., 2009; Hines et al., 2009; Just et al., 2010; Zimmerman-Downs et al., 2010; Braun et al., 2011; Romero-Franco et al., 2011; Buckley et al., 2012; Meeker et al., 2012; Parlett et al., 2012; Casas et al., 2013; Li et al., 2013). However, in comparison, exposure predictor studies in children are much more limited in number and have considered a far less variety of BPA and phthalate sources. These child exposure predictor studies have been conducted in infants (Calafat et al., 2004, 2009; Green et al., 2005), toddlers (Sathyanarayana et al., 2008), preschoolers (Casas et al., 2013), and school-aged children (Colacino et al., 2011; Nahar et al., 2012; Li et al., 2013). Additional, more comprehensive studies concerning predictors of BPA and phthalate exposure in children at all stages are needed to better inform targeted behavior modifications and policy for reducing exposures to these endocrine-disrupting chemicals.

In this study, the primary aim was to identify the determinants of urinary BPA and phthalate metabolite concentrations in 108 children from Mexico City, Mexico aged 8–13 years. A secondary aim of this study was to determine whether childhood and maternal-third trimester urinary concentrations are correlated in 99 mother–child pairs. This study considered a greater variety of BPA and phthalate sources than previous child exposure predictor studies and, to our knowledge, this is the first study to examine the relationship between BPA and phthalate exposures at these two time points.

2. Materials and methods

2.1. Study participants

This study used data from the Early Life Exposure in Mexico to ENvironmental Toxicants (ELEMENT) project that was started in 1994 and consists of three sequentially-enrolled birth cohorts from Mexico City maternity hospitals (Gonzalez-Cossio et al., 1997; Hu et al., 2006; Surkan et al., 2008). The mission of ELEMENT is to examine the influence of environmental toxicant exposures on the development and future health of the fetus and infant. Across these three cohorts, 2098 mothers were recruited during the first trimester of pregnancy or at delivery and followed at 1, 7, and 12 months postpartum and at ages 2–5 years for their offspring (n = 1710) depending on the specific study. Socio-demographic, dietetic, anthropometric, and biomarker (urine, blood and bone) measures were collected at each follow-up visit. Spot urine and blood samples were collected and archived from mothers and children at different stages, including pregnancy, as well. In 2010, a subset of these children was contacted again at ages 8–13 years (n = 250) through their primary caregiver based on availability of archived biomarker measures, and data from the first available 108 children were included in this current study. Urine samples and questionnaire data from these children were used in this analysis, along with urine samples from their mothers collected during third trimester when available (n = 99). The questionnaire was administered by trained study nurses and filled out by the children with assistance from their primary caregiver (i.e. proxy-assisted). The research protocols were approved by the Ethics and Research Committees of all participating institutions (National Institute of Public Health, National Institute of Perinatology, and University of Michigan).

2.2. Urinary BPA and phthalate metabolites

Total (free + glucuronidated) BPA and nine phthalate metabolites were measured in maternal and child urine samples by isotope dilution–liquid chromatography–tandem mass spectrometry (ID–LC–MS/MS) at NSF International (Ann Arbor, MI, USA). The nine phthalate metabolites included: monoethyl phthalate (MEP), metabolite of diethyl phthalate (DEP); mono-n-butyl phthalate (MBP), metabolite of di-n-butyl phthalate (DBP); mono-isobutyl phthalate (MIBP), metabolite of di-isobutyl-phthalate (DIBP); mono(3-carboxypropyl) phthalate (MCPP), metabolite of DBP and