Polychlorinated dibenzo-p-dioxins and dibenzofurans in blood and breast milk samples from residents of a schistosomiasis area with Na-PCP application in China

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ABSTRACT

Schistosomiasis has prevailed in some areas of China for a long time. Chinese technical sodium pentachlorophenate (Na-PCP) has been used to control the spread of snail-borne schistosomiasis since the 1960s. Polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs), impurities contained in the Na-PCP, enter the soil and may accumulate in the food chain. In order to evaluate their potentially harmful effects on local residents, 50 breast milk samples and 20 blood samples were collected in 2004 from residents in the Dongting Lake area, one of China's known schistosomiasis areas. Levels of 17 PCDD/F congeners were measured in all samples, and DNA damage was simultaneously assessed in blood samples. The PCDD/F congener distribution patterns in human tissue samples from the Dongting Lake area were similar to those in Na-PCP, and the octachlorodibenzodioxin (OCDD) congener was predominant in all samples. We also had a primary investigation that the breast milk WHO-TEQ associated with some factors such as: age, dietary habit, body mass index (BMI) and the total menses times. In blood samples, the samples with higher OCDD level had higher DDS (DNA damage score) values than those samples with low OCDD level, which indicated that the higher DNA damage value in general population might be caused directly or indirectly by PCDD/Fs. The results also indicated that the WHO-TEQ values in blood were associated with age ($r = 0.6$, $p = 0.007$).

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1. Introduction

Polychlorinated dibenzodioxins (PCDDs) and dibenzofurans (PCDFs) are ubiquitous environmental pollutants that have been found in human blood, breast milk and adipose tissue. Exposure to PCDD/Fs can result in adverse health effects including cancer, the disturbance of the reproductive and immune systems, and harmful effects on the skin (Pelclova et al., 2001; Jongbloet et al., 2002; Wang et al., 2003). PCDD/Fs accumulated in women's bodies have been found to be passed onto their babies both trans-placentally and lactationally (Päpke, 1998; Schecter et al., 1998). Due to lactational transfer, contaminant levels are expected to be higher in infants that are breastfed for a longer time, with a concomitant decrease of levels in the mother (Rogan et al., 1991). Exposure to higher background levels through breast milk may cause immune disorders such as atopic dermatitis (Yang et al., 2002). Although levels of PCDD/F exposure vary among countries, the benefits of breastfeeding were still deemed to outweigh the risk of dioxin exposure (LaKind et al., 2004; Nickerson, 2006; Li et al., 2009). Taking into account breast milk's nutritional, immunologic,

anticancer, and detoxifying effects, the World Health Organization (WHO) reiterated its recommendation for breastfeeding based on a reevaluation of dioxins and dioxin-like compounds in 1998 (Brouwer et al., 1998).

Asian schistosomiasis has been endemic in some regions of China for centuries. Dongting Lake in Hunan Province and Poyang Lake in Jiangxi Province have been areas with serious schistosomiasis. *Oncomelania hupensis* Gredler is the only lodging host of *Schistosoma japonicum* and plays a vital role in the spread of schistosomiasis. In China, large amounts of sodium pentachlorophenate (Na-PCP) have been sprayed around Dongting Lake and Poyang Lake since the 1960s to kill *Oncomelania hupensis* Gredler. It is well known that pentachlorophenol (PCP) and its derivatives (Na-PCP and PCPL) contain PCDD/Fs (predominantly HpCDD/Fs and OCDD/F) as impurities and are one of the main historic PCDD/F sources with contemporary relevance (Weber et al., 2008).

Together with the application of the PCP or other pesticides, PCDD/Fs have entered the environment from such activities (Bao et al., 1995). As a previous study demonstrated (Masunaga et al., 2001), a high level of dioxin had been detected in sediments in Japanese lakes and bays due to the extended and intensive use of agrochemicals such as PCP and chloronitrofen (CNP). In the Dongting Lake area, PCDD/Fs levels up to 890 pg I-TEQ g⁻¹ dry weight

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were also detected in sediment samples (Zheng et al., 1997). Furthermore, according to Weber's report (2008), PCDD/Fs from historic reservoir sources represent an important source of food contamination and human exposure. It has been shown that there could be correlation between the 2,3,7,8-congener patterns of HxCDDs in contemporary human breast milk from Japan (Tawara et al., 2006) and PCDD/F impurities in historical PCP products. Likewise, contaminants found in the Dongting Lake area may not only cause pollution against the environment but also affect the health of local people.

Human samples such as breast milk, serum/plasma and adipose tissue have been used as biomarkers to assess the extent of human exposure to PCDD/Fs and the associated risk they pose to human health (Tuinstra et al., 1994). Also, the Stockholm Convention relies on breast milk and human blood to evaluate the effectiveness of the treaty in reducing emissions of POPs (Li et al., 2009). In the current studies, 20 general population blood samples and 50 breast milk samples were collected in the Dongting Lake area and PCDD/F levels were determined. Simultaneously, DNA damage in blood samples was assessed. Based on the analysis data, both the correlation between the PCDD/F levels and DNA damage in blood samples and the correlations between the PCDD/F levels in breast milk samples and various factors such as demographic characteristics and diet before and after pregnancy were investigated.

2. Materials and methods

2.1. Human breast milk

Fifty breast milk samples were collected from the Dongting Lake area from February to April 2004. All of the participants completed questionnaires concerning maternal age, height and weight before pregnancy, the age of menarche, duration of residency in their present home region, diet including meat and fish consumption before and after pregnancy, and details of possible occupational exposures and personal health history. The 50 breastfeeding mothers were primiparas, between 20 and 33 years old and had lived in the community since they were born; the specimens were collected between 3 and 12 d postpartum.

2.2. Human blood

At the same time, twenty blood samples were also collected from the Dongting Lake area. All volunteers were asked to complete a health and dietary questionnaire. This included demographic characteristics (age, gender, height and weight), lifestyle (alcohol intake and tobacco usage) and occupational history. The 20 volunteers (8 men and 12 women) were between 30 and 58 years old and had lived in the community since they were born; they were farmers without any history of disease. Approximately 50 mL samples of venous blood were drawn from each volunteer into clean glass bottles. The plasma was separated by centrifugation and the obtained serum was immediately frozen at -20°C until analysis.

2.3. DNA damage

The comet assay reported by Singh et al. (1988) was used to evaluate DNA damage. Details of the method have been described previously (Yanez et al., 2004).

2.4. PCDD/F analysis

The fat content in breast milk was determined by the weight method reported by Patterson et al. (1987). In brief, 50 mL of breast

milk was spiked with a $^{13}\text{C}_{12}$ -PCDD/F standard solution (EDF-8999, Cambridge Isotope Laboratories, USA), and allowed to equilibrate at room temperature for 30 min. Then the sample was mixed with 10 mL of saturated potassium citrate and 50 mL of ethanol, and extracted with 20 mL diethylether and 60 mL hexane in a 500 mL separatory funnel. The extraction steps were repeated twice. The hexane phases were combined and washed with water, dried and weighed. The fat content of primipara breast milk was $2.7 \pm 0.36 \text{ g/50 mL}$.

The serum was spiked with a standard solution containing a mixture of $^{13}\text{C}_{12}$ -PCDD/Fs (EDF-8999, Cambridge Isotope Laboratories, USA), and allowed to equilibrate at room temperature for 30 min in a glass bottle with a cap. The sample was mixed with saturated ammonium sulfate and ethanol, extracted with hexane, and the hexane layer was separated. The extraction steps were repeated twice. The hexane extract was then washed with water and dried. The detailed steps have been described by Patterson et al. (1987). The extract was evaporated to dryness and constant weight, and the total extractable lipid was measured gravimetrically. The fat content of the blood samples ranged from 0.4% to 0.65%. After gravimetric determination, total extracted lipid was dissolved in hexane for clean up. The clean up, analysis and quality assurance procedures have been described by Zhao et al. (2005).

2.5. Quality control

Before the analysis of the breast milk and human blood samples, the cow milk and pig blood samples were separately performed to determine the initial precision and recovery. Recoveries of spiked cow milk samples with the EPA 1613-LCS mixture were in the range of 60–110% with RSD <20%. Recoveries of spiked pig blood samples with the EPA 1613-LCS mixture were in the range of 55–120% with RSD <20%. Blank determinations were performed concurrently with all analytical procedures. Furthermore, the ongoing precision and recovery were investigated. The results obtained for breast milk samples were in the range of 50–125% with RSD <30%. For human blood samples, the results obtained were in the range of 40–130% with RSD <30%. The results were satisfied the requirement of EPA method 1613.

3. Results and discussion

3.1. Levels of PCDD/Fs in human tissue

PCDD/F levels in individual breast milk and blood samples were quantified. In order to facilitate the comparison of results with previous studies, the WHO TEF 1998 scheme has been adopted (Van den Berg et al., 1998). Figs. 1 and 2 show the results given as mean $\pm$ standard deviation (SD) concentrations of PCDD/F in 1 g of fat from blood and breast milk. The PCDD/F congeners that were below the limit of determination were regarded as the limit values when the average and SD were calculated.

The total average WHO-TEQ value in serum specimens from the Dongting Lake area was 26 pg g^{-1} lipid and ranged from 5 to 109 pg g^{-1} lipid. In the 50 individual primipara breast milk samples, PCDD/F concentrations ranged from 0.43 to 11.4 pg g^{-1} lipid WHO-TEQ, with a mean value of 5.5 pg g^{-1} lipid WHO-TEQ. The subjects had lower total WHO-TEQ levels in breast milk than those reported in previous studies conducted in the general population at a comparable age (Johansen et al., 1996; Calvert et al., 1998; Schecter, 1998; Kiviranta et al., 2002; Wang et al., 2004). Possible reasons may be that (1) the predominant OCDD congener has little contribution to the total TEQ levels, and (2) the subjects have different dietary habits.

Fig. 1. PCDD/F levels in blood samples ($n = 20$) from general population in Dongting Lake area.

Fig. 2. PCDD/F levels in breast milk samples ($n = 50$) from Dongting Lake area.

3.2. Profiles of PCDD/F congeners in human tissue

In general, risk assessment of human exposure to dioxins is expressed via the total TEQ obtained from congener specific data. Therefore, attention should be paid to the congener distribution of PCDD/Fs and their contributions to the total TEQ in the breast milk and blood samples.

The profiles of PCDD/F congeners in the blood samples, primipara breast milk samples were similar to those observed in the Chinese technical Na-PCP product and those in blood and breast milk pool samples from the Poyang Lake area (Schecter et al., 1994) (Figs. 1–3). OCDD was the predominant congener and PCDD congeners make the main contribution to the total PCDD/Fs (blood, 80%; breast milk, 91%; Na-PCP, 87%). The patterns of PCDD/Fs in this study were quite different from those in breast milk samples from another area in China where Na-PCP had been never used (Sun et al., 2006), and those in human blood and breast milk sam-

Fig. 3. PCDD/F levels in Chinese Na-PCP products (Bao et al., 1995).

ples of some developed countries (Focant et al., 2002; Guan et al., 2006).

The congeners such as OCDD, OCDF, 1,2,3,4,7,8-HxCDD and 1,2,3,4,6,7,8-HpCDD were detected at higher levels than other congeners in the blood samples, and OCDD, 2,3,4,7,8-PeCDF, 1,2,3,4,6,7,8-HpCDD, 1,2,3,4,7,8-HxCDD, 1,2,3,4,7,8-HxCDF and 1,2,3,6,7,8-HxCDF were found in higher levels than other congeners in the breast milk. However, in blood samples, 1,2,3,7,8-PeCDD, 2,3,7,8-TCDD, 2,3,4,7,8-PeCDF and 1,2,3,4,7,8-HxCDD congeners contributed more to the total TEQ than other congeners. And in breast milk samples, the main contributors to the total TEQ were 2,3,4,7,8-PeCDF, 1,2,3,7,8-PeCDD, 2,3,7,8-TCDD and 1,2,3,4,7,8-HxCDF.

It should be also noted that 1,2,3,4,7,8-HxCDD and 1,2,3,4,7,8-HxCDF were respectively the main isomer of the toxic HxCDDs and HxCDFs in all test samples. Actually, except OCDD, 1,2,3,4,7,8-HxCDF and 1,2,3,4,7,8-HxCDD are also markers for processes using elemental chlorine and can therefore be found in several Organochlorine Pesticides such as in the PCP (Bao et al., 1995; Wolz et al., 2008). This result was similar to the Chinese technical Na-PCP applied in the Dongting lake area, but different from that obtained in a previous study (Masunaga et al., 2001) which reported that the 1,2,3,6,7,8-HxCDD was the main isomer of the toxic HxCDDs in some PCP products from Japan. This is because technical product PCP or Na-PCP from different manufacturers has different PCDD/F congener profiles. Among the 2,3,7,8-substituted HxCDFs, it was also observed the relative content of 1,2,3,6,7,8-HxCDF in blood and milk samples was higher compare to that observed in the Na-PCP. This may be due to the impact of other sources on the PCDD/F patterns.

In addition, variations between test samples and Chinese technical Na-PCP could be observed in lower chlorinated dioxin/furan isomer patterns. Averagely, the ratio between 1,2,3,7,8-PeCDD and 1,2,3,4,7,8-HxCDD in Na-PCP was far less than 0.5, yet larger than 0.5 in blood and breast milk samples in this study. For PeCDF, the concentration of 1,2,3,7,8-PeCDF was higher than that of 2,3,4,7,8-PeCDF in Na-PCP, yet smaller than that of 2,3,4,7,8-PeCDF in test samples. The reason may be due to the different biomagnification and transfer factors of the congeners. According to Malisch (2000), higher chlorinated PCDD/PCDF (e.g. OCDD or OCDF) have a much lower transfer factor from feed to milk fat compared to lower chlorinated TCDD/F or PeCDD/F (e.g. 2,3,7,8-TCDD, 1,2,3,7,8-PeCDD

Fig. 4. Correlation between OCDD levels and DNA damage in blood samples.

Fig. 5. Correlation between WHO-TEQ levels and age of volunteers in blood samples.

and 2,3,4,7,8-PeCDF), and the elevated levels of the congeners 2,3,7,8-TCDD and 1,2,3,7,8-PeCDD, 2,3,4,7,8-PeCDF, HxCDF and even OCDF in the milk samples were consistent with the different bioavailability of PCDD/F congeners.

3.3. Correlations between PCDD/F levels and DNA damage

DNA damage was primarily assessed in blood samples from the schistosomiasis area. The DDS value was found to be 12.89% on average (range: 7.84–18.96%), which is higher than the DDS value in the nearby uncontaminated area, which was determined to be 2.6%. There have been some studies reporting a correlation between 2,3,7,8-TCDD and DNA damage (IARC, 1997; Valic et al., 2004), but very few studies have showed the correlation between OCDD and DNA damage. However, some blood samples with higher OCDD levels had higher DDS values (Fig. 4), but OCDD content or WHO-TEQ levels were not significantly associated with data on DNA damage. Further studies are thus needed on this subject.

3.4. Correlations between PCDD/F levels and age

In addition to examining the correlation between the PCDD/F levels and DNA damage, the relationship between the human

Table 1

Correlations between PCDD/F levels and various factors in breast milk samples from Dongting Lake region.

	Correlation coefficient		p-Value (n = 50)	
	OCDD	WHO-TEQ	OCDD	WHO-TEQ
<i>Demographic characteristics</i>				
Maternal age	−0.058	−0.009	0.687	0.951
Menses time	−0.006	−0.009	0.968	0.949
BMI	−0.086	−0.164	0.552	0.255
<i>Dietary (times/month)</i>				
<i>Before pregnancy</i>				
Meat	−0.214	−0.269	0.135	0.059
Fish	0.173	−0.056	0.230	0.701
<i>After pregnancy</i>				
Meat	−0.093	0.091	0.520	0.528
Fish	0.104	−0.145	0.473	0.317

blood TEQ values/OCDD levels and the subject's age was examined. As shown in Fig. 5, the TEQ values increased with age. There was a positive correlation between TEQ concentration and age ($r = 0.6$, $p = 0.007$), indicating that the total PCDD/F level increased continuously over a life span. Chen et al. (2005) also reported that the serum levels of PCDD/Fs were positively associated with age. However, in contrast to this result, OCDD levels had no correlation with age ($p > 0.05$).

3.5. Correlations between PCDD/F levels in breast milk and various factors

Table 1 shows the correlations between PCDD/F levels in breast milk and various factors. The WHO-TEQ values and OCDD levels of breast milk samples were not correlated with demographic characteristics such as maternal age, BMI, or total menses times. The correlation between PCDD/F levels in breast milk samples and dietary habits was also investigated, because the major source of dioxin exposure for humans is through food, particularly food containing animal fat (Shaw and Connell, 1986; Schecter and Piskac, 2001). The results showed that PCDD/F levels had no significant association with maternal food consumption patterns, including fish and meat consumption, before or after pregnancy.

4. Conclusion

In summary, we could conclude historic use of PCP or Na-PCP (and probably other pesticides) seems an important source of PCDD/Fs for contemporary breast milk and therefore still a contamination source for babies. This study has provided an indication of the PCDD/F body burden of a group of childbearing women and the general population in the Dongting Lake area. The results indicated the positive correlation between the blood WHO-TEQ levels and the age of the volunteers was in agreement with most other studies. DNA damage levels were higher in some blood samples with higher OCDD concentrations than those with lower OCDD levels. The profile of PCDD/Fs in this study indicated the origin of the contamination was Na-PCP. Despite the TEQ in breast milk being low in this area, the exposure of babies to PCDD/Fs during the breast-feeding period is still a matter of concern.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.chemosphere.2010.02.042](https://doi.org/10.1016/j.chemosphere.2010.02.042).

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