Available online at www.sciencedirect.com
ScienceDirect
Chemosphere 70 (2008) 1676–1684
CHEMOSPHERE
www.elsevier.com/locate/chemosphere

Placental transfer of polychlorinated biphenyls, their hydroxylated metabolites and pentachlorophenol in pregnant women from eastern Slovakia

June-Soo Park [a,b,*], Åke Bergman [c], Linda Linderholm [c], Maria Athanasiadou [c], Anton Kocan [d], Jan Petrik [d], Beata Drobna [d], Tomas Trnovec [d], M. Judith Charles [e], Irva Hertz-Picciotto [a]

[a] Department of Public Health Sciences, University of California-Davis, Davis, CA 95616, United States
[b] Department of Toxic Substances Control, California Environmental Protection Agency, Berkeley, CA 94710, United States
[c] Department of Environmental Chemistry, Stockholm University, SE-106 91 Stockholm, Sweden
[d] Department of Toxic Organic Pollutants, Slovak Medical University, Bratislava, Slovak Republic
[e] Department of Environmental Toxicology, University of California-Davis, Davis, CA 95616, United States

Received 18 December 2006; received in revised form 11 July 2007; accepted 16 July 2007
Available online 30 August 2007

Abstract

The aim of the present study was to understand the placental transfer of polychlorinated biphenyls (PCBs), specific hydroxylated PCB metabolites (OH-PCBs), and pentachlorophenol (PCP) in blood serum, in a birth cohort from eastern Slovakia. During the period 2002–2004, cord blood specimens were collected in parallel with maternal specimens from women delivering in the two eastern Slovak districts of Michalovce and Svidnik/Stropkov. A total of 92 pairs of mother-cord specimens at delivery were selected for this study. 4-OH-CB107, 3-OH-CB153, 4-OH-CB146, 3′-OH-CB138, 4-OH-CB187, and 4′-OH-CB172 were quantified. The median concentrations of Σ_{17}PCBs, Σ_6OH-PCBs, and PCP in cord serum were 0.92, 0.33, and 0.69 ng/g wet wt., respectively and highly correlated with the corresponding maternal serum levels (correlations were $R^2 = 0.61$, 0.78, and 0.82, respectively). The median cord to mother ratios of the Σ_{17}PCBs, Σ_6OH-PCBs, and PCP were 0.18, 0.75, and 1.10, respectively. The median ratio of the Σ_6OH-PCBs to the Σ_{17} PCBs in the cord serum was 0.38 from wet weight based concentrations, which was about four times higher than the ratio of these compounds in maternal serum (0.09). PCP was more abundant than any PCB or OH-PCB congener measured in cord serum. The higher cord to maternal ratios of OH-PCB metabolites as compared with the parent compounds suggests either a higher placental transfer rate or greater metabolism in the fetus as compared with the maternal compartment. These findings are consistent with their preferential binding to TTR that can cross the placenta. The cord to maternal ratio varies by congener (e.g., 4-OH-CB107 = 0.58, 4-OH-CB146 = 0.74, 3′-OH-CB138 = 1.01).

Keywords: Cord blood; Hydroxylated PCB metabolites; Polychlorinated biphenyls; Pentachlorophenol; Slovakia

1. Introduction

In the 1970s and 1980s, countries around the world including USA, Japan, Germany, and Slovakia took regulatory actions to restrict or ban the production and use of PCBs (polychlorinated biphenyls), and over the subsequent decades, a decline in PCB levels in the biota including human milk has been observed (Bignert et al., 1998; Norén and Meironyte, 2000). However, PCBs are still one of the world′s most widespread contaminants. PCBs were involved in several food poisoning incidents; i.e. Yusho (Masuda and Yoshimura, 1984), Yucheng (Hsu et al., 1985), and the Belgian chicken feed contamination

* Corresponding author. Address: Department of Toxic Substances Control, California Environmental Protection Agency, Berkeley, CA 94710, United States. Tel.: +1 510 540 2925; fax: +1 510 540 2930.
E-mail address: jpark@dtsc.ca.gov (J.-S. Park).

0045-6535/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.chemosphere.2007.07.049

(Bernard et al., 1999), as well as the contamination of neighborhoods surrounding production sites in Anniston, Alabama (now closed) (Hansen et al., 2003), and Michalovce, Slovak Republic (Hovander et al., 2004; Kocan et al., 2004; Pavuk et al., 2004).

PCBs are capable of crossing the placenta to reach the fetus (Covaci et al., 2002; Ayotte et al., 2003; Fukata et al., 2005). Animal experiments have demonstrated PCBs to be toxic to numerous systems, including alterations in the thyroid hormone system (Porterfield and Hendry, 1998), and adverse effects on cognitive and neurosensory development (Schantz et al., 1991; Goldey et al., 1995).

Studies in human also suggest adverse effects associated with *in utero* exposure to PCBs: lower birth weight (Hertz-Picciotto et al., 2005; Rylander et al., 1996), possible retardation of postnatal growth (Patandin et al., 1998), impaired immune response (Weisglas-Kuperus et al., 1995), and neurodevelopmental deficits (Stewart et al., 2004). Some studies specifically observed impairments in mental performance tests associated with cord blood PCBs (Rogan et al., 1986; Stewart et al., 2003).

The apparent negative effects of PCBs on human health might have been the result of PCBs themselves, their metabolites such as OH-PCBs, or their contaminants, such as PCDFs. The metabolism of PCB congeners results in the formation of a large number of OH-PCB congeners (Letcher et al., 2000). OH-PCBs have been shown to be transferred to the fetal compartment both in humans (Guvenius et al., 2003; Soechitram et al., 2004) and in animals (Brouwer et al., 1998; Sinjari and Darnerud, 1998; Meerts et al., 2002). Those OH-PCB metabolites with a *para*- or a *meta*-substituted hydroxyl group adjacent to chlorine atoms have a particularly high affinity for transthyretin (TTR) (Brouwer et al., 1998). Although TTR is not the primary transport protein for thyroid hormone in human blood, it still crosses the placenta and blood-brain barrier, resulting in the delivery of T4 and possibly OH-PCBs. In experimental animals, OH-PCB metabolites reduce thyroxine (T_4) levels in the brain and blood of the fetus (Brouwer et al., 1998; Sinjari and Darnerud, 1998; Meerts et al., 2002) and therefore have the potential to affect behavioral development.

Unlike the parent PCB compounds, OH-PCBs are transferred in very low amounts via milk (Fängström et al., 2005). The studies of neurodevelopment in relation to postnatal exposure via breast milk have been inconsistent and often not significant (Jacobson and Jacobson, 2004). For this reason, although PCB exposure is higher through breastfeeding than *in utero* (Fukata et al., 2005; Guvenius et al., 2003), the prenatal exposure is believed to pose a greater threat to the infant than postnatal exposure. The analysis of umbilical cord blood is, therefore, central to the assessment of developmental effects, since it provides a direct measure of *in utero* exposure to PCBs and their metabolites.

Pentachlorophenol (PCP) is also of interest because it is present at high concentrations, higher than other halogenated phenolic compounds (HPCs) dominant in cord blood (Guvenius et al., 2003; Sandau et al., 2002), and is documented as an endocrine disruptor (Beard and Rawlings, 1999; Ishihara et al., 2003).

The present study of prenatal exposure to PCBs, PCP, and OH-PCBs was conducted in eastern Slovakia, in an area with PCB exposures among the highest in the world (Hovander et al., 2004; Kocan et al., 1994; Pavuk et al., 2004). We characterized and quantified the levels of 17 PCBs, 9 OH-PCB metabolites and PCP in cord blood sera specimens collected from mother-child pairs at delivery in two eastern Slovakian districts, Michalovce and Svidnik/Stropkov, to assess and compare the placental transfer and prenatal exposures to those compounds. Our ultimate goal is to improve the understanding of the relationship between prenatal exposure to halogenated endocrine disruptors and early childhood immune- and neurodevelopment.

2. Materials and methods

2.1. Cohorts

During the period 2002–2004, over 1100 mothers were enrolled into a birth cohort study in the Michalovce district, where the Chemko, Inc. chemical plant produced PCBs from 1959 to 1984, and in Svidnik/Stropkov district as a lower exposure area with similar population characteristics, about 70 km to the north. Hospital staff trained in the study protocols administered informed consent to all participants and collected the maternal and cord blood at delivery. The study participants gave written informed consent. A total of 762 and 341 women participated from Michalovce and Svidnik/Stropkov districts, respectively. We collected a total of 1087 pairs of both maternal and cord sera. The general characteristics of our study cohort were described in previously (Park et al., 2007). This study complied with all applicable US and international requirements with regard to research on human subjects and was approved by the respective Institutional Review Boards at the University of California, Davis and the Slovak Medical University.

2.2. Samples

A Medican cannula was used, instead of standard needles, to collect umbilical cord blood samples just after the delivery. An adapter was used to connect the cannula to 9-ml plastic vacutainer tube (S-Monovette, Sarstedt, Germany). An adequate volume of blood was aspirated into the S-Monovette tubes without adding anticoagulant. The blood samples were allowed to clot no more than two h at 5–10 °C. After clotting, blood was centrifuged at 3000 rpm for 15 min. Isolated serum was stored frozen at −18 °C in pre-cleaned glass tubes with polytetrafluoroethylene (PTFE) liner screw caps. All the samples were