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Urinary biomarkers of polycyclic aromatic hydrocarbons in pre- and peri-pubertal girls in Northern California: Predictors of exposure and temporal variability

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ABSTRACT

Background: Polycyclic aromatic hydrocarbons (PAHs), a class of chemicals produced as combustion by-products, have been associated with endocrine disruption. To understand exposure in children, who have been less studied than adults, we examined PAH metabolite concentrations by demographic characteristics, potential sources of exposure, and variability over time, in a cohort study of pre- and peri-pubertal girls in Northern California.

Methods: Urinary concentrations of ten PAH metabolites and cotinine were quantified in 431 girls age 6–8 years at baseline. Characteristics obtained from parental interview, physical exam, and linked traffic data were examined as predictors of PAH metabolite concentrations using multivariable linear regression. A subset of girls (n = 100) had repeat measures of PAH metabolites in the second and fourth years of the study. We calculated the intraclass correlation coefficient (ICC), Spearman correlation coefficients, and how well the quartile ranking by a single measurement represented the four-year average PAH biomarker concentration.

Results: Eight PAH metabolites were detected in ≥ 95% of the girls. The most consistent predictors of PAH biomarker concentrations were cotinine concentration, grilled food consumption, and region of residence, with some variation by demographics and season. After adjustment, select PAH metabolite concentrations were higher for Hispanic and Asian girls, and lower among black girls; 2-naphthol concentrations were higher in girls from lower income households. Other than 1-naphthol, there was modest reproducibility over time (ICCs between 0.18 and 0.49) and the concentration from a single spot sample was able to reliably rank exposure into quartiles consistent with the multi-year average.

Conclusions: These results confirm diet and environmental tobacco smoke exposure as the main sources of PAHs. Controlling for these sources, differences in concentrations still existed by race for specific PAH metabolites and by income for 2-naphthol. The modest temporal variability implies adequate exposure assignment using concentrations from a single sample to define a multi-year exposure timeframe for epidemiologic exposure-response studies.

1. Introduction

Polycyclic aromatic hydrocarbons (PAHs) are a class of ubiquitous chemicals generally produced as combustion by-products; of these chemicals, only naphthalene is produced commercially in the United States (ATSDR, 1995, 2005). People are usually exposed to a complex mixture of PAHs rather than individual chemicals (CDC, 2009). Non-occupational exposure sources include vehicle exhaust, residential

Abbreviations: AADT, average annual daily traffic; BCERP, Breast Cancer and the Environment Research Program; BMI, body mass index; CDC, Centers for Disease Control and Prevention; CEHTP, California Environmental Health Tracking Program; CI, confidence interval; ETS, environmental tobacco smoke; GM, geometric means; ICC, intraclass correlation coefficients; IQR, interquartile range; IRB, institutional review board; KPNC, Kaiser Permanente Northern California; LOD, limit of detection; NHANES, National Health and Nutrition Examination Survey; OH-PAHs, monohydroxy- polycyclic aromatic hydrocarbons; PAHs, polycyclic aromatic hydrocarbons; SES, socioeconomic status

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heating sources, smoke from wood, coal, or gas, cigarette smoke, and grilled foods (ATSDR, 1995). PAHs are absorbed by the body (i.e., skin, respiratory tract, and gastrointestinal tract), and can be metabolized into monohydroxy-PAHs (OH-PAHs), and eliminated in the urine or feces within a few days (Chetiyanukornkul et al., 2006; Ramesh et al., 2004). Urinary OH-PAHs have therefore been used as biomarkers for assessing recent exposure to PAHs because biomonitoring accounts for all possible routes (e.g., inhalation, diet) (Aquilina et al., 2010; Li et al., 2010a; Nethery et al., 2012; Scherer et al., 2000). Metabolism of PAHs differs among exposure sources and varies by person (Jacob and Seidel, 2002; Li et al., 2012b, 2016; Lin et al., 2016).

Previous studies have detected OH-PAHs in children not exposed to residential biomass fuels, not near occupational sites, nor smoking (CDC, 2017; Health Canada, 2015; Hemat et al., 2012; Thai et al., 2016; Wilhelm et al., 2008). However, only a handful of studies have quantified an array of PAH urinary metabolites in children to assess sources of exposure (Alghamdi et al., 2015; Jung et al., 2014; Kang et al., 2002; Yoon et al., 2012). Many studies solely measured 1-hydroxypyrene (Cavanagh et al., 2007; Fiala et al., 2001; Freire et al., 2009; Martinez-Salinas et al., 2010; Morgan et al., 2015; Mucha et al., 2006; Ochoa-Martinez et al., 2016; van Wijnen et al., 1996), which is not representative of the mixture of PAHs in general environmental exposures.

Limited published data exist on the temporal variability of OH-PAH urinary concentrations. A recent study found that a person's PAH metabolite concentrations in urine spot samples, first morning voids, and 24-h voids have a high degree of correlation (Li et al., 2010b). Time intervals of a few days (Fiala et al., 2001) or seasons (Peters et al., 2017; van Wijnen et al., 1996) have previously been studied. Data on the temporal variability of OH-PAHs across years, especially among children, are sparse (Jung et al., 2014) but important because health outcomes are associated with exposures over time intervals longer than the few days of metabolite elimination. We used a Breast Cancer and the Environment Research Program (BCERP) cohort to evaluate demographic differences, potential sources, and temporal variability of OH-PAH urinary concentrations among pre- and peri-pubertal girls in Northern California.

2. Methods

2.1. Study population

The BCERP cohort is comprised of over 1200 girls who were enrolled in 2005–2006 into a longitudinal study of puberty at three U.S. sites: Mount Sinai School of Medicine, Cincinnati Children's Hospital, and Kaiser Permanente Northern California (KPNC) (Biro et al., 2010; Hiatt et al., 2009). Eligibility criteria included female sex, 6–8 years of age, and no underlying endocrine-associated medical conditions. This analysis included only girls recruited from the KPNC Health Plan in the San Francisco Bay Area, as other sites did not measure PAHs. The site obtained informed consent from a parent or guardian and child assent, approved by KPNC's institutional review board (IRB) with the Centers for Disease Control and Prevention (CDC) reliance upon the KPNC IRB.

2.2. Data collection

Demographics, anthropometry, and urine were obtained at baseline and annually thereafter. The girl's parent or guardian completed an annual questionnaire, including girl's race/ethnicity, diet, other demographic variables, and residential history. The baseline variables were used for this analysis. The girl's race/ethnicity was classified in the following priority order: black (regardless of ethnicity), Hispanic (any race other than black), Asian or Pacific Islander (non-Hispanic), and white (non-Hispanic) (hereafter referred to as black, Hispanic, Asian, and white). The parent or guardian was asked for the total, pre-tax income from all income sources by all family members in the child's household in the past year, using a series of questions to determine the income group: less than $12,000, $12,000- < $25,000, $25,000- < $50,000, $50,000- < $75,000, $75,000- < $100,000, $100,000 or more. For this analysis, household income was categorized as < $50,000, $50,000- < $100,000, and ≥$100,000. Recent grilled food consumption was defined by a "Yes" response to the question "During the past two days, has (child's name) eaten any foods that were cooked on a grill or barbeque? Please do not include foods that may have been cooked on an electric grill such as a George Foreman grill." Traffic metrics have been described previously (McGuinn et al., 2016). Briefly, baseline residential addresses (2005–2006) were geocoded using the California Environmental Health Tracking Program's (CEHTP) geocoding tool, and then the address was linked to traffic exposure data (California Department of Transportation Highway Performance Monitoring System data from 2004) using the CEHPT's Traffic Volume Linkage Tool. Distance-weighted traffic density (highest average annual daily traffic (AADT) with Gaussian weight based on distance from residence) was calculated within a 150 m buffer zone around each geocoded address. Using residential city, the girl's region of residence was classified as the San Francisco Peninsula (i.e., the City and County of San Francisco, San Mateo County), North Bay (i.e., Marin County, Sonoma County), or East Bay (i.e., Alameda County, Contra Costa County, San Joaquin County, Stanislaus County, Solano County).

Height and weight were assessed at annual clinic visits by study staff who had been uniformly trained and certified to use calibrated scales and stadiometers. Body mass index (BMI) was calculated as weight/height-squared and then classified by age- and sex-specific BMI percentiles based on the 2000 growth charts from the CDC (CDC, 2002). Categories of baseline BMI were defined as normal (below the CDC age and sex-specific 85th percentile) and overweight (above the 85th percentile). Spot urine samples were collected annually. The season of sample collection, based on the date of the baseline urine sample, was classified as: spring (March–May), summer (June-August), fall (September–November), or winter (December–February).

2.3. Quantification of biomarkers

Girls with sufficient baseline urine sample volume for PAH biomarker measurements were included in this study (N = 431). In addition, samples from a subset of 100 girls with stored urine available at both the second and fourth years of the study (year 2 and year 4, respectively henceforth) were selected to assess temporal variability of PAH biomarkers concentrations. Urinary concentrations of ten OH-PAH metabolites (i.e., 1-naphthol, 2-naphthol, 2-hydroxyfluorene, 3-hydroxyfluorene, 9-hydroxyfluorene, 1-hydroxyphenanthrene, 2-hydroxyphenanthrene, 3-hydroxyphenanthrene, 4-hydroxyphenanthrene, 1-hydroxypyrene) as well as urinary cotinine, a nicotine metabolite, were measured at the National Center for Environmental Health laboratories at the CDC using previously published methods (Bernert et al., 2005; Li et al., 2006, 2014). Briefly, the PAH metabolite conjugates in urine were hydrolyzed enzymatically and extracted using pentene through liquid-liquid extraction; the extracts were evaporated and the PAH metabolites derivatized. The baseline samples were quantified using gas chromatography isotope dilution high-resolution mass spectrometry (Li et al., 2006); annual samples thereafter were quantified using gas chromatography isotope dilution tandem mass spectrometry (Li et al., 2014). Quality control and quality assurance checks have been previously described (Li et al., 2006, 2014). Urinary cotinine was quantified by high performance liquid chromatography/atmospheric pressure ionization tandem mass spectrometry; each analytical run included one water blank and two quality control samples (Bernert et al., 2005; McGuffey et al., 2014). Two girls were missing 1-hydroxypyrene measurements; 12 girls were missing cotinine measurements. Creatinine was also measured at CDC using the Roche Creatinine Plus Assay (Roche Diagnostics, Indianapolis, IN) on a Roche Hitachi 912 Chemistry Analyzer (Hitachi Inc., Pleasanton, CA).