Does One Size Fit All? Revisit of the Hair-to-Blood Concentration Ratio for Evaluation of Mercury Exposure

Y.S. Lin, S. Ramasamy, J. Xue, A.M. Kadry, D. Segal, L. Kopylev

U.S. Environmental Protection Agency, Office of Research and Development

*Contact : Yu-Sheng Lin | Lin.Yu-Sheng@epa.gov | 202-565-7253

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Abstract

Background: Mercury (Hg) is considered by the World Health Organization (WHO) as one of the priority chemicals that affect human and ecologic health worldwide. Although WHO recommends a constant concentration ratio (250:1) of hair-to-blood Hg for assessing mercury exposure, the mechanisms underlying variability in that ratio remain to be elucidated. **Objective:** To identify key determinants of the hair-to-blood ratio of total mercury in US women. **Methods:** The data were obtained from 1306 women aged 16-49 years, each of whom provided valid measurements of blood and hair Hg, in the National Health and Nutrition Examination Survey 1999-2000. The impact on the hair-to-blood ratio of factors, such as age, race, body mass index, socioeconomic status, seafood consumption, liver function (assessed by serum levels of alanine aminotransferase [ALT] and aspartate aminotransferase [AST]), hair treatment, and smoking, are examined by linear regression analysis. Logarithmic transformations were applied when necessary. **Results:** Although hair Hg level is well correlated with blood Hg concentration (Spearman correlation=0.71, $p < 0.05$), there is a great deal of variability in the hair-to-blood Hg ratio in the study population (mean= 282; median [interquartile range] = 215 [129-330]). Of the physiological and sociodemographic parameters investigated, race is the leading factor followed by smoking in determining the hair-blood Hg ratio and while African-American women had the lowest estimated ratio, women in "All Other Races (including Asians)" have the highest hair-blood Hg ratio. Moreover, the hair-blood Hg ratio is approximately 13% higher among current and former smokers than their counterparts after covariate adjustment. On the other hand, the hair-blood Hg ratio among subjects with impaired liver function is 16% lower (p=0.08) than that in subjects with normal liver enzyme levels. **Conclusions:** Conclusions: While this study generally supports the WHO recommendation of using a hair-to-blood Hg ratio of 250 for mercury assessment, there is a range of interindividual variation in the ratio. As dose metric conversion of Hg biomonitoring data is important in estimating body burden of Hg exposure, further research is warranted to confirm our findings.

Background

Mercury (Hg) is a toxic metal that has been associated with a variety health issues including developmental neurotoxicity and cardiovascular diseases worldwide. While there are multiple routes of exposure to Hg, the most common way people in the U.S. are exposed to Hg is through the consumption of seafood and fish contaminated with methylmercury (MeHg).[1] Although the WHO recommends a hair-to-blood ratio of 250:1 for the conversion between Hg hair levels (μg/g) and those in whole blood (μg/L) for assessing Hg exposure,[2] there are reports of interindividual variation in biokinetics (e.g., biological half-life) and the hair-to-blood ratio for Hg.[1] As evaluation of Hg toxicity depends on the estimation of body burden from Hg exposure to humans, improved understanding of the causes underlying variability in hair-blood Hg ratio could inform the selection of dose conversion parameters in toxicity or exposure studies of Hg. The goal of this study is, therefore, to investigate the key determinants of the hair-to-blood Hg ratio using the data from a large-scale, nationally representative health survey of the U.S. non-institutionalized population, the National Health and Nutrition Examination Survey (NHANES).[3]

Materials and Methods

Data from NHANES 1999-2000 were used in this study. The protocol was approved by the NHANES Institutional Review Board, and all subjects provided written informed consent. A spot blood sample was collected from each subject and were stored at -70°C until analysis. Total mercury in whole blood was measured by flow injection cold vapor atomic absorption analysis with on-line microwave digestion. Prior to hair collection, subjects were asked whether their hair had been treated (e.g., hair dye) within the last month. Total hair mercury was analyzed according to the method described previously.[4] Demographic information (e.g., age, race, and seafood consumption) was self-reported. Serum liver enzyme activity was measured by the Beckman Synchron System (Beckman Coulter, Brea, CA). Impaired liver function was defined as elevation in serum ALT levels (> 30 U/L) and serum AST levels (>33 U/L). Two subjects with hair-blood Hg ratio > 5000 were excluded. Logarithmic transformations were applied to normalize the distributions of the continuous data whenever necessary. Generalized linear regression models were used to investigate crude and adjusted relationships of interest. Sampling weight was used in the analyses to account for the complex survey design (e.g., oversampling of minorities), survey non-response, and post-stratification to ensure that estimates are representative of the U.S. civilian non-institutionalized population. Statistical significance is set at 0.05.

Results

Table 1 presents the collected demographic characteristics and laboratory values for the subject cohort stratified by race-ethnicity groups. While White women are older, have higher socioeconomic status (assessed by poverty income ratio) and use more tobacco products, Black (African-American) women tend to have higher BMI, have more hair treatment, consume more seafood, and have higher levels of blood total Hg but lower hair Hg concentrations, as compared to other racial groups. This observation may be explained, at least in part, by a previous report that hair treatment (e.g., straightening, perm, etc.) can reduce total Hg in hair.[5] Thus, although hair Hg level is generally well correlated with blood Hg (Spearman correlation=0.71, $p < 0.05$, data not shown), there is a great deal of variability in the overall hair-to-blood Hg ratio in the study population (mean: 282; median [inter-quartile range, IQR]: 215 [129-330]). Figure 1 gives the distribution of hair-to-blood Hg ratio by the sociodemographic and physiological characteristics of 1306 study subjects. Of the parameters evaluated in the study, race is the leading factor and African-American women had the lowest estimated ratio as compared to other races. Recent hair treatment and smoking are also associated with the hair-to-blood Hg ratio (p<0.05). Nevertheless, only race and smoking remain statistically significant when all factors are considered together in the multivariate regression analysis (data not shown). While Black women have the lowest estimated ratio, women in "All Other Races" have the highest hair-blood Hg ratio. Moreover, the hair-blood Hg ratio is approximately 13% higher among current and former smokers than their counterparts after covariate adjustment. Interestingly, liver function becomes marginally significant (p=0.08) that hair-blood Hg ratio among subjects with impaired liver function is 16% lower than that in subjects with normal liver enzyme levels.

Table 1. Demographics of study participants (women aged 16-49 yrs)˟

Characteristics	Race-Ethnicity			
	White	Black	Hispanics	Others
N	485	245	427	149
Age (yrs)[a,˟]	34.3 (0.84)	32.2 (0.94)	29.6 (1.04)	30.0 (1.24)
BMI (kg/m^2)[a,˟]	25.6 (0.51)	29.7 (1.03)	27.4 (0.78)	26.1 (0.78)
Serum AST (U/L)[a]	18.7 (0.33)	17.8 (0.36)	19.3 (0.30)	18.3 (0.56)
Serum ALT (U/L)[a]	16.2 (0.27)	15.1 (0.27)	17.8 (0.61)	16.0 (0.78)
Blood Hg (μg/L)[a,˟]	0.88 (0.10)	1.29 (0.14)	0.86 (0.06)	1.24 (0.29)
Hair Hg (μg/g)[a,˟]	0.20 (0.03)	0.14 (0.02)	0.19 (0.01)	0.28 (0.06)
Seafood consumption (>4 times past month, %)[b,c,˟]	33.2 (4.20)	34.2 (2.70)	20.1 (3.04)	26.4 (5.32)
Poverty income ratio (>1.3, %)[b,d,˟]	79.6 (3.86)	62.6 (4.43)	52.1 (2.16)	55.8 (7.12)
Ever smoking (yes, %)[b,˟]	44.7 (3.03)	30.3 (4.43)	26.7 (2.49)	27.9 (4.29)
Recent hair treatment (yes) [b,e,˟]	32.7 (1.43)	64.4 (3.92)	26.7 (2.33)	39.7 (6.24)

[a]Median (SE), [b]Percentage (SE) in the category, [c]Include fish and shellfish. [d]Poverty income ratio (PIR), a federal poverty level index accounting for household income and number of household members, was used as the surrogate of social economic status (SES). A low PIR (≤1.3) is defined as low SES. [e]Hair had been given a permanent or been treated with a hair dye or straightener within the last month. ˟Statistically significant difference (p<0.05) across racial groups. SE, standard error.

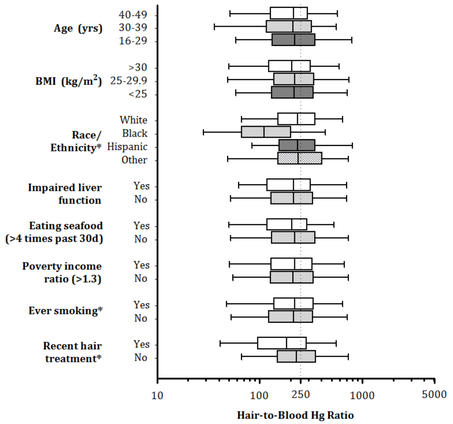

Figure 1. Distribution of hair-to-blood Hg ratio by demographic characterististics (box-and-whiskers plots with median and 5–95 percentile, univariate analysis). ˟Significant difference across groups.

Conclusions

Estimation of body burden of Hg based on biological monitoring of hair and blood Hg levels is important in assessing Hg toxicity. While this U.S. population-based study generally supports the WHO recommendation of using a hair-to-blood Hg ratio of 250 for Hg assessment, there is a range of interindividual variations in that ratio. A better understanding of causes that reflect the uncertainty and variability in the ratio could inform the adoption of dose conversion parameters for advancing Hg exposure assessment.

Selected references

[1] U.S. ATSDR, 1999. Toxicological Profile for Mercury. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. [2] World Health Organization (WHO). 1990. Environmental Health Criteria No 101: Methyl Mercury. Geneva: WHO. [3] U.S. Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey (NHANES): Questionnaires, Datasets, and Related Documentation. Hyattsville, MD. Available at: http://www.cdc.gov/nchs/nhanes.htm. [4] Pellizzari ED et al. Analysis of mercury in hair of EPA Region V population. J Expo Anal Environ Epidemiol. 1999;9:393–401. Nuttall KL. Interpreting hair mercury levels in individual patients. Ann Clin Lab Sci. 2006;36:248-61.

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