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Associations between human exposure to polybrominated diphenyl ether flame retardants via diet and indoor dust, and internal dose: A systematic review

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ABSTRACT

The aim of this review was to identify and appraise the current international evidence of associations between concentrations of polybrominated diphenyl ethers (PBDEs) in humans and their indoor dusts and food. We systematically searched Medline, Embase, Web of Science and Scopus (up to Jan 2015), using a comprehensive list of keywords, for English-language studies published in peer-reviewed journals. We extracted information on study design, quality, participants, sample collection methods, adjustments for potential confounders and correlations between PBDE concentrations in internal and external matrices. Of 131 potential articles, 17 studies met the inclusion criteria and were included in the narrative synthesis. We concluded that three key factors influenced correlations between external and internal PBDE exposure; half-life of individual congeners in the human body; proximity and interaction between PBDE source and study subject; and time of study relative to phase out of PBDE technical products. Internal dose of Penta-BDE technical mix congeners generally correlated strongly with dust. The exception was BDE-153 which is known to have higher persistence in human tissues. Despite the low bioaccessibility and short half-life of BDE-209, its high loading in dusts gave strong correlations with body burden where measured. Correlations between PBDE concentrations in duplicate diet and body burden were not apparent from the included studies. Whether dust or diet is the primary exposure source for an individual is tied to the loading of PBDE in dust or food items and the amounts ingested. Simple recommendations such as more frequent hand washing may reduce PBDE body burden.

1. Introduction

Polybrominated diphenyl ethers (PBDEs) are a class of brominated flame retardant, which have been widely used to meet fire safety regulations for fabrics, furnishings, electronics and vehicles since the 1970s. PBDEs are additive flame retardants, meaning that they are mixed into plastics or foam without forming chemical bonds. Fabrics and textiles can also be treated with PBDE commercial mixtures to provide protection. During the lifetime of products, PBDEs can leach out, thus becoming ubiquitous in indoor air and dust (Harrad et al., 2010). From there they migrate further into the wider environment and bioaccumulate through food chains (Harrad and Diamond, 2006). The human body burden of PBDEs increased dramatically from the 1970s until the 1990s (Frederiksen et al., 2009b; Hites, 2004; Meironyte et al., 1999) reflecting both wide use and persistence of these lipophilic chemicals. It is likely that regulations restricting PBDE use, e.g. Directives 2002/95/EC and 2003/11/EC and EC Designation 2008/C116/4, have been instrumental in reducing human exposure (Frederiksen et al., 2009b). However, the effects of such measures are slow to impact on levels found as contaminants in human tissue. Furthermore, recovery and recycling of electronics, particularly where unregulated in developing countries, is an additional new source of exposure (Athanasiadou et al., 2008; Ionas et al., 2014; Labunska et al., 2014; Liu et al., 2008). Potential adverse human health effects of PBDE exposure and body burden are well documented and include reproductive toxicity, neurotoxicity, endocrine activity, DNA damage and immune effects (EFSA, 2011; Kim et al., 2014; Linares et al., 2015; Lyche et al., 2015; US-EPA, 2010). The bioaccessibility of ingested PBDEs has been estimated to be 32-60% for tri- to hepta-BDEs, and 14-25% for deca-BDE (Abdallah et al., 2012; Fang and Stapleton, 2014). PBDE bioaccessibility generally decreases with increasing octanol-water partitioning coefficient (Log K_{ow}) a measure of relative solubility in lipid and water (Abdallah et al., 2012; Fang and Stapleton, 2014). It is widely accepted that PBDEs can have substantial half-lives in humans. There is a general trend of shorter half-lives for the higher brominated compounds, with estimates of residence time for

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BDE-209 of just a few days, and for main congeners of the technical Penta-BDE mixture (i.e. BDE-47, -99, -100) around two to four years (Geyer et al., 2004; Thuresson et al., 2006). Over the last few years, a number of studies have investigated matched internal and external PBDE exposure. A thorough review of such studies may reveal common patterns, which may generate recommendations for reducing exposure and identify future research needs. This new evidence will help to determine whether external exposure measurements can be used as indicators of human internal PBDE exposure. The aims of this systematic review were: (1) to identify, appraise and summarise the current international literature on the association between PBDE concentrations measured in food items and indoor dusts with human body burdens; and (2) to determine the relative contributions made by indoor dust ingestion and dietary exposure to PBDE body burden for general non-occupational human exposure.

2. Methods

2.1. Literature search and selection criteria

The process of this review followed the guidance for conducting systematic reviews from the Centre for Reviews and Dissemination (CRD, 2009) and 'Preferred Reporting Items for Systematic Reviews' guidelines (Moher et al., 2009). Papers were identified through searches of the environmental and medical literature databases (Medline, Embase, Web of Science, Scopus) using relevant terms for PBDEs, internal dose, external exposure and matched exposure. The Boolean operators 'AND' and 'OR' were used to combine topic areas; *i.e.* ($bde OR pbde OR pbdes OR (polybrominated and ('diphenyl' de OR diphenyl) and ('ethers' de OR ethers))) AND (serum$ OR plasma$ OR blood$ or milk$ OR internal OR body burden$ OR exposure$) AND (diet$ OR food$ OR dust$ OR air$ OR indoor$ OR environment$ OR exposure$ OR factor$ OR lifestyle$ OR source$ OR behav$) AND (match$ OR pair$ OR relation$ OR association$ OR evidence$ OR predict$). A comprehensive description of the search strategy is available in SI1. Reference lists of the identified published studies were also scanned and experts in the field were consulted.

Studies were included if they met the following inclusion criteria: a) explored correlations in PBDE concentrations between paired human internal dose (serum or milk) and indoor house dust, and/or correlations between paired human internal dose (serum or milk) and diet, b) were published in the English language, c) were full original papers which were published in a peer-reviewed journal available either on-line or from the British Library. Databases were searched for papers published between 1974 to January 2015. There were no limits on the year of publication (up until Jan 2015) or the age of study participants. Studies were not included if the dust exposure measurement was purely occupational or from a hobby.

One reviewer (LB) scanned through all abstracts after the initial article selection and excluded only obvious non-eligible studies. A second reviewer scanned titles and abstracts of a 15% sample of the identified studies and confirmed decisions on inclusion. A sample of the papers that met the inclusion criteria (20%) were formally reviewed by two independent reviewers using a data extraction form modified from Glinianaia et al. (Glinianaia et al., 2004). Data extracted included information on study design, sample descriptors and collection methods, analytical and statistical methods, confounders and correlations. Concentrations of PBDE in human serum or milk (lipid weight) were used to indicate internal dose. Concentrations of PBDE in indoor dusts or in duplicate diets (per body weight) were used as the indicators of exposure. The correlations calculated for pairs of internal dose and exposures were explored.

We present a narrative synthesis of the data, as a formal meta-analysis was not possible given the heterogeneity of samples, particularly differences in: a) fire prevention regulations and technical product usage between countries (and between states in the USA); b) sample collection methods; c) congeners analysed and reported; and d) analysis and reporting of correlations between internal and external exposures.

2.2. Study quality

The quality data extraction form was based on that used by Roth and Wilks (2014) and 'Harmonization of Neurodevelopmental Environmental Epidemiology Studies' (HONEES) criteria (Youngstrom et al., 2011). Quality assessment evaluated study design (description of setting, location, data collection dates, study size), study population and sampling (eligibility criteria, recruitment methods, response rate, participant description, representation of population to whom results would be generalised), variables for adjustment (discussion of and accounting for confounders and bias), data measurement (methods of measurement, quality controls, fit with literature) and outcome measurement (statistical methods and description). Laboratory measurement quality considerations included ^{13}C internal standardisation coupled with GC-HRMS measurement, and the successful use of regular procedure blanks and reference materials. Studies were classified, regarding provision of this information, as: yes (1), no or unclear (0), or partially (0.5). Based on these criteria, three quality groups were formed: scores of 10–12 were rated high, 4–9 moderate and 0–3 low. When drawing conclusions, studies with a low quality score were given less weight. Throughout the review process we referred to recommendations from 'Strengthening the Reporting of Observational Studies in Epidemiology' (STROBE) guidelines (von Elm et al., 2007).

3. Results

A flow diagram of numbers of articles identified by the literature searches, screened, assessed for eligibility and included in the review, with reasons for exclusion at each stage is presented in Fig. 1. Database searches elicited 408 articles. A title and abstract review resulted in 131 original peer reviewed papers. The abstracts and, where necessary, full articles were reviewed in detail resulting in further exclusions. Twenty-three articles were included in the systematic review, concerning 17 studies which met our inclusion criteria and were included in the narrative synthesis (Fig. 1). For six of these studies, key information was extracted from additional papers to those containing the correlation analysis. The additional papers are referred to in Tables 1 and 2.

3.1. Participant characteristics and study methods

A summary of study designs, participant characteristics, sampling methods, adjustments for confounders and quality assessment for the 17 included studies is presented in Table 1. Seven of the studies took place in Europe — predominantly Scandinavia and Northern Europe, six studies took place in the USA, three took place in Australasia, and one in South Central Asia. The specific countries where the studies were conducted are included in Table 1. Only one study stated its design, this was a convenience cross-sectional sample, (Watkins et al., 2012) so recruitment information was used to deduce design for the other studies where possible. Samples recruited from a previous study's cohort or by word-of-mouth appeared to be on the basis of convenience (Coakley et al., 2013; Imm et al., 2009; Sahlström et al., 2015; Stasinska et al., 2014; Toms et al., 2009; Whitehead et al., 2015). Where participants were recruited because they were pregnant or were undergoing medical treatment, the design appeared to be prospective (Frederiksen et al., 2010; Wu et al., 2007). If recruitment was based on specific businesses or accommodation, the studies were considered to be retrospective (Ali et al., 2014; Roosens et al., 2009). Remaining studies were classed cross-sectional (Bjorklund et al., 2012; Cequier et al., 2015; Fromme et al., 2009; Johnson et al., 2010; Stapleton et al., 2012) or of unclear design (Karlsson et al., 2007).

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