Hair Mercury Levels in Six Iranian Sub-populations for Estimation of Methylmercury Exposure: A Mini-review

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ABSTRACT
Background: Mercury is widespread and persistent in the environment. One organic form of mercury, Methylmercury (MeHg), can accumulate in the food chain in aquatic ecosystems and lead to high concentrations of MeHg in fish, which, when consumed by humans, can result in an increased risk of adverse effects. Currently, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) has established provisional tolerable weekly intakes (PTWIs) for total mercury at 5 µg/kg body weight and for methylmercury at 1.6 µg/kg body weight. Mercury concentration in blood or hair has been widely used for estimation of methylmercury exposure.

Materials and Methods: In this review article, we calculated methylmercury exposure from hair mercury levels among six subpopulations (i.e. students, dentists, dental nurses, women with amalgam fillings, pregnant women in Mahshahr, and Women of a port town, Mahshahr, Iran). Some of the experiments had been performed by this group in previous years.

Results: The mean exposure level (µg/kg bw/day) in three Iranian groups (dentists, pregnant women, and women in Mahshahr) was higher than RfD and PTWIs.

Conclusion: As people are exposed to methylmercury mainly through their diet, especially from fish and other marine species, pregnant women should reduce fish consumption, especially predatory fish, and dentists should use preventive measures (like masks and gloves).

Keywords: Hair mercury, Iran, Methyl mercury Exposure.

INTRODUCTION
Mercury exposure is considered a health hazard throughout the world (1). Exposure to toxic levels of mercury may result in impaired health in adults, toxicological effects on the developing central nervous system and general physiological systems of children, and adverse effects on the cardiovascular system (1, 2, 3). The major exposure way of methylmercury (MeHg) to human is consumption of fish and shellfish which accumulate MeHg through the food web in an aquatic environment. In human body, MeHg is rapidly absorbed by the gastrointestinal tract and is distributed in various tissues like the brain which eventually imposes hazardous neurotoxic effects (4, 5, 6, 7, 8, 9). Methylmercury (MeHg) is biomagnified throughout the food chain, and in the larger and long-lived predatory fish, MeHg reaches high concentrations (5, 10, 11). Therefore, when these animals are consumed by human, mercury concentrations in human tissues reach high levels (12). In human, 90-100% of MeHg is absorbed through the gastrointestinal tract (1, 5, 13), whereas inorganic salts of Hg are less readily absorbed (7–15%) (13). After absorption MeHg easily enters the bloodstream and spreads throughout the body. In the bloodstream, more than 90% of the methylmercury is accumulated in red blood cells and plasma, where it is mainly bound to the plasma proteins.

To date, three major episodes of methylmercury poisoning have occurred due to fish consumption. The first episode occurred near Minamata City on the shores of Minamata Bay, Kyushu, Japan, in the early 1950s. Effluent from a chemical factory was discharged into Minamata Bay where it accumulated in the
tissues of fish and shellfish that were dietary staples of the population (14). Another major episode occurred in Niigata, Japan in 1965 and was very similar to that in Minamata in the previous decade. Like the high concentration exposures in Japan, methyl mercury poisoning also occurred in Iraq in the 1960s and 1970s which lasted for approximately 6 months, respectively.

For these disastrous poisonings and the toxic nature of mercury, the EPA defines an RfD as an estimate of daily exposure in human populations that is likely to be without an appreciable risk of deleterious effects during a lifetime (15). The current EPA RfD for MeHg is 0.1 µg/kg-day. In fact, RfD is an important risk-characterization tool that is broadly used as a measure of the “acceptability” of population exposure levels. RfD for MeHg is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfD, the potential for adverse health effects increases (16).

The potential risk of health hazards to humans via mercury exposure has been estimated by examining the metal contents in breast milk, blood, hair, nail, adipose tissues, and various organs (17). The two biomarkers most frequently used to determine individual exposures to methylmercury are the Hg levels in scalp hair and in whole blood (18). Therefore, in toxicological studies, researchers use human blood and hair for monitoring Hg intake (18, 19). In some studies, hair and blood Hg are measured for comparison. More often, hair is used as the sole biomarker of exposure (20). Therefore, in the present study, we reviewed the hair mercury levels in different Iranian sub-populations to estimate the current MeHg exposure levels.

**MATERIALS AND METHODS**

Data needed for this review were collected from the previous study which had been done by this group in previous years. The method for mercury detection in hair sample generally was as described below.

After primary preparation, hair samples mercury was measured by the LECO AMA 254 advanced mercury analyzer according to ASTM standard No. D-6722. In order to assess the analytical capability of the proposed methodology, accuracy of total Hg analysis was checked by running three samples of Standard Reference Materials (SRM), National Institute of Standards and Technology (NIST), SRM 1633b, SRM 2709, and SRM 2711 in seven replicates (21, 22). Recovery was between 94.8 % and 105 %. The detection limit of the instrument used was 0.001 µg/g of dry weight.

**Calculation of exposure to methylmercury**

The concentration of mercury in hair is assumed to be 250 times the concentration in blood. In human, the steady-state mercury concentration in blood can be related to the average daily intake. Calculation of the steady-state ingestion (µg/kg bw/day) of methylmercury from a hair-mercury concentration requires two steps to be taken into account: conversion of the concentration in hair to that in blood, and conversion of the blood concentration into intake. A ratio of 250:1 was used to convert hair Hg concentration (mg of Hg/kg of hair) to blood Hg concentration (mg of Hg/L of blood) to derive the RfD critical dose. The exposure level to MeHg can be estimated from hair mercury level using the following formula (5, 15):

\[
d = \frac{C \times b \times V}{A \times f \times bw}
\]

\(C=\) mercury concentration in blood (µg/l) = hair level (µg/g) × 1000/250,
\(b=\) elimination rate constant (0.014/day),
\(V=\) blood volume (9% of body weight),
\(A=\) fraction of the dose absorbed (expressed as a unitless decimal fraction of 0.95),
\(f=\) absorbed fraction distributed to the blood (unitless, 0.05),
\(bw=\) body weight (kg), and
\(d=\) dose (µg/kg bw/day).
RESULTS

Through this formula, exposure level to MeHg was estimated among different Iranian

Table 1. Calculation of the daily MeHg exposure level (µg/kg bw/day) from mercury concentrations in hair among different groups of people in Iran

<table>
<thead>
<tr>
<th>Sample</th>
<th>Mean Hg in hair (mg/kg)</th>
<th>Estimated blood Hg concentration (µg/l)</th>
<th>Exposure level (µg/kg bw/day)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Students</td>
<td>0.45</td>
<td>1.8</td>
<td>0.0477</td>
<td>(31)</td>
</tr>
<tr>
<td>Dentists</td>
<td>2.84</td>
<td>11.36</td>
<td>0.3013</td>
<td>(34)</td>
</tr>
<tr>
<td>Dental nurse</td>
<td>0.92</td>
<td>3.68</td>
<td>0.0976</td>
<td>(34)</td>
</tr>
<tr>
<td>Women with amalgam fillings</td>
<td>1.28</td>
<td>5.12</td>
<td>0.1358</td>
<td>(17)</td>
</tr>
<tr>
<td>Pregnant women in Mahshahr</td>
<td>3.52</td>
<td>14.08</td>
<td>0.3734</td>
<td>(30)</td>
</tr>
<tr>
<td>Women of a port town</td>
<td>2.95</td>
<td>11.8</td>
<td>0.3130</td>
<td>(32)</td>
</tr>
</tbody>
</table>

The results show that the exposure level (µg/kg bw/day) in three Iranian groups (dentists, pregnant women, and women in Mahshahr) is higher than RfD. After multiplying the exposure levels (showed in Table 1) in 7 (weekdays) the exposure levels of MeHg in dentists, pregnant women and women in Mahshahr were found to be more than PTWI.

DISCUSSION

Hair mercury concentration among Iranian people and inhabitants of other countries

Almost all people have at least trace amounts of methylmercury in their tissues. Generally, these low levels of exposure are not likely to cause health hazards (16). Human body (70 kg) contains 13 mg of Hg on average (12). People are exposed to methylmercury mainly through their diet, especially from fish and other marine species. They may also be exposed to elemental or inorganic mercury through inhalation of ambient air during occupational activities and from dental amalgams. However, inhalation is the primary route of exposure for elemental mercury. The main pathways for human exposure to mercury are shown in Figure 1. The toxicokinetics (absorption, distribution, metabolism, and excretion) of Hg is highly dependent on the form of mercury to which a person has been exposed (16). The different factors that determine the occurrence of adverse health effects are the duration of exposure, route of exposure (inhalation, ingestion, or dermal contact), dose and chemical form of mercury, age of the person exposed (developing systems are susceptible), and dietary patterns of fish and seafood consumption. Methylmercury bio-accumulated in fish and consumed by pregnant women may lead to neuro-developmental problems in the developing fetus (16, 23, 24). Neurological symptoms include mental retardation, seizures, vision and hearing loss, delayed development, language disorders, and memory loss. In children, a syndrome characterized by red and painful extremities called acrodynia has been reported to result from chronic mercury exposure. Methylmercury is excreted slowly over a period of several months, mostly as inorganic mercury in the faeces (16).
In the present study, different groups of Iranian people, such as pregnant women, dentists, and students were studied. The studies have mainly focused on 3 organs, such as hair, nails, and saliva. Minimum and maximum levels of mercury in hair in different group were 0.07 µg/g and 53.56 µg/g. Research results showed that the main parameters affecting the amount of mercury in Iranians, include fish consumption, dental amalgam fillings which other studies conducted by other researchers present similar results (2, 9, 17, 19, 20, 25, 26, 27, 28, 29).

Although the average rate of per capita fish consumption in Iran (≈ 7 kg.) is less than the global average, fishermen who live in coastal areas may be consuming more than the average rate in Iran. Therefore, it is essential that more fish consumption limit is expressed in these areas.

Among Iranian dentists a significant difference related to the age, number of patients visited per day, use of masks, and fish consumption was observed (30). Zolfaghari et al.’ study (2007) on Iranian dentists concluded that the use of gloves had a significant effect on nails’ Hg. Furthermore, the masks had a significant effect on Hg in the hair and nails of dentists. The use of the mask resulted in significant decreases in the Hg levels among dentists because it can limit the inhalation of Hg particles through the nose (31). These data are similar to findings of Harakeh al.’ study (31). Therefore, precautionary measures could limit exposure to Hg among dentists.

**Figure 1.** The main pathways of exposure to mercury

Amalgam surfaces release mercury vapor into the mouth and lungs depending upon the number of amalgam fillings and other factors. The estimated average of daily absorption of mercury vapor from dental fillings varies between 3 and 17 µg mercury (16). When mercury vapors are inhaled, 80% is readily absorbed in the blood through the lungs and distributed in various organs, mainly in the kidneys where it may become incorporated before being excreted. According to the results of Fakor et al.’s study (2010) in Iran, individuals who have many amalgam fillings and consume large amounts of fish have higher levels of mercury than others. In 82 healthy Iranian women (mean age of 29 years; ranging from 20 to 56 years), the average mercury values in saliva and hair were 4.14 µg/l and 1.28 mg/kg, respectively. Conversely, in subjects without amalgam fillings, mercury concentrations in saliva samples were very low (almost zero). A comprehensive study showed that arithmetic mean (M) hair Hg concentrations
for people who ate fish 1-4 times each month were in several countries: Australia, 2.5 mg/kg; Canada, 1.2 mg/kg; China, 0.9 mg/kg; West Germany, 0.5 mg/kg; Hong Kong, 3.0 mg/kg; Italy, 1.5 mg/kg; Japan, 3.9 mg/kg; Monaco, 1.7 mg/kg; New Zealand, 1.3 mg/kg; Papua New Guinea, 1.8 mg/kg; South Africa, 1.9 mg/kg; U.K., 1.6 mg/kg, and USA, 2.4 mg/kg (19). The arithmetic mean hair mercury concentrations (mg/kg) and standard deviation (SD) of males and females from these 13 countries who ate fish once a month or less (A), twice a month (B), every week (C), and every day (D) were: M males, excluding D: 2.2 mg/kg (SD = 1.7, range = 0.1–9.2 mg/kg); M females, excluding D: 2.1 (SD = 1.6, range = 0.3–8.0 mg/kg); M(A): 1.4 (SD = 1.3, range = 0.1–6.2); M(B): 1.9 (SD = 1.5, range = 0.2–9.2); M(C): 2.5 (SD = 2.2, range = 0.2–16.2); M(D): 11.6 (SD = 6.6, range = 3.6–24.0) (19). Generally, the data are similar to mean hair mercury concentrations in Iran.

The Joint FAO/WHO Expert Committee on Food Additives (JECFA), which also evaluates chemical contaminants in the food supply, PTWIs for total mercury at 5 µg/kg body weight and for methylmercury at 1.6 µg/kg body weight (33, 16). The PTWI is the amount of a substance that can be consumed weekly over an entire lifetime without appreciable risk to health and is an end-point used for food contaminants. In the case of adults, JECFA considered that intakes of up to about two times higher than the PTWI would not pose risks of neurotoxicity in adults, although in the case of women of childbearing age, the intake should not exceed the PTWI in order to protect the embryo and fetus. However, the PTWI level, corresponding to hair mercury of 2.2 ppm, is lower than the lowest level which may cause adverse effects. The current PTWI is limited in pregnant women because fetus in utero is susceptible to MeHg. Normally, MeHg exposure should have no adverse health effects on most population even if it is several times higher than the PTWI. However, in pregnant woman, more attention should be paid to PTWI.

In another study focusing on obtaining the usual value of Pb, Cd, and Hg in normal human blood in Tehran, Iran (34) was found that mercury concentration in blood was 4.42 ± 0.42 µg/L (for a 60 Kg person equal to 0.2249 µg MeHg/kg bw/day or 1.57 µg MeHg /kg bw/week). This amount of Hg in blood exactly was within the range of estimated Hg in blood (mean 1.8-14.08 µg/L) in other studies in Iran.

CONCLUSION

Overall, hair mercury can contribute to such decisions as providing information on MeHg exposure levels. It is recommended that dentists use preventive measures (like masks and gloves) to protect themselves against MeHg exposure. In addition, it is essential that pregnant women and those who may become pregnant in Mahshahr reduce their fish meals, especially predatory fish, and consume fish that contain lower mercury levels. Moreover, it is suggested that governmental organizations produce a program to regulate the consumption of fish. However, not only the risk of mercury contamination, but also nutritional benefits may have to be considered when determining a regulatory standard for fish and shellfish consumption.

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