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Exposure determinants of phthalates, parabens, bisphenol A and triclosan in Swedish mothers and their children

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ABSTRACT

Chemicals such as phthalates, parabens, bisphenol A (BPA) and triclosan (TCS), used in a wide variety of consumer products, are suspected endocrine disrupters although their level of toxicity is thought to be low. Combined exposure may occur through ingestion, inhalation and dermal exposure, and their toxic as well as combined effects are poorly understood.

The objective of the study was to estimate the exposure to these chemicals in Swedish mothers and their children (6–11 years old) and investigate potential predictors of the exposure. Urine samples from 98 mother–child couples living in either a rural or an urban area were analyzed for the concentrations of four metabolites of di-(2-ethylhexyl) phthalate (DEHP), three metabolites of di-iso-nonyl phthalate (DiNP), mono-ethyl phthalate (MEP), mono-benzyl phthalate (MBzP) and mono-n-butyl phthalate (MnBP), methylparaben (MetP), ethylparaben (EthP), propylparaben (ProP), butylparaben, benzylparaben, BPA, and TCS. Information on sociodemographics, food consumption habits and use of personal care products, obtained via a questionnaire, was used to investigate the associations between the urinary levels of chemicals and potential exposure factors. There were fairly good correlations of biomarker levels between the mothers and their children. The children had generally higher levels of phthalates (geometric mean ΣDEHP 65.5 μg/L; ΣDiNP 37.8 μg/L; MBzP 19.9 μg/L; MnBP 76.9 μg/L) than the mothers (ΣDEHP 38.4 μg/L; ΣDiNP 33.8 μg/L; MBzP 12.8 μg/L; MnBP 63.0 μg/L). Conversely, the mother's levels of parabens (MetP 37.8 μg/L; ProP 13.9 μg/L) and MEP (43.4 μg/L) were higher than the children's levels of parabens (MetP 6.8 μg/L; ProP 2.1 μg/L) and MEP (28.8 μg/L). The urinary levels of low molecular weight phthalates were higher among mothers and children in the rural area (MBzP $p = <0.001$; MnBP $p = 0.001–0.002$), which is probably due to higher presence of PVC in floorings and wall coverings in this area, whereas the levels of parabens were higher among the children in the urban area (MetP $p = 0.003$; ProP $p = 0.004$) than in the rural area. The levels of high molecular weight phthalates were associated with consumption of certain foods (i.e. chocolate and ice cream) whereas the levels of parabens were associated with use of cosmetics and personal care products.

1. Introduction

Chemicals such as phthalates, parabens, bisphenol A (BPA) and triclosan (TCS), used in a wide variety of consumer products, are suspected endocrine disrupters although their level of toxicity is thought to be low. Combined exposure may occur through ingestion, inhalation and dermal exposure, and their toxic as well as combined effects are poorly understood.

Phthalates are industrial chemicals which are used for a wide range of applications. They are primarily used as plasticizers in PVC found in consumer products such as shoes, gloves and packing materials as well as in building materials, floorings and wall coverings. Some phthalates are

Abbreviations: BenP, benzylparaben; BPA, bisphenol A; BBzP, butylbenzyl phthalate; ButP, butylparaben; DEHP, di-(2-ethylhexyl) phthalate; DEP, diethyl phthalate; DiNP, di-iso-nonyl phthalate; DnBP, di-n-butyl phthalate; EthP, ethylparaben; MetP, methylparaben; 5-cx-MEPP, mono(2-ethyl-5-carboxy-pentyl) phthalate; 5-OH-MEHP, mono(2-ethyl-5-hydroxy-hexyl) phthalate; 5-oxo-MEHP, mono(2-ethyl-5-oxo-hexyl) phthalate; cx-MiNP, mono-(carboxy-isooctyl) phthalate; OH-MiNP, mono-(hydroxyl-isononyl) phthalate; oxo-MiNP, mono-(oxo-isononyl) phthalate; MBzP, mono-benzyl phthalate; MEP, mono-ethyl phthalate; MEHP, mono(2-ethylhexyl) phthalate; MnBP, mono-n-butyl phthalate; ProP, propylparaben; TCS, triclosan.

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also used in non-plastic products such as pharmaceuticals, personal care products, paints and adhesives (Frederiksen et al., 2007; Wittassek et al., 2011). Phthalates can be released from products and exposure may occur in humans through food, dust, air and direct use of personal care products (Janjua et al., 2008; Wittassek and Angerer, 2008; Wormuth et al., 2006). After absorption, the parent phthalates are metabolized into respective monoesters, which can be further hydroxylated, oxidized and/or glucuronidated before excretion in urine as free or conjugated monoesters (Frederiksen et al., 2007). The presence of phthalate metabolites in urine indicates recent exposure to respective parent compound (Townsend et al., 2013). Some phthalates, such as di-(2-ethylhexyl) phthalate (DEHP), butylbenzyl phthalate (BBzP) and di-n-butyl phthalate (DnBP) are endocrine disrupters. These phthalates have been shown in animal studies to affect the development of the reproduction system in male offspring, referred to as the "phthalate syndrome" including e.g. shortened anogenital distance, hypospadias and cryptorchidism (Foster, 2006; Gray et al., 2000; Mylchreest et al., 2000). Similar effects have been observed after in utero exposure in humans (Suzuki et al., 2012; Swan et al., 2005). Due to their supposed toxic effects, DEHP, BBzP and DnBP have been prohibited within the EU from the production of toys, childcare articles (EC, 2005) and cosmetic products (EC, 2009) and the migration levels from food contact materials are regulated (EC, 2007). Di-iso-nonyl phthalate (DiNP) is prohibited only from toys which can be put in the mouth by the child (EC, 2005).

BPA (2,2-bis(4-hydroxyphenyl)propane) is a high production volume chemical used in polycarbonate plastics and epoxy resins, which are used in e.g. CDs and DVDs, tooth fillings, cash receipts, plastic bottles, inner coatings of cans, and relining of water pipes. Food is the main source of exposure in humans because BPA can migrate from cans coated with epoxy as well as other plastics in contact with food or beverages (Geens et al., 2012). In addition, BPA has been detected in indoor dust which may contribute to the exposure (Geens et al., 2009; Loganathan and Kannan, 2011). After ingestion, BPA is readily absorbed, glucuronidated or sulfatated and subsequently excreted in urine with an elimination half-life of less than 6 h (Völkel et al., 2002). The levels of BPA in spot-urine samples reasonably reflect the ongoing average exposure on a population/group level (Christensen et al., 2012; Ye et al., 2011). BPA is a well-known endocrine disruptor with estrogenic potency. The toxicity of BPA shown in animal studies has mainly been attributed to effects on the development and function of the reproductive organs as well as the nervous system and behavior (Richter et al., 2007). However, the low-dose effects shown for BPA are debated (Beronius et al., 2010). Aiming to lower the exposure, the use of BPA in baby bottles and cosmetics has been banned within the EU (EC, 2009, 2011).

Parabens are used as antimicrobial preservatives in personal care products, cosmetics and pharmaceuticals. The maximum level of parabens in cosmetics is restricted by the European Cosmetic Directive to 0.4% for one ester and 0.8% for a mixture of esters (EC, 2009). Methylparaben (MetP), ethylparaben (EthP) and propylparaben (ProP) are also permitted as food preservatives in confectionary and dried meat (EC, 1995). Parabens are readily absorbed orally and to a lesser extent dermally. After absorption, parabens can be hydrolyzed to parahydroxybenzoic acid (PHBA) and/or conjugated and are then excreted in urine as free or conjugated parabens and PHBA within hours (Janjua et al., 2008; Ye et al., 2006a). Despite their short half-life, the levels of parabens in a spot urine sample reasonably represent an individual's exposure over several months (Smith et al., 2012). The use of parabens has raised concern due to their weak estrogenic activity confirmed in in vivo and in vitro studies. The potency seems to increase with the length of the alkyl chain, thus the long-chain parabens (e.g. ProP and butylparaben (ButP)) are of highest concern (Boberg et al., 2010; Routledge et al., 1998; Witorsch and Thomas, 2010). In 2010, the EU Scientific Committee on Consumer Safety (SCCS) evaluated the safety of parabens and concluded that the use of MetP and EthP below the maximum permitted levels is considered safe, whereas the safety of ProP and ButP at the maximum levels is more uncertain due to lack of data (SCCS, 2011).

TCS (5-chloro-2-(2,4-dichlorophenoxy)phenol) is used as an antimicrobial agent in personal care products such as deodorants, toothpastes, mouth washes and shower gels, and also in consumer products such as cleaning products, plastics and toys (Bedoux et al., 2012). TCS is approved by the European Cosmetic Directive for use in cosmetic products in concentrations up to 0.3% (EC, 2009), but is no longer permitted for use in food contact materials (EC, 2010). TCS is readily absorbed by the gastrointestinal tract, whereas the uptake via the oral cavity and skin is lower (SCCP, 2009). After absorption, TCS is almost completely converted to glucuronic and sulphuric acid conjugates and is subsequently excreted predominately in urine as glucuronide conjugates. The elimination half-life in humans after oral administration is estimated to be 13–29 h (SCCP, 2009). Serial measurements of TCS in morning urine have shown relatively high consistency over time (ICC = 0.56; (Lassen et al., 2013)). TCS has been shown in animal studies to cause endocrine effects, especially on the levels of thyroid hormones (Crofton et al., 2007; Dann and Hontela, 2011; Kumar et al., 2009; Zorrilla et al., 2009). The Scientific Committee on Consumer Products (SCCP) has concluded that the current maximum concentration of 0.3% is not safe when the aggregate exposure from all cosmetic products is considered. However, the maximum concentration is considered safe for individual products such as toothpastes, soaps and deodorants, but not in products that stay on the skin (e.g. body lotions) or mouth wash (SCCP, 2009).

The objectives of the present study were to evaluate the levels of 10 phthalate metabolites, 5 parabens, BPA and TCS in urine from Swedish children (6–11 years old) and their mothers, in relation to demographics, lifestyle, housing and different potential sources of exposure to these chemicals. The study is part of a harmonized approach for biomonitoring on the European level; the COPHES (COnsortium to Perform Human biomonitoring on a European Scale) and DEMOCOPHES (DEMOnstration of a study to COordinate and Perform Human biomonitoring on a European Scale) twin projects.

2. Materials and methods

2.1. Recruitment and sampling

The participants were selected via inhabitant registers, based on the age of the child (6–11 years) and the living area. The mother–child couples were either from the urban area of Uppsala with a population of 140,000 inhabitants, or a sparsely populated area in the county of Västerbotten in northern Sweden. Inclusion criteria included that the mother was under 45 years of age, had lived in the study area for at least 3 years, that the child lived more than half of the time at the mother's address, and that the mother or child had no chronic kidney or liver disease. The sampling was performed according to the harmonized approach developed within the COPHES/DEMOCOPHES projects (Becker et al., 2014). First morning urine samples were collected in polypropylene tubes. The urine samples were frozen at −20 °C and transported to the analyzing laboratories for analysis. Ethical permission was granted by the regional ethical review board in Stockholm (Dnr 2011/1024-31/1).

2.2. Questionnaires

The mothers answered an extensive questionnaire (developed by the COPHES/DEMOCOPHES consortium) covering questions about living environment, food consumption, use of personal care products, smoking, lifestyle and sociodemographics. The questionnaires were answered through face-to-face interviews with field workers or online. The Computer Assisted Personal Interviewing system SOCRATOS (Ivox, Belgium) was used for interviews and self-administered questionnaires. The information reported through questionnaires was