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Risk assessment of methylmercury based on internal exposure and fish and seafood consumption estimates in Taiwanese children

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ABSTRACT

Fish and seafood consumption is a major source of human exposure to methylmercury (MeHg). This study evaluated the potential health risk of MeHg in Taiwanese children from fish and seafood consumption using a toxicokinetic model, hazard quotients and hazard indices (HIs). Two biomonitoring programs provided an important resource for blood specimens for assessing MeHg exposure in human populations. For internal exposures, total mercury (THg) was measured as a biomarker of MeHg in whole blood (WB) and red blood cells using inductively coupled plasma mass spectrometry and cold-vapor atomic absorption spectroscopy, respectively. The THg concentrations were used to estimate MeHg concentrations. Consumption of fish and seafood was assessed using the National Food Consumption database in Taiwan, while mercury concentrations in edible fish and seafood were collected from published studies in Taiwan. Our results indicated that 1) the highest median THg (representing estimated MeHg) daily intakes were found to decrease with increasing age in children consuming saltwater fish for age groups 0–3, 4–6, 7–12, and 13–18 years: 0.03 > 0.02 > 0.017 > 0.007 ($\mu g\,kg\text{-}BW^{-1}\,day^{-1}$); 2) HI greater than one, based on WB-THg, was found in 28% of 4–6-year-old children and 3) internal exposure estimates based on WB-THg, though slightly higher, were comparable to those based on fish and seafood consumption. The results support the use of dietary intake estimates as surrogates for internal blood MeHg levels in Taiwanese children to assess their exposure.

1. Introduction

Mercury (Hg) is a heavy metal widely used in industrial, medicinal, agricultural and other applications (Kidd and Batchelar, 2011). In addition to the human activities, Hg is released into the aquatic environment from natural sources (Ullrich et al., 2001). There are three forms of Hg in the aquatic ecosystems: elemental Hg (Hg^0), inorganic Hg and organic Hg, such as methylmercury (MeHg). Inorganic Hg released into the air and deposited in the environment can be transformed into MeHg, which bioaccumulates and biomagnifies in the aquatic food web (Kidd and Batchelar, 2011). MeHg has been a worldwide concern for its potential impact on human health and ecosystems because of its persistence, bioaccumulation potential, widespread occurrence and toxicity (WHO, 1990). The developmental neurotoxicity of MeHg in humans and its potential adverse effects on cardiovascular and immune system have been documented (WHO, 2008; Roman et al., 2011; Nyland et al., 2012).

Humans are exposed to MeHg mainly through the consumption of freshwater and marine fish and other animals that eat fish (e.g., marine mammals) (WHO, 2008). However, the extent of human MeHg exposure depends on the species of fish and frequency of consumption (Cho et al., 2014; Sheehan et al., 2014). Fish and seafood are primary sources of proteins and lipids (i.e., omega-3 fatty acids) essential for preventing hypertension and coronary heart diseases (Eshak et al., 2014; Sioen et al., 2007).

Human exposure to environmental chemicals can be estimated indirectly by calculating dietary intake, from aggregating data on MeHg concentrations in edible fish and seafood tissues and consumption rates of fish and seafood, or directly by quantifying MeHg in individual's biological materials. Biomarkers, such as total Hg (THg) levels in hair, whole blood (WB) or red blood cells (RBCs), have been used to reflect MeHg exposure (Groth, 2010; Karagas, 2012; WHO, 1990). Various studies have shown that 70–95% of THg in blood is in the form of MeHg (Mortensen et al., 2014) and bound to the sulfhydryl groups of

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hemoglobin (Weed et al., 1962). There is a strong linear correlation between MeHg in WB and MeHg in RBCs (Berglund et al., 2005; Oken et al., 2008). The presence of Hg in blood indicates recent or current exposure to Hg, and there is a direct relationship between Hg concentrations in human blood and consumption of fish contaminated with MeHg (WHO, 2008). In this study, all THg concentrations in blood were used to estimate MeHg concentrations. But references to toxicity, hazard and risk were associated with MeHg.

Recently, increased attention has been focused on the vulnerability of children and adolescents to environmental chemicals (Ha et al., 2014; Ochoa-Martinez et al., 2016). MeHg may disturb the development of the nervous system in children, such as impairing their ability to learn and process information (Kim and Lee, 2010). In Taiwan, data on MeHg exposure assessment in children and adolescents are underrepresented (Hsi et al., 2016; Lee et al., 2012).

Seafood is an essential part of the Taiwanese diet among all ages of the general population, and its consumption was estimated at approximately 48% of total animal food consumption during 2014 (Taiwan CoA, 2017). Accordingly, the present study was undertaken to determine: 1) internal THg dose based on blood measurements; 2) intakes of THg from fish and seafood consumption and THg levels in the regional fish/seafood species of interest using data collected from previous surveys, and 3) the hazard indices (HIs) based on internal doses and intake estimates from fish/seafood consumption.

2. Materials and methods

2.1. Internal exposure assessment

2.1.1. Subject data collection

Two Taiwan human biomonitoring programs, mainly for children and adolescents, were used to assess the internal doses: 1) the "Nutrition and Health Survey in Taiwan, NAHSIT" between 2005–2008 (7–18-year-olds) (Tu et al., 2007), and 2) the "Taiwan Maternal and Infant Cohort Study, TMICS" during 2003 (4–6-year-olds) (Wang et al., 2004). In the NAHSIT database, children aged less than 7 years were not sampled. The TMICS database was used to provide data for preschool children aged 4–6 years. For those aged over 7 years, WB was centrifuged to obtain the RBCs and plasma, for quantifying nutrients and lipids while Hg was only measured in RBC.

To assess internal exposure from blood measurements, preschool children aged 4–6 years, school children aged 7–12 years and adolescents aged 13–18 years were chosen. A total of 815 subjects were randomly stratified by age and gender according to the population distribution in Taiwan. The participants' inclusion criteria were described by Tsai et al. (2016). Institutional Review Board approvals from the Taiwan National Health Research Institutes were obtained for this study.

2.1.2. Determination of THg

For NAHSIT study, venous fasting blood specimens were obtained from children whose parents gave written informed consent in the TMICS study during 2003. A total of 10 ml WB was collected into a heparinized tube and centrifuged immediately. One milliliter of RBCs was transferred to a polypropylene tube and stored in liquid nitrogen. The samples were kept in at −20 °C during transportation to the Taiwan National Health Research Institutes laboratory (NHRI) and stored at −80 °C in Taiwan NHRI laboratory before analysis for THg. Detailed blood drawing and management flow were described by Tu et al. (2007).

THg levels were measured in 1 ml of WB from children aged 4–6 years using inductively coupled plasma mass spectrometry (ICP/MS, NexION 350X, Perkin-Elmer, UK) at the Linkou Chang Gung Memorial Hospital Department of Laboratory Medicine, Taoyuan, Taiwan. Duplicate samples were used to check the precision of the ICP/MS analysis. The relative standard deviation was less than 10%. All data used in the trend analysis met the certified laboratory's QA/QC standards. The detection limit of WB-THg was 0.02 μg L^{-1}.

Approximately 1 ml of the archived RBCs from children aged 7–18 years was used to quantify THg levels using an atomic absorption spectrometry (AAS, AAnalyst 100, Perkin-Elmer, USA). The instrument was equipped with a cold-vapor flow injection analysis system (CV-FIAS 100, Perkin-Elmer, USA) and located at the Taiwan NHRI. Intra-assay precision was performed, in triplicate, by calculating the average of the area under the curve, standard deviation and relative standard deviation. The blank and spiked RBC samples were processed and analyzed concurrently with blood samples, to check the accuracy of the method, which was 101.5%. The recovery ranged from 94 to 108% and the mean relative error for duplicate analyses was less than 6%. The detection limit of RBC-THg was 0.13 μg L^{-1}.

2.1.3. Blood Hg-based toxicokinetic (TK) model

We used a simple blood THg-based TK model developed by the WHO (1990) to assess MeHg body burden in children based on WB-THg concentrations that can be estimated according to the following formula:

$$D_b = \frac{c_b \times b \times V}{A \times f \times BW}, \quad (1)$$

where

D_b is the estimated daily intake dose of THg (representing estimated MeHg) (μg kg-BW^{-1} day^{-1}),

C_b is the THg concentration in the WB (WB-THg) (μg L^{-1}),

b is the elimination constant for MeHg (0.014 day^{-1}),

V is the blood volume (9% of BW),

A is the fraction of MeHg in diet that is absorbed (0.95),

f is the absorbed fraction of MeHg distributed to the blood volume (0.05), and

BW is the body weight (kg) of children estimated from the NAHSIT 2005–2012. The input values of the parameter (such as b, A, and f) were adopted from Legrand et al. (2010).

An empirical equation (Eq. (2), Kershaw et al., 1980) was used to calibrate RBC-THg concentration ($C_{b,RBC}$) and estimate the WB-THg concentration (C_b), as indicated below:

$$C_b = C_{b,RBC} \times h + C_p\,(1 - h), \quad (2)$$

where

$C_{b,RBC}$ is the RBC-THg concentration that is derived from this study in children aged 7–12 and 13–18 years (μg L^{-1}),

h is the hematocrit (39%) (Yen et al., 2008), and

C_P is the plasma-THg concentration.

Here, because the ratio of RBC-THg concentration ($C_{b,RBC}$) to plasma-THg concentration (Cp) is 6.3–1 (Berglund et al., 2005), the value of ($0.16 \times C_{b,RBC}$) can be used to substitute the C_P.

2.2. External exposure assessment

2.2.1. Fish and seafood consumption

The data on fish and seafood consumption, obtained from the Taiwan National Food Consumption Database (TNFCD), during NAHSIT 2005–2012, targeting different populations and time periods. The NAHSIT 2005–2012 utilized a 24-h recall method that was based on the amount of daily intake per person. Targeted populations were preschoolers (2005–2008), elementary school students (2005–2008), and junior and senior high-school students (2010–2011). Detailed information on the study subjects and the sampling design were described by the Taiwan Ministry of Health and Welfare (TMHW, 2015).

We assessed external exposure by reanalyzing the daily intake rates of fish and seafood in children 0–3, 4–6, 7–12, and 13–18 years old, individually. Three categories of fish and seafood were included: (1) freshwater fish (F), (2) saltwater fish (S), and (3) shellfish, cephalopods