Different Outcomes Associated with Prenatal and Postnatal Exposure to PCBs/PCDFs in Yucheng Children

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Abstract

In 1978-9, an episode of poisoning due to ingestion of rice-oil contaminated with polychlorinated biphenyls (PCBs)/polychlorinated dibenzofurans (PCDFs) occurred in central Taiwan. This study was conducted to determine the dose-response relationship between the health outcomes and the transplacental and lactational doses of PCBs/PCDFs in perinatally exposed children. The children born between June 1978 and March 1985 after their mothers' consumption of the contaminated oil were examined in 1985, 1992, and 1993. Symptoms reported by mothers and physical examination were recorded. Serum levels of PCBs/PCDFs were measured for 31 of these children in 1991 and for 56 of their mothers in 1992. Using serum half-life of 9.6 yr, 7.8 yr, and 10 yr for 2,3,4,7,8-pentachloro-dibenzofuran (PnCDF), 1,2,3,4,7,8-hexachloro-dibenzofuran (HxCDF), and total PCBs respectively, serum levels of PCBs/PCDFs in Yucheng children were back-extrapolated to one year of age and those in mothers to the time of childbirth. Extrapolated mother serum HxCDF level at child's birth was associated with white eye discharge, hyperpigmentation, deformed nail at birth; pigmented or deformed nails and lymphadenopathy in 1985; and deformed nails in 1992. Estimated mother PCB level at child's birth was associated with eyelid swelling, natal teeth, and irritated or swollen gum at birth; genital pigmentation and hypertelorism in 1985. Estimated child's PnCDF level at one year of age, mostly from lactational exposure, was associated with genital hyperpigmentation in 1985, and middle ear diseases in 1993. We concluded that in children perinatally exposed to PCBs/PCDFs, different outcomes might be associated with prenatal or postnatal exposure to different toxicants.

Introduction

Polychlorinated biphenyls (PCBs), polychlorinated dibenzofurans (PCDFs), and polychlorinated dibenzodioxins (PCDDs) are ubiquitous environmental pollutants found throughout the world and in all human populations. The primary route of human exposure to these chemicals is through contaminated food, such as meat and fresh water fish[1)]. PCBs and their heat degradation products have long half lives in human[2)], cross the placenta[3,4)] and are excreted in breast milk. Prenatal exposure to PCBs and tetrachloro-dibenzodioxin (TCDD) have caused significant teratogenic and developmental toxicities in animals[5)]. In the human, transplacental and possibly lactational exposure caused detectable

adverse effects[6]. Although in animal studies, different outcomes are associated with transplacental and lactational exposure, information on perinatally exposed human is lacking. This study was conducted to examine the dose-response relationship between the health outcomes and the transplacental and lactational doses of PCBs/PCDFs in exposed humans.

Subjects and Methods

In 1978-9, over 2000 Taiwanese people ingested rice oil contaminated with PCBs and PCDFs. They developed chloracne, hyperpigmentation, peripheral neuropathy, and other signs and symptoms which were later called Yucheng in Taiwan and were very similar to Yusho disease described in the 1970s in Japan. The outbreak and the discovery of etiology of Yu-cheng have been reviewed elsewhere[7]. The repeated heating partially degraded the PCBs into PCDFs and polychlorinated terphenyls and quarterphenyls (PCTs and PCQs)[8]. Some congeners of these PCDFs, e.g., 2,3,4,7,8-pentachloro-dibenzofurans (PnCDF), are highly toxic in animals, with potencies approaching that of the most toxic PCDDs, 2,3,7,8-tetrachlorodibenzodioxin (TCDD) in animal and *in vitro* studies[9]. Of 39 Yucheng babies in utero during the time the mothers ingested the contaminated oil, eight died in the first few years of life[7]. In September 1985, a field survey was conducted of 128 living children who were in utero during or after the period of oil contamination. History and physical examination of these children's development were performed and compared with 117 controls[10]. The parents of 118 children gave permission for their children to be followed yearly. For the follow-up study, another unexposed child was selected as a control for each Yucheng child, matching for neighborhood (same township), age (within 15 days for those under one year, and within one month for those older), sex, mother's age (within 3 years), parents' combined educational level (within about 3 years for the total), and occupation (within 1 class of 5 classes from unskilled laborer to professional)[11]. Skin examination was done in 1992[12] and ear examination was done in 1993[13]. Serum levels of PCBs/PCDFs were measured for 30 of these children in 1991[14] and for their mothers in 1992[15] by high resolution gas chromatography-high resolution mass spectrometry (HRGC/HRMS) using sample enrichment and isotope dilution. In brief, a mixture of C13-compounds, i.e., six 2,3,7,8-chlorinated PCDD congeners, six 2,3,7,8-chlorinated PCDF congeners plus 1,2,7,8-TCDF, and 3,3'4,4'-TCB, 3,3'4,4'5-PnCB, 3,3'4,4'5,5'-HxCB (IUPAC #'s 77, 126, 169) were added to the weighed samples. All non-polar organochlorine compounds including the non-ortho or planar, the mono-ortho, and the di-ortho PCBs, and the PCDFs/PCDDs in the serum were extracted with a mixture of ethanol, saturated aqueous ammonium sulfate, hexane. The weighed residue was used to estimate the serum lipid content after evaporation of the organic solvents. The samples were defatted with concentrated sulfuric acid, and purified by column chromatography on acid-base silica. The planar PCBs (pPCBs)/PCDFs/PCDDs were separated from the non-planar PCBs and other common organochlorines by chromatography on Florisil (second fraction; dichloromethane), followed by further fractionation on activated carbon. On the same purified extract, identification and measurement of pPCBs/PCDFs/PCDDs was carried out by HRGC/HRMS. To examine the dose-response relationship between serum levels and health outcomes, serum levels of PCBs/PCDFs in Yucheng mothers were back-extrapolated to the time of each child's birth, and serum levels of PCBs/PCDFs in Yucheng children were back-extrapolated to one year of age using half-life of 2,3,4,7,8-PnCDF, 1,2,3,4,7,8-HxCDF, and nonplanar PCBs as 9.6 yr, 7.8 yr, and 10 yr, respectively. In child, body weight change was also taken into consideration in calculating the one-year-old concentration. The mothers' levels of PCBs/PCDFs at child's birth was considered to be the major source of transplacental exposure, and lactational exposure was considered

responsible for the child's levels at one year of age. These levels were compared with history and physical findings of Yucheng children.

Results and Discussions

Extrapolated mother serum HxCDF level at child's birth was associated with white eye discharge, hyperpigmentation, deformed nail at birth, and acne scar by mother's history; pigmented or deformed nails, and lymphadenopathy by physical examination in 1985; and deformed nails in 1992. Estimated mother PCB level at child's birth was associated with eyelid swelling, natal teeth, and irritated or swollen gum at birth; genital pigmentation and hypertelorism by examination in 1985 (Table). Estimated child's PnCDF level at one year of age, mostly from lactational exposure, was associated with genital hyperpigmentation in 1985, and middle ear diseases by otolaryngologist's examination in 1993. We concluded that in children perinatally exposed to PCBs/PCDFs, different outcomes might be associated with prenatal or postnatal exposure to different toxicants.

Table. Relationship between extrapolated serum levels of PCBs/PCDFs and child's health outcomes by logistic regression analysis. Entities are logistic regression coefficients ($^{+}p<0.1$, $*p<0.05$, $**p<0.01$).

	Mother's level at childbirth			Child's level at one year		
	PnCDF[1]	HxCDF	PCBs	PnCDF	HxCDF	PCBs
By history						
White eye discharge at birth[2]		0.21*				
Eyelid swelling at birth			18.3+			
Teeth present at birth			24.8*			
Irritated or swollen gum at birth			38.1**			
Hyperpigmentation at birth		0.13+				
Deformed nail at birth		0.14+				
Acne scar		0.26*				
By examination in 1985						
Genital pigment			18.4+	2.4*		
Pigmented or deformed fingernail		0.20*				
Lymphadenopathy		0.17*				
Hypertelorism			18.7+			
Deformed nails in 1992		0.30**				
Middle ear disease in 1993				3.3*		

[1]PnCDF: 2,3,4,7,8-pentachloro-dibenzofurans, ng/g lipid base; HxCDF: 1,2,3,4,7,8-hexachloro-dibenzofurans, ng/g lipid base; PCBs: polychlorinated biphenyls, ng/g whole base.

[2]None of the above serum levels was associated with history of acne at birth, pneumonia/bronchitis in first 6 months, and hair loss, physical findings of tooth chipping, intraoral hyperpigmentation, head or face pigmentation, eyebrow flare, hirsutism, or unclear lung by auscultation in 1985.

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