Environmental Research 141 (2015) 118–124

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Case study: Possible differences in phthalates exposure among the Czech, Hungarian, and Slovak populations identified based on the DEMOCOPHES pilot study results

Milena Černá [a,b,*], Marek Malý [a], Peter Rudnai [c], Szilvia Középesy [c], Miklós Náray [d], Katarina Halzlová [e], Michal Jajcaj [e], Anna Grafnetterová [a], Andrea Krsková [a], Danuše Antošová [a], Kateřina Forysová [f], Elly Den Hond [o], Greet Schoeters [g,l], Reinhard Joas [h], Ludwine Casteleyn [i], Anke Joas [h], Pierre Biot [j], Dominique Aerts [j], Jürgen Angerer [k], Louis Bloemen [m], Argelia Castaño [n], Marta Esteban [n], Holger M. Koch [k], Marike Kolossa-Gehring [p], Arno C. Gutleb [q], Jana Pavloušková [a], Karel Vrbík [a]

[a] National Institute of Public Health, Šrobárova 48, Prague 10 100 42, Czech Republic
[b] Charles University, Third Faculty of Medicine, Prague, Czech Republic
[c] National Institute of Environmental Health, Budapest, Hungary
[d] National Labour Office, Department for Occupational Health, Budapest, Hungary
[e] Authority of Public Health of the Slovak Republic, Bratislava, Slovakia
[f] Public Health Agency based in Liberec, Czech Republic
[g] VITO, Environmental Risk and Health Unit, Boeretang 200, 2400 Mol, Belgium
[h] BiPRO, Munich, Germany
[i] KU Leuven—Centrum Menselijke Erfelijkheid, Belgium
[j] Federal Public Service Health, Food Chain Safety and Environment—DG Environment, Brussels, Belgium
[k] Institute for Prevention and Occupational Medicine of the German Social Accident Insurance—Institute of the Ruhr-Universität Bochum (IPA), Germany
[l] Department of Biomedical Sciences, University of Antwerp, Antwerp, Belgium
[m] Environmental Health Sciences International, Hulst, The Netherlands
[n] Instituto de Salud Carlos III, Madrid, Spain
[o] Flemish Institute for Technological Research (VITO), Environmental Risk and Health, Belgium
[p] Federal Environment Agency (UBA), Berlin, Germany
[q] Centre de Recherche Public—Gabriel Lippmann, Belvaux, Luxembourg

ARTICLE INFO

Article history:
Received 4 August 2014
Received in revised form
23 September 2014
Accepted 15 October 2014
Available online 19 December 2014

Keywords:
DEMOCOPHES
Urinary phthalate metabolites
Czech Republic
Slovakia
Hungary

ABSTRACT

Objective: Phthalates and their metabolites are classified as endocrine modulators. They affect the hormonal balance in both children and adults.

The aim of this publication was to compare the urinary levels of phthalate metabolites in selected populations of the Czech Republic (CZ), Slovakia (SK), and Hungary (HU) in relation to the sources of phthalate exposure identified by means of questionnaire (personal care products, floor and wall coverings, plastic toys, and some kinds of foods).

Methods: Data were obtained through the twin projects 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) from 2009 to 2012. The target groups were children aged 6–11 years old and their mothers up to 45 years of age. The metabolites of phthalates (monomethyl phthalate (MMP), monoethyl phthalate (MEP), monobenzyl phthalate (MBzP), mono-cyclohexyl phthalate (MCHP), mono-(2-ethylhexyl) phthalate (MEHP), mono-(2-ethyl-5-hydroxyhexyl) phthalate (5OH-MEHP), and mono-(2-ethyl-5-oxohexyl) phthalate (5OXO-MEHP)) were analysed in first morning urine samples. After enzymatic glucuronide cleavage, the urine sample analyses were performed using ultra-high-performance liquid chromatography–electrospray ionization tandem mass spectrometry (UHPLC–ESI-MS/MS) in one laboratory that qualified in the External Quality Assessment exercises organised by COPHES.

Results: Significant differences in phthalate exposure between countries were revealed for children only but not for mothers. The concentrations of 5-OH-MEHP ($P<0.001$), 5OXO-MEHP ($P<0.001$), and their sum ($P<0.001$) were the highest in SK compared to CZ and HU. The health based guidance values for the sum of

* Corresponding author at: National Institute of Public Health, Šrobárova 48, Prague 10 100 42, Czech Republic.
E-mail address: mcerna@szu.cz (M. Černá).

http://dx.doi.org/10.1016/j.envres.2014.10.025

DEHP metabolites 5-OH MEHP and 5OXO-MEHP established by the German Commission for biomonitoring of 300 μg/L and 500 μg/L for women adults and children, respectively, were only exceeded in one mother and three boys. A significant difference was also found for MEP ($P=0.0149$), with the highest concentrations detected in HU. In all countries, the increasing frequency of using personal care products significantly elevated the concentrations of MEP.

Conclusion: Some differences were observed between countries in the concentrations of individual urinary phthalate metabolites in children. However, the questionnaire results give no direct explanation for the differences between the countries except the variation in using personal care products.

1. Introduction

Human biomonitoring (HBM) is a tool for evaluating population exposure to potentially critical chemicals found in the environment, contaminated foodstuffs, lifestyle, use of different products, and other sources. This approach allows characterising the body burden from all exposure sources and has been increasingly applied in environmental health surveys in the last decade all over the world (Angerer et al., 2007; Needham et al., 2007).

Although HBM has been practiced for several years in several European countries (Becker et al., 2002, 2003; Černá et al., 2007; Fréry et al., 2012; Cañas, et al., 2014; Schindler et al., 2014), Europe as such—unlike the USA (CDC, 2013)—has no comparable data on the levels of environmental chemicals in the body for their population. Results produced by individual European countries are not always comparable as the studies may differ in the methodological steps like recruitment of body fluid donors, choice of population groups, selection of biomarkers and analytical procedures.

Therefore, the European Environment and Health Action Plan 2004 prioritized the need to harmonise HBM in Europe to be able to obtain internationally comparable data (EHAP, 2004; Joas et al., 2012). Unified protocols developed by the COPHES project (COnsortium to Perform Human biomonitoring on a European Scale) and the practical use of these Standard operational procedures (SOPs) in the DEMOCOPHES project (DEMOnstration of a study to COordinate and Perform Human biomonitoring on a European Scale) allowed to produce comparable data by means of harmonized methodological procedures within the DEMOCOPHES pilot study (Becker et al., 2014; Schindler et al., 2014).

For the DEMOCOPHES pilot study, children aged between 6 and 11 years old were chosen as the main target group. The reason being that children belong to the most vulnerable population group, and that the protection of children's health is a main priority for the environmental health policy. The exposure of infants and children to environmental toxic compounds early on in life may adversely influence their quality of life in later periods (Au, 2002). Additionally, the children's mothers were included. The population group of mothers as women of reproductive age is another known vulnerable group with similar lifestyle characteristics and habits to the children under study.

Several environmental pollutants with known biomarkers of exposure (cadmium and cotinine in urine and mercury in hair) were selected for the DEMOCOPHES pilot study based on ongoing knowledge of HBM requirements taking into account the demands of participating countries discussed in the Consultative Forum in the frame of the EU Environment and Health Action Plan (Becker et al., 2014; Joas et al., 2012). Contrary to the existing HBM scenarios in which generally the population exposure to traditional environmental pollutants covered by sufficient analytical experience like heavy metals or persistent organic pollutants is monitored, this pilot study also included phthalates. They represent a relatively new group of emerging types of environmental contaminants, identified due to increasing public and political awareness (Zimmer et al., 2012), which started to be included into the spectrum of monitored biomarkers only in the last decade (Barr et al., 2003; Koch et al., 2003a).

Some phthalates such as di(2-ethylhexyl) phthalate (DEHP) have been widely used as plasticizers in numerous products (Lyche et al., 2009). Other phthalate derivatives are also used for different purposes dependent on their molecular weight, e.g. as additives in the textile industry (DEHP, di-isononyl phthalate (DiNP), and di-isodecyl phthalate (DiDP), etc.), personal care products (dimethyl phthalate (DMP), diethyl phthalate (DEP), di-*n*-butyl phthalate (DBP), etc.), paints and construction materials (DiNP, DiDP) or adhesives (ATSDR, 2002; Heudorf et al., 2007). At present, the US general population is exposed to phthalates to quite a large extent (Hauser and Calafat, 2005). As phthalates are classified as endocrine disruptors and reproductive toxicants, the exposure of children is of particular concern (Swan et al., 2005). Phthalates enter the human body by ingestion, inhalation and dermal absorption (Wittassek et al., 2011). They are quickly metabolised in the organism and metabolites are excreted in urine (Koch et al., 2006). Urinary metabolites of phthalates are considered relevant indicators of phthalate exposure (Koch et al., 2003b, 2006). Therefore metabolites were included in the range of biomarkers monitored in the DEMOCOPHES pilot study. At the beginning of this study, only very few laboratories were able to analyse the most important metabolites of phthalates so as to match Interlaboratory Comparison Investigation/External Quality Assessment Scheme (ICI/EQUAS) tests (Schindler et al., 2014). The laboratory of the National Institute of Public Health (NIPH) in Prague was one of the few which succeeded in the ICI/ EQUAS exercise). Therefore, the analyses of selected phthalate metabolites in the samples from the Czech Republic, Slovakia and Hungary were performed in the NIPH laboratory.

Data regarding the concentration of urinary phthalate metabolites obtained in the Democophes study for all 17 participating European countries have shown marked differences and the highest mean urinary DEPH metabolite concentrations were found in children from Slovakia (Den Hond et al., 2015). Therefore the main objective of this manuscript was to try to identify the possible causes of this finding taking into account responses obtained in basal questionnaire (Fiddicke et al., 2015) and explain higher concentrations of urinary phthalate metabolites in Slovak children compared with neighbouring states.

2. Materials and methods

2.1. Sampling and questionnaire

In the Czech Republic and Hungary, 120 pairs of children aged 6 to 11 years old and their mothers from urban and rural areas each were examined while in Slovakia 129 such pairs were enrolled. In all three countries study subjects were recruited through schools, equally in urban and rural areas as defined according to regional standards. Generally samples and sampling were not