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Demographic and dietary risk factors in relation to urinary metabolites of organophosphate flame retardants in toddlers

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HIGHLIGHTS

- 100% of toddler urine contained organophosphate flame retardants metabolites.
- Maternal income impacted toddler diphenyl phosphate (DPP) concentrations.
- Toddler dietary factors were below level of significance but showed trends.

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ABSTRACT

Organophosphate flame retardants (OPFRs), including Tris (1,3-dichloro-isopropyl) phosphate (TDCPP), triphenyl phosphate (TPP), and isopropylated triphenyl phosphate (ITP), are increasingly used in consumer products because of the recent phase out of polybrominated diphenyl ether (PBDE) flame retardants. OPFRs have been widely detected in adults and have been linked to reproductive and endocrine changes in adult males. Carcinogenicity and damage to immunologic, neurologic and developmental systems have been observed in human cell lines. Young children are especially vulnerable to OPFR exposure, but little is known about exposure levels or exposure risk factors in this population. We examined parent-reported demographic and dietary survey data in relation to OPFR urinary metabolite concentrations in 15- to 18-month old toddlers (n = 41). OPFR metabolites were detected in 100% of subjects. The metabolite of TPP, diphenyl phosphate (DPP) was detected most commonly (100%), with TDCPP metabolite, bis(1,3-dichloro-2-propyl) phosphate (BDCPP), detected in 85–95% of samples, and ITP metabolite, monoisopropylphenyl phenyl phosphate (ip-DPP), detected in 81% of samples (n = 21). Toddlers of mothers earning <$10,000 annually had geometric mean DPP concentrations 66% higher (p = 0.05) than toddlers of mothers earning >$10,000/year (7.8 ng/mL, 95% CI 5.03, 12.11 and 4.69 ng/mL, 95% CI 3.65–6.04, respectively). While no dietary factors were significantly associated with OPFR metabolite concentrations, results suggested meat and fish consumption may be associated with higher DPP and BDCPP levels while increased dairy and fresh food consumption may be associated with lower DPP, BDCPP, and ip-DPP levels. Research with larger sample sizes and more detailed dietary data is required to confirm these preliminary findings.

1. Introduction

Organophosphate flame retardants (OPFRs) are chemicals used to reduce the flammability of numerous consumer products and building materials. Yearly manufacture of flame retardants (FRs)

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worldwide is predicted to approach 6 billion pounds by 2019, with phosphorus-based flame retardants projected to account for 16% of global market share (BBC Research, 2015). Prior to 2004, three types of FRs were used in the United States (US); the penta and octa forms of polybrominated diphenyl ethers (PBDEs), and Tris (1,3-dichloroisopropyl) phosphate (TDCPP). Accumulating evidence of environmental persistence and toxicity to human and animal health led to a national phase out of all penta and octa PBDEs by 2012 (USEPA, 2015). Since the PBDE phase out, the use of TDCPP, and other OPFRs, has increased (Stapleton et al., 2008; Dodson et al., 2012; Bradman et al., 2014; Stapleton et al., 2014). However, concerns have mounted regarding the safety of these replacement FRs (Van Bergen and Stone, 2014; Hoffman et al., 2016).

In animal studies, OPFRs have induced immunologic, metabolic, genetic and endocrine disruptive changes (Liu et al., 2012, 2013; Farhat et al., 2013; Patisaul et al., 2013; Wang et al., 2013; Farhat et al., 2014). Rats exposed to OPFR contaminated food at environmentally relevant doses, comparable to human exposure, have been found to demonstrate increased obesity and characteristics of metabolic syndrome (Patisaul et al., 2013). Toxicity data is incomplete but OPFRs are linked to reproductive and endocrine changes in humans (Meeker et al., 2013a). Carcinogenicity and damage to immunologic, neurologic, and developmental systems have been observed in human cell lines (Dishaw et al., 2011; Faust and August 2011).

TDCPP is the most frequent flame retardant found in US furniture foam, and California's Proposition 65 lists TDCPP as a known carcinogen (Cooper et al., 2016; Faust and August 2011). TDCPP is designated by the US Environmental Protection Agency (EPA) as environmentally persistent and a hazard to human reproductive, genetic and developmental functions. Although several US states have banned its use in children's products or residential furniture foam, recent US studies have detected TDCPP in >90% of urine samples from adult men, pregnant women and toddlers (Hoffman et al., 2015, 2016; Cooper et al., 2016).

Triphenyl phosphate (TPP), and isopropylated triphenyl phosphate (ITP), together make up approximately 50% of the commonly used PBDE replacement, Firemaster® 550 (Belcher et al., 2014). Both TPP and ITP induce obesogenic activity in human cells and disrupt cardiac development in non-human vertebrates (McGee et al., 2013; Belcher et al., 2014). The EPA has designated ITP a high hazard to human developmental, neurologic, and reproductive systems and has designated both TPP and ITP as moderate carcinogen hazards (USEPA, 2015; Faust and August 2011). TPP is associated with altered hormone levels and decreased sperm count in a sample of US men (Meeker et al., 2013a; USEPA, 2015). Behl et al. compared eleven flame retardant compounds and recommended TPP and ITP for priority action due to evidence of developmental and neurologic toxicity (Behl et al., 2015).

Most FRs are not tightly bound to product matrices and therefore, migrate easily into the surrounding environment (Hou et al., 2016). They may be carried long distances, by air and water, or accumulate in indoor environments (Hou et al., 2016). This has resulted in the widespread detection of OPFRs in air, water, soil, indoor environments, and human food sources. In one study of 75 commonly consumed foods in China, including dairy, grains, meats and produce, OPFRs were detected in 100% of food samples, with rice reported to be a potential major source of human OPFR exposure (Zhang et al., 2016). Although ingestion is a known human exposure route, few studies have examined the association between human OPFR exposure levels and dietary patterns (Hou et al., 2016). In a study examining associations between placental OPFR concentrations and maternal diet, levels of TPP were higher in the placentas of women who reported more frequent vegetable consumption before pregnancy (Ding et al., 2016). A study of 48 school-age children in Norway, using 24-h recall food journals, found urinary metabolites of TDCPP were associated with reported sugar consumption. No other food associations with OPFR metabolites were found and the authors concluded that food is not a major OPFR exposure source (Cequier et al., 2015). However, the authors acknowledged their recruitment methods may have resulted in the biased selection of “particularly health concerned mothers,” which may have decreased the study population's exposure relative to the general population.

Children are more vulnerable to ingestion of toxics compared to adults, due to faster and more efficient nutrient absorption (Van den Eede et al., 2015). Additionally, young children are undergoing sensitive periods of metabolic, epigenetic, neurologic and organ development, which may be disrupted by OPFR exposure (Breton et al., 2017). Early exposure to toxics increases the time available for exposure-related disease to manifest later in life (Van den Eede et al., 2015). Currently, very little data exists regarding early childhood OPFR exposure concentrations or the risk factors for exposure. More research is needed to investigate whether contaminated food is a significant exposure source for young children. This study aims to fill that research gap.

This study sought to confirm previous findings regarding prevalence of OPFR exposure in young children, as well as investigate associations between toddlers' metabolite levels and dietary practices and demographic characteristics. We measured dietary and demographic factors in relation to three OPFR metabolite concentrations (BDCPP, DPP and ip-DPP) in the urine of 41 toddlers in Washington State, USA (Table 1) (Meeker et al., 2013a; Butt et al., 2014, 2016; Hoffman et al., 2015; Cooper et al., 2016; Hoffman et al., 2016).

2. Materials and methods

2.1. Study population

We recruited a convenience sample of children from the Bright Start Study in Seattle, WA, administered by the Seattle Children's Research Institute. Bright Start was designed to examine the effects of socio-demographic factors on child neurodevelopment. The Bright Start Study recruited English speaking, first-time mothers, between the ages of 18–23 years old, during the postpartum period, while they were in the hospital. Data was obtained at multiple time points from both mothers and children. The sample population for the current OPFR study consisted of a randomly selected subset of 41 Bright Start mother/child pairs. Selected subjects were contacted by phone to schedule their 15–18 months old Bright Start visit and invited to participate in an additional environmental exposure study. The children were aged 15–18 months old when the food journals and urine sampling were completed. All study procedures and protocols were approved by the Seattle Children's Research Institute Institutional Review Board.

2.2. Questionnaires and food journals

Mothers completed self-administered Bright Start questionnaires when children were born, and again at 12–15 months old. Information obtained included demographic factors (e.g. child race, maternal annual income, maternal educational status, public assistance, adequacy of resources to purchase food, and food insecurity) and lifestyle factors (e.g. mother's work or school outside home, cohabitation). We included income factors, such as maternal income and public assistance, in our analyses because of the demonstrated association between lower household income and FR exposure (Zota et al., 2008). Mothers' work or school outside home was included in our analysis as a potential indicator of time in