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Co-exposure to non-persistent organic chemicals among American pre-school aged children: A pilot study

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ABSTRACT

Background: General population human biomonitoring programs such as the National Health and Nutrition Examination Survey (NHANES) in the United States suggest that chemical exposures are common. Exposures during childhood may affect health later in life, but biomonitoring data in NHANES among pre-school aged children are limited.

Methods: A convenience group of 122 3–5 year old American boys and girls were recruited in 2013 for a pilot study to assess the feasibility of collecting urine from young children and analyzing it for select chemical exposure biomarkers for future NHANES. Children were primarily Hispanic (64.8%); the remainder was divided between non-Hispanic black, and non-Hispanic white and "other." We measured 52 urinary biomarkers: 13 phthalates and one non-phthalate plasticizer, five phenols and four parabens, 10 polycyclic aromatic hydrocarbons (PAHs), and 19 pesticides. For each biomarker, we calculated descriptive statistics. We also calculated the number of biomarkers detected within each child, and performed principal components analysis (PCA).

Results: NHANES staff obtained permission to attempt collection of 60 mL urine from 3 to 5 year olds who participated in the 2013 NHANES health examination; 83% of children successfully provided the target volume. We detected 24 individual biomarkers of pesticides, phenols and parabens, phthalates/non-phthalate plasticizers, and PAHs in 95–100% of children. The median number of biomarkers detected was 37: nine pesticides, five phenols and parabens, 13 phthalates and non-phthalate plasticizers, and 10 PAHs. Biomarkers concentrations appear to be similar to national estimates among 6–11 year old children from previous NHANES. PCA suggested high within-class correlations among biomarkers.

Conclusions: These young children successfully adhered to the collection protocol and produced enough urine for the quantification of environmental biomarkers currently being measured in NHANES participants 6 years of age and older. Using the same analytical methods employed for the analysis of samples collected from older NHANES participants, in this sample of pre-school aged children we detected multiple chemicals including plasticizers, combustion products, personal-care product chemicals, and pesticides. Starting with NHANES 2015–2016, the NHANES biomonitoring program will include urinary biomarkers for 3–5 year old children to provide exposure data to select chemicals at the national level among this age group.

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Abbreviations: BPA, bisphenol A; CDC, Centers for Disease Control and Prevention; DCBA, 3-diethyl-carbamoyl benzoic acid; DINCH, di(isononyl) cyclohexane-1,2-dicarboxylate; DEET, *N,N*-diethyl-*m*-toluamide; EPA, Environmental Protection Agency; ERB, Ethics Review Board; GM, geometric mean; LOD, limit of detection; MEC, Mobile Examination Center; NCEH, National Center for Environmental Health; NCHS, National Center for Health Statistics; NHANES, National Health and Nutrition Examination Survey; PAH, polycyclic aromatic hydrocarbon; PCA, principal components analysis; RDC, Research Data Center.

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1. Introduction

Interest exists in understanding the extent of chemical exposures during critical periods of human development, including childhood (US EPA, 2013). Children, because of their specific behaviors and physiology, experience different exposure situations than do adults (EPA, 2008). Therefore, identifying these differences as well as the exposure determinants is important for evaluating potential health hazards of these exposures.

Biomonitoring studies suggest that exposures to contemporary-use chemicals are common in modern societies (National Research Council, 2012). General population human biomonitoring programs are particularly useful for investigating such exposures (CDC 2015; Haines and Murray, 2012; Schulz et al., 2007). Interestingly, many contemporary chemicals are not persistent in people, and exposure biomarkers in urine are increasingly used to evaluate exposures to these compounds and to inform chemical risk assessments (Sobus et al., 2015). Compared to blood and other matrices, collecting urine is generally considered a non-invasive and relatively easy procedure, at least for adults. However, collecting urine from young children who cannot easily void in regular urine collection containers can pose logistic challenges (Lee and Arbuckle, 2009).

In the United States, the National Health and Nutrition Examination Survey (NHANES) collects data and biospecimens from persons aged one year and older to evaluate participants' general health and nutritional status (CDC, 2014). Blood and urine, collected during the participant's medical examination at the mobile examination center (MEC), are also used to assess exposure to environmental chemicals (Calafat, 2012). NHANES has collected urine specimens in its MEC since 1960, but, although urine has been successfully collected from young children for other studies by using various strategies including urine bags, diapers, and commode insert pans (Lee and Arbuckle, 2009), up to 2013–2014, only participants 6 years of age and older provide urine in the MEC. Therefore, information on Americans' exposure to environmental chemicals is more limited for children than for adults even though exposures during early childhood may be relevant to understand potential adverse effects on health later in life (US EPA, 2013).

To facilitate future efforts in the United States for closing this information gap, the National Center for Health Statistics (NCHS) in collaboration with the National Center for Environmental Health (NCEH) designed a feasibility study to demonstrate that urine specimens from 3 to 5 year old children can be collected and analyzed for select chemical exposure biomarkers as part of NHANES. In this paper, to evaluate the feasibility of the urine collection, we describe the results of the analysis of the urine for metabolites of pesticides, plasticizers, combustion products, and personal-care product chemicals. To identify correlation patterns among these biomarkers, we also performed principal components analysis (PCA).

2. Materials and methods

2.1. Study population

A convenience sample of 3–5 year old American boys and girls who participated in the 2013 NHANES health examination were recruited for this feasibility study, conducted during four months in 2013 (Table 1). Although NHANES is a nationally-representative survey (CDC, 2014), this convenience sample of children was not. The 3–5 year old children, whose parent/guardian allowed them to provide a urine specimen, in addition to the examination component of NHANES (CDC, 2014), voided on a plastic commode insert pan placed on the toilet bowl at the MEC restroom by MEC staff, in the presence of their parent/guardian. As done for the urine collection materials used for older NHANES participants, the commode insert had been acid washed and individually packaged to eliminate metal contamination and ensure that the collected urine could also be analyzed for select metals (http://www.cdc.gov/nchs/features/nhanes_mec_collects_health_data.htm). Participating children had up to two attempts during their scheduled MEC exam to provide the urine; target volume was 60 mL. The urine collection protocol for 3–5 year old children included specific steps for the placement and use of the commode insert pan. MEC staff provided detailed instructions to the child's parent/guardian for the proper collection and handling of the commode insert to minimize external contamination. MEC staff also collected the urine container from the parent/guardian immediately after the child urinated and delivered to the MEC lab where the specimen was processed following NHANES approved procedures for the collection of urine from participants ≥6 years old (e.g., https://www.cdc.gov/nchs/data/nhanes/nhanes_15_16/2016_MEC_Laboratory_Procedures_Manual.pdf). The study protocol as well as the NHANES protocol were approved by the NCHS Research Ethics Review Board (ERB).

We accessed the demographic variables from NHANES and restricted biomarkers data from the present pilot study through the NCHS Research Data Center (RDC). Analysis of restricted data through the NCHS RDC was approved by the NCHS ERB.

2.2. Urinary biomarker concentrations

The urine samples were shipped on dry ice to CDC's NCEH laboratory and stored at or below −20 °C until analyzed. We used isotope-dilution coupled to mass spectrometry for the quantification of 52 urinary biomarkers (Table 2), already measured among NHANES participants ≥6 years of age, using previously described analytical chemistry methods (Davis et al., 2013; Kuklenyik et al., 2013; Li et al., 2014; Odetokun et al., 2010; Silva et al., 2013; Ye et al., 2005, 2006). Based on the volume of urine collected, the number of samples varied slightly by method: phenols and parabens (N = 118); phthalates and plasticizers (N = 118); polycyclic aromatic hydrocarbons (PAHs, N = 119); and pesticides (N = 122). Calibration standards, quality control, and reagent blank samples were included in each analytical batch along with the study samples. The 52 urinary biomarkers and limits of detection (LOD), which, depending on the analyte, ranged from 0.01 μg/L to 1.0 μg/L are shown in Table 2.

2.3. Statistical analysis

We used SAS (version 9.3; SAS Institute Inc.; Cary, North Carolina) to perform statistical analyses. Of note, because of the convenience sampling nature of the population included in this pilot study, all analyses were unweighted (as opposed to weighted methods appropriate for the complex survey data typically used for NHANES biomarkers results). For concentrations below the LOD, we imputed a value equal to the LOD divided by the square root of 2 (Hornung and Reed, 1990).

On the basis of information reported by the child's parent or guardian, we categorized race/ethnicity as non-Hispanic black, non-Hispanic white and other, and All Hispanic. For each sex and race/ethnic group, we calculated the geometric mean (GM), if the frequency of detection was greater than 60%, and distribution percentiles for both volume-based (μg/L) and creatinine-corrected concentrations (μg/g creatinine). For the calculations of creatinine-corrected concentrations, we did not exclude any creatinine values, even those <30 mg/dL, an arbitrary cutoff concentration suggestive of excessive urine dilution in adults (Barr et al., 2005), because creatinine excretion depends on muscle mass which is much lower in young children compared to adults (Koch et al., 2011).