Assessing Children’s Exposure to Organophosphate Flame Retardants using Passive Air Samples from the Home Environment

Stephanie C. Hammel, Kate Hoffman, Amelia M. Lorenzo, Meredith Frenchmeyer, Bridget Flaherty, Allison L. Phillips, Albert Chen, Thomas F. Webster, Heather M. Stapleton

a Nicholas School of the Environment, Duke University, Durham, NC, USA
b Department of Environmental Health, Boston University School of Public Health, Boston, MA, USA

Introduction

Organophosphate flame retardants (PFRs) are commonly applied to polyurethane foam to meet flammability standards. This use has led to ubiquitous PFR detection in air and dust from an array of indoor environments.1–3 As such, human exposure is widespread, and PFR metabolites are frequently detected in human urine.4–8 PFR exposure has been associated with negative health outcomes, including lower hormone levels in humans, and carcinogenicity, endocrine disruption, and neurotoxicity in animal studies.9–12 This is particularly concerning for children who often have higher PFR exposures and are at greater risk for adverse health effects which could persist into adulthood. While PFRs have been measured in indoor air and inhalation is suspected to contribute heavily to personal exposure, no studies to date have measured paired indoor air samples and urinary biomarkers. The current study examined the association between PFRs measured in passive air samples from the home and corresponding PFR metabolites in children’s urine.

Materials & Methods

Study Design. Families with toddlers (24-60 months) were recruited through an existing cohort in North Carolina to participate in a study characterizing children’s exposure to semi-volatile organic compounds in homes. In Sep 2014 to Apr 2016, 200 home visits were conducted during which sorbent-impregnated polyurethane (SIP) foam passive air samplers were placed in homes for 3 wks. Each child provided 3 urine samples collected over a 48h period. Urine samples were pooled, and all samples were stored at -20°C until analysis.

Air Sampler Extraction. SIP foam disks (n=49) were Soxhlet-extracted using 4:1 hexane:acetone for 12h, a method adapted from Shoeib et al.13 Extracts were concentrated then cleaned via solid phase extraction (Supelclean ENVII-Florisil cartridges). PFRs were eluted with 10mL ethyl acetate and quantified using gas chromatography-mass spectrometry.

Urine Extraction. Urine samples (n=181) were analyzed for PFR metabolites using previously characterized methods.6,8,14 Briefly, urine samples were digested with enzymes then extracted via mixed-mode anion-exchange solid-phase extraction. Analytes were measured using liquid chromatography-tandem mass spectrometry.
Statistics. All analyses were performed using SAS software (Version 9.4). Analyses were conducted for analytes with detection >50%. Non-detects were replaced by MDL/2. PFR masses on SIPS and urinary metabolites were log-normally distributed. Spearman correlations ($r_s$) were used to assess associations between air samples and metabolites.

Results & Discussion

**PFRs on SIPS.** Air samples were analyzed for tris(1-chloro-2-propyl)phosphate (TCIPP), tris(2-chloroethyl)phosphate (TCEP), tris(1,3-dichloroisopropyl)phosphate (TDCIPP), and triphenyl phosphate (TPHP), with geometric means (GMs) of PFR masses measured on the SIPS ranging from 24-204 ng. TCIPP and TCEP were detected in every sample and at the highest levels.

**Urine.** Urine samples were assessed for 6 PFR metabolites: bis(1-chloro-2-isopropyl)phosphate (BCIPP), bis(1-chloro-2-isopropyl) 1-hydroxy-2-isopropyl phosphate (BCIPHIP), bis(1,3-dichloroisopropyl)phosphate (BDCIPP), diphenyl phosphate (DPHP), isopropylphenyl phenyl phosphate (ip-PPP), and tert-butyl diphenyl phosphate (tb-DPHP). All metabolites were detected in ≥80% of urine samples (GM=0.2-5.8 ng/mL).

**Air & Urine Associations.** The TDCIPP mass measured on air samplers was significantly correlated with BDCIPP urine concentrations ($r_s=0.3$, p<.05). TPHP mass on the SIPS was also highly correlated with DPHP, ip-PPP, and tb-DPHP urine levels ($r_s=0.3-0.4$, p<.05). Levels of these 3 metabolites were also significantly correlated with each other ($r_s=0.3-0.5$, p<.01). ip-PPP is a suggested metabolite of mono-isopropylated triaryl phosphate, and parent compounds of tb-DPHP are likely a mix of tert-butylated phenyl diphenyl phosphate isomers. These correlations suggest similar use patterns in products or similar exposure routes for TPHP and the other PFR compounds. Positive correlations between parent PFRs (TDCIPP and TPHP) in air and corresponding urinary metabolites suggest that household air is a significant source of PFR exposure for children and indicate that inhalation is an important pathway that must be considered in exposure assessments.

**Urine & Demographics.** PFR metabolites and various demographic factors were also examined using linear regression. Child’s race was associated with significant differences in urinary BDCIPP, BCIPP, BCIPHIP, and ip-PPP. When compared to white non-Hispanic children, white Hispanic children had half the levels of BDCIPP and BCIPP ($10^\beta=0.5$, p<.01). In contrast, black, non-Hispanic children and white Hispanic children had over 1.5 times higher levels of BCIPHIP and ip-PPP ($10^\beta=1.5-1.9$, p<.05) (Figure 1). Mother’s education was also associated with urinary metabolites. Significantly higher levels of BCIPHIP, ip-PPP, and tb-DPHP ($10^\beta=1.5-2.0$, p<.01) and lower levels of BCIPP ($10^\beta=0.6$, p<.01) were observed among households where the mother had some college education or less. This suggests that socioeconomic status may be impacting
PFR exposures, and further research is warranted to understand what factors are contributing to these disparities.

**Figure 1.** 95% CIs for BDCIPP and BCIPHIP in urine based on child’s race.

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**References**


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