Environment International 114 (2018) 1–11

Contents lists available at ScienceDirect

Environment International

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

Quantitative estimation of mercury intake by toxicokinetic modelling based on total mercury levels in humans

Abass K.[a,*,1], Huusko A.[a], Knutsen H.K.[b], Nieminen P.[c], Myllynen P.[d], Meltzer H.M.[b], Vahakangas K.[e], Rautio A.[a]

[a] Arctic Health, Faculty of Medicine; and Thule Institute, University of Oulu, Finland
[b] Division for Infection Control and Environmental Health, Norwegian Institute of Public Health, Norway
[c] Medical Informatics and Statistics Research Group, University of Oulu, Finland
[d] Northern Laboratory Centre NordLab, Oulu FI-90220, Finland
[e] Faculty of Health Sciences, School of Pharmacy/Toxicology, University of Eastern Finland, Finland

ARTICLE INFO

Handling Editor: Yong Guan Zhu

Keywords:
Mercury exposure
Food frequency questionnaire
Multi-compartment toxicokinetic modelling

ABSTRACT

Mercury is a toxic metal that can be disseminated into the environment from both natural and anthropogenic sources. Human exposure to the metal stems mainly from food, and more particularly from the consumption of fish and other seafoods. Examining dietary exposure and measuring mercury levels in body tissues are two ways of estimating exposure to mercury. In this study, we utilized a modelling system consisting of three linear toxicokinetic models for describing the fate of methyl mercury, inorganic mercury, and metallic mercury in the body, in order to estimate daily intake of mercury as measured through total mercury concentrations in the blood. We then compared the results stemming from our modelling system to those of the detailed semi-quantitative food frequency questionnaire (FFQ) of the Norwegian Fish and Game (NFG) Study, a project that focused on dietary mercury exposure.

The results indicate that toxicokinetic modelling based on blood levels gave higher daily intake values of mercury compared to those of the FFQ. Furthermore, the former had a wider range of estimates than the latter. The properties of the toxicokinetic model or limitations in the dietary exposure assessment could be posited as reasons for the differences between the respective methods. Moreover, the results may have been influenced by sources of mercury exposure that cannot be described as dietary, such as amalgam fillings.

1. Introduction

Mercury (Hg) is a toxic metal that can be passed into the environment via both natural and anthropogenic sources (ATSDR, 1999), Hg undergoes – in nature – a variety of intricate transformations and cycles between the interrelated systems of atmosphere, oceans and land. While elemental (metallic, Hg^0) Hg is aqueous, it swiftly dissipates into a hazardous vapor form (Bernhoft, 2012; Crespo-López et al., 2009; Gupta, 2012; Selin, 2011). Hg has the ability to bind to other elements (e.g. chlorine, sulfur, or oxygen), thereby forming inorganic mercurous (Hg^{1+}) and mercuric mercury (Hg^{2+}) salts; and inorganic Hg can be altered to organic Hg by microbial activity. Toxicologically, the most important organic form is methyl mercury (MeHg) (ATSDR, 1999).

Humans are primarily exposed to Hg through food, with consumption of fish and seafood being the major source (Sheehan et al., 2014). Another source of elemental Hg in humans is dental amalgam (Richardson et al., 2011). Conversely, the atmosphere and drinking water generally have such low levels of Hg that they cannot be seen as significant sources of exposure to the wider public (Amos et al., 2014; Jaffe et al., 2014; Quétel et al., 2014).

The degree to which Hg is toxic varies from case to case, depending on the form of the metal and its route of exposure (Bridges and Zalups, 2017; Ynalvez et al., 2016). Continual exposure to high levels of MeHg mainly affects the nervous system (Rice et al., 2014). Consequences of such exposure include disturbances in neurological function such as vision, hearing and muscle weakness, with children and unborn babies the groups most at risk (Sheehan et al., 2014; Solan and Lindow, 2014). Furthermore, a number of complex nervous system effects have been observed in populations that consume a good deal of seafood as part of their regular diet. Within such social groups, exposure to MeHg in the womb and/or soon after birth has been associated with issues such as altered memory, attention and language development in children

* Corresponding author at: Faculty of Medicine, Arctic Health, University of Oulu, FI-90014 Oulu, Finland.
E-mail addresses: khaled.megahed@oulu.fi, khaled.m.abass@gmail.com (K. Abass).
[1] Permanent address: Department of Pesticides, Menoufia University, P.O. Box 32511, Egypt.

https://doi.org/10.1016/j.envint.2018.02.028
Received 7 November 2017; Received in revised form 8 February 2018; Accepted 14 February 2018
0160-4120/ © 2018 Elsevier Ltd. All rights reserved.

(reviewed by Grandjean and Landrigan (2014)). However, it should be stressed that this connection has not been made in other studies (Myers et al., 2003; Nieminen et al., 2015; Orlando et al., 2014).

MeHg is freely absorbed from the gastrointestinal tract. In the human body, 1 to 10% of MeHg is absorbed from the GI tract and distributed to the blood. About 5% of MeHg is distributed to tissues within a few days and approx. 1% of the body's MeHg is found in one liter of adult human blood (70 kg) (WHO, 2000). Fish and other types of seafood are the main source of human MeHg exposure (Mergler et al., 2007). In fish, approximately 95% of MeHg is absorbed and distributed to tissues within thirty hours, with around 7% of the ingested dose accounted for by the blood level (Gupta, 2012). MeHg is visible in the body as soluble complexes mainly attached to the sulfur atom of thiol ligands. It passes the blood-brain barrier as a MeHg-L-cysteine complex, transported by the L-system (leucine preferring) amino acid carrier (Gupta, 2012). The MeHg is demethylated over an extended period to mercuric Hg in tissue macrophages, intestines, and the liver, including fetal liver. Bile and feces are significant as the major routes of excretion of MeHg, with 90% of MeHg being excreted as the ionic form in the latter after demethylation. While breast milk is another notable excretion route (Greenwood et al., 1978), the substance is yet to be detected in urine (CDC, 2016; Schindler et al., 2014; Smith et al., 1994). The results of different studies present an enormous variety in the elimination half-life of MeHg in humans, varying from 32 to 164 days (Miettinen et al., 1971; Smith et al., 1994) after an intravenous dose. In people who come into contact with MeHg on a regular basis, it takes approximately five elimination half-lives to reach a steady-state body burden (WHO, 2000).

In the case of inorganic Hg, toxicokinetics is different. There is an estimate of 7–15% for absorption of inorganic Hg from the gastrointestinal tract after an oral dose. The ingested ionic Hg quickly spreads to the blood and organs, while the vast majority of it is excreted in urine and smaller amounts through saliva, bile, sweat, and breast milk. Some is even exhaled.

There is a great deal of variety in the excretory half-lives of metallic and mercuric Hg, and this can be attributed to the organ of deposition and redox state. Values can range from a few days to anything up to several months. Mercuric Hg is primarily excreted via urine and stool (Berlin et al., 2007; Björnberg et al., 2005). Half-lives of metallic and mercuric Hg give the appearance of being multiphasic. When it comes to the former, human studies suggest an effective half-life of 42 days for 80% of an oral tracer dose, while the final 20% seems not to have a rate of excretion that can be measured (Rahola et al., 1971). This could point towards a mechanism yet to be defined or perhaps simply trapping in other organs.

Measuring Hg levels in body tissues, such as blood, urine, human milk, and hair, can help to estimate Hg exposure (Berglund et al., 2005; Björkman et al., 2007; Needham et al., 2011; Sheehan et al., 2014) as they provide an indication of the internal dose. This can be then be utilized to assess the likelihood of health problems (World Health Organization, 2003), although one must take great care in choosing the correct biomarker in order to accurately anticipate internal exposure (Berglund et al., 2005). In terms of the population of this study, Jenssen et al. (2012) have demonstrated the link between consumption of fish and seafood contained Hg, and total Hg concentrations in blood. According to the literature, currently the best proxy for long term MeHg exposure in individuals is the concentration of Hg in hair (Sheehan et al., 2014). Moreover, it is considered that an excellent biomarker for inorganic Hg is Hg level in urine (Berglund et al., 2005).

The key influences on the amount of urinary Hg excretion without occupational exposure are amalgam fillings and fish consumption (Apostoli et al., 2002; Dutton et al., 2013; Johnsson et al., 2005). Amalgam fillings tend to liberate Hg and up to 80% of this metallic Hg can be absorbed through lungs (ATSDR, 2009). After this, the body transports Hg quickly to major organs such as the brain, the liver and the kidneys. In blood, Hg either dissolves in serum or attaches to red cell membranes. In erythrocytes, metallic Hg is rapidly oxidized to mercuric Hg by catalase and hydrogen peroxide. This is a phase with a half-life of approximately two days, after which Hg functions in the same manner as mercuric Hg. Dutton et al. (2013) found that individuals with amalgam fillings had higher urinary Hg levels than those without. The average difference between the two groups was 0.55 μg Hg/g creatinine (0.04 μg Hg/g creatinine per amalgam surface).

During the course of this study we used a linear toxicokinetic model based on the total Hg level in blood for describing the fate of MeHg, inorganic Hg, and metallic Hg in the body, in order to estimate daily intake of Hg from food. The Norwegian Fish and Game (NFG) Study (part C) – a cross sectional study carried out by the Norwegian Institute of Public Health (NIPH) in 2003–2004 – provided us with the published biological data now used in this study for comparison and modelling (Jenssen et al., 2012). While the published literature includes several multi-compartment models for Hg (Farris et al., 1993; Smith et al., 1994), the models of Carrier et al. (2001a, 2001b) and Farris et al. (2008) stand out as being well-documented and for having been utilized in different studies (Noisel et al., 2011). Thus, we have applied both of these models in constructing a new combined model. The linear toxicokinetic model by Carrier et al. (2001a, 2001b) is used for modelling the fate of MeHg in the body, and the model of the Farris et al. (2008) for modelling the fate of inorganic Hg in the body. These models are connected through a blood circulation model and organic blood compartment. Due to the fact that models are linear and do not overlap, we consider the concurrent use of all three models to be justifiable.

2. Materials and methods

The population data are from the Norwegian Fish and Game Study (NFG) which was conducted in 2003–2004 (Jenssen et al., 2012). One of the aims of the original study was to measure total Hg in blood and urine and estimate the dietary exposure of Norwegians with a wide range of seafood and game consumption (Knutsen et al., 2008; Kvalem et al., 2009). Participants delivered blood samples and answered an extensive FFQ. Dietary information for the preceding 12 months was obtained by using a detailed semi-quantitative FFQ designed and validated for the Norwegian mother and Child Cohort study and contained 340 questions covering 255 different food items (Brantsæter et al., 2008; Meltzer et al., 2008). The present study included all participants who were ≥18 years with complete dietary intake information and measured total Hg concentration in blood and urine (n = 176). For three participants, the concentration of creatinine was lacking, and for these, the median level was imputed. Analytical methods used in analysis of blood and urine concentrations of Hg are described in Jenssen et al. (2012). In our study we have used total Hg concentrations in blood for modelling total Hg intake. In Table 1 the main characteristics of the study participants are presented as well as the distribution statistics of total Hg concentration in blood.

The dynamic equations in the toxicokinetic modelling system are solved by the Runge-Kutta method as a one linear differential equation system. The model was implemented using a Mathematica – package (Wolfram Research, Inc., Mathematica, Version 10.0, Champaign, IL) and run into the steady state condition.

Statistical visualization of results (box-and-whisker, residual and Bland-Altman plots) was conducted using the Mathematica – package, and the intra class correlation coefficient was calculated using IBM SPSS Statistics package.

2.1. Toxicokinetic modelling system of the study

The block diagrams of the toxicokinetic modelling system are presented in Fig. 1. The modelling system consists of the inorganic model of Farris et al. (2008) (model A) and the organic Hg model of Carrier et al. (2001a, 2001b) (models C and D). These models are connected through a blood circulation (model B) and organic blood compartment

Download English Version:

https://daneshyari.com/en/article/8855303

Download Persian Version:

https://daneshyari.com/article/8855303

Daneshyari.com