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Association of Blood and Hair Mercury with Blood Pressure and Vascular Reactivity

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Abstract

Background—Some studies suggest that high levels of blood and hair mercury (Hg) increase the risk of atherothrombotic diseases, an effect that may be explained by oxidative damage to the vascular endothelium.

Objectives—We tested whether high Hg levels impair the vasodilating function of the vascular endothelium or increase blood pressure.

Methods—We measured the association between high blood and hair Hg and brachial artery flow mediated vasodilation (FMD%), middle cerebral artery reactivity to CO_2 (MCAR%) and hypertensive status in 101 participants in the Wisconsin Sleep Cohort Study (mean age of 59.4 years; 52.5% male). Whole blood total Hg and hair total Hg were tested using inductively coupled plasma mass spectrometry and cold vapor atomic fluorescence spectrometry, respectively.

Results—Geometric mean blood and hair Hg were 1.16 μg/L and 270.1 ng/g. Blood and hair Hg were not significantly associated with FMD% and MCAR%. However, after adjustment for other risk factors, people in the upper quartile of blood Hg were 1.9 times (P=0.23) more likely to be hypertensive and those in the upper quartile of hair Hg were more than 4 times more likely (P=0.02).

Conclusion—High hair and blood Hg levels do not seem to influence vascular reactivity, but may increase the risk of hypertension.

Introduction

Exposure to mercury (Hg) is a growing public health concern in the United States. Approximately 8% of the US population is exposed to levels of methyl Hg (MeHg) above the US Environmental Protection Agency (EPA) allowable intake (0.5 to 0.1 μg/kg/day),[1] and 12% of women have hair Hg above the level at which stopping consumption of highly

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contaminated fish would be advisable (1.0 μg/g).[2] Evidence from epidemiologic studies suggest that people with high levels of urine, hair or toenail Hg have an increased risk of cardiovascular diseases.[3–4] However, the effects of MeHg accumulation on the cardiovascular system are still uncertain. Experiments in human cell models suggest that Hg could increase oxidative stress and alter the vasodilating function of the normal vascular endothelium, but no studies have been conducted in human subjects. We evaluated whether high levels of Hg are related to impaired endothelial function and blood pressure in human subjects. This could help understand the mechanisms underlying the effects of Hg accumulation on cardiovascular diseases.

Methods

We conducted a pilot study in a cross-sectional sample of 101 consecutive participants in the Wisconsin Sleep Cohort study (WSCS).[5] Data on vascular function measures (brachial artery flow mediated dilation [FMD]), middle cerebral artery reactivity to CO_2 (MCAR%), and blood pressure were obtained as part of the original study. Blood pressure was measured by conventional standard mercury sphygmomanometer using the left arm with an appropriate-sized cuff. This was measured after participants had been seated for 15 minutes. Two readings were recorded at 5-minute intervals and the average was used in the analysis. Total Hg concentration were measured in the Toxicology Section, Wisconsin State Laboratory of Hygiene, using cold vapor atomic fluorescence spectrometry (hair) and inductively coupled plasma mass spectrometry (blood).[6]

Levels of Hg were described and compared using geometric means. Linear regression was used to estimate the effect of Hg levels on brachial artery flow mediated vasodilation (FMD %) and middle cerebral artery reactivity to CO_2 (MCAR%). A large proportion of the participants were receiving antihypertensive medication (n=49). Excluding these participants from the analysis would have resulted in bias. Therefore, censored normal regression was used for the analysis of the association between Hg exposure and systolic and diastolic blood pressure to account for censored values due to antihypertensive treatment.[7] Logistic regression was used to estimate the effect of the exposure on hypertension. For all analyses, individuals in the upper quartile of the blood and hair Hg levels were considered exposed (≥496 ng/g for hair and ≥2.01 μg/L for blood Hg).

Results

We studied 101 individuals 44–75 years old (mean age 59.4; 52.5% male). Mean blood and hair Hg were 1.16 μg/L (95% confidence interval [95% CI]: 0.98, 1.38) and 270.1 ng/g (95% CI: 226.1, 322.6; Table 1). The correlation between hair and blood Hg was 0.90 (95% CI: 0.85, 0.93). Blood Hg was 29%, and hair Hg was 10% higher in men, but these differences were not statistically significant (P=0.13 and 0.59, respectively). Blood and hair Hg levels also tended to increase with age, but the trends were not statistically significant (P=0.75 and 0.26, respectively). Average fish intake was 23.5 ounces per month and was significantly correlated with total blood and hair Hg. In fact, compared to individuals in the lowest quartile of fish intake, blood Hg increased 60% (P=0.04), 83% (P<0.001), and 150%

(*P*<0.001), and hair Hg increased 76% (*P*=0.02), 112% (*P*<0.001), and 156% (*P*<0.001) in those in the second, third, and fourth quartiles of fish intake.

Crude levels of FMD, MCAR, and systolic and diastolic blood pressure were similar in exposed and nonexposed subjects (Table 2). In contrast, the crude prevalence of hypertension was 2.05 times higher in those in the upper quartile of blood Hg (95% CI: 0.79, 5.37) and 4.81 times higher in those in upper quartile of hair Hg (95% CI: 1.63, 14.19) than in those in lower quartiles of the corresponding Hg levels. After adjustment for gender, age, body mass index, and fish intake, individuals in the upper quartile of blood and hair Hg had considerably higher but non-statistically significant levels of systolic blood pressure (Table 3). Moreover, participants with the highest blood Hg levels were 1.93times more likely (*P*=0.23) and those with the highest levels of hair Hg were more than 4 times more likely to be hypertensive (*P*=0.02) than participants with lower Hg levels.

Discussion

The average total blood Hg observed in our study was about 40% higher than the national average (0.83 μg/L; 95% CI: 0.77–0.89),[8] and 10% of our subjects were above the EPA advisory level of 1.0 μg/g for hair Hg.

Hg accumulation can affect endothelial function by inhibiting NO synthesis,[9] and by increasing reactive oxygen species,[10] lipid peroxidation,[3] and TNF-α and interleukin-6.[11] However, we found no evidence that Hg has an effect on FMD or MCAR, 2 clinical measures of endothelial function. This discrepancy could be the result of differences in acute exposures to Hg, as used in cell and animal models, and cumulative exposures, as evaluated in our study.

Individuals in the highest quartile of blood and hair Hg had higher systolic blood pressure and were significantly more likely to be hypertensive. An effect of Hg on blood pressure could be the result of kidney toxicity,[12] although Hg-related renal dysfunction of clinical significance seems to be rare.[13] Little additional data exists on the effect of Hg on blood pressure in adults. In a sample of 1240 women aged 16–49 who participated in the National Health and Nutrition Examination Survey (1999–2000), Vupputuri et al[14] found a significant increase in systolic blood pressure with increasing levels of blood total Hg, but only among non-fish consumers: 1.83 mm Hg for each increase of 1.3 μg/L in blood total Hg (95% CI: 0.36, 3.30; interaction *P*=0.02). The cross-sectional nature of the data is an important limitation of our study since we can not establish if fish consumption and, therefore, Hg levels were a consequence of dietary changes following the diagnosis of hypertension. Altogether the available information suggests that Hg exposure could increase the risk of hyper-tension, but this remains uncertain due to the lack of prospective data.

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Table 1

Characteristics of the Studied Population

Variable	Mean	95% Confidence Interval
Age (years)	59.4	58.0, 60.9
Body mass index (kg/m^2)	32.0	30.8, 33.3
Systolic BP (mm Hg)	123.3	120.7, 126.0
Diastolic BP (mm Hg)	79.1	77.1, 81.0
FMD%	6.0	5.0, 7.0
MCAR%	5.0	4.5, 5.5
Total hair Hg (ng/g)	270.1	226.1, 322.6
Total blood HG (μg/L)	1.16	0.98, 1.38

Abbreviations: Hg, mercury; BP, blood pressure; FMD, brachial artery flow mediated dilation; MCAR, middle cerebral artery reactivity to CO_2.

Table 2

Crude Effects of Blood and Hair (Hg levels on Clinical Measures of Endothelial Function and Blood Pressure

	Blood Hg Exposed			Hair Hg Exposed		
	No	Yes[a]	*P*-value	No	Yes[a]	*P*-value
FMD (%)	5.8	6.7	0.48	6.1	5.7	0.77
MCAR (%)	5.1	4.7	0.56	5.1	4.7	0.58
Systolic BP (mm Hg)	122.8	125.5	0.41	122.6	126.0	0.29
Diastolic BP (mm Hg)	79.3	78.7	0.81	79.0	79.4	0.86
Hypertension (%)	49.3	66.7	0.14	79.2	44.2	<0.01

[a] ≥496 ng/g for hair and ≥2.01 μg/L for blood Hg.

Abbreviations: Hg, mercury; BP, blood pressure; FMD, brachial artery flow mediated dilation; MCAR, middle cerebral artery reactivity to CO_2.

Table 3

Difference in Vascular Function Parameters in Subjects in the Upper and Lower Quartiles of Mercury (Hg) Levels

	Blood Hg		Hair Hg	
	Difference[a]	*P*-value	Difference[a]	*P*-value
FMD%	0.47 (−0.50, 1.42)	0.34	0.50 (−1.81, 2.81)	0.67
MCAR%	0.14 (−0.40, 0.67)	0.61	−0.85 (−2.21, 0.51)	0.22
Diastolic BP (mm Hg)	1.0 (−4.8, 6.8)	0.74	1.47 (−4.4, 7.3)	0.62
Systolic BP (mm Hg)	7.7 (1.0,16.5)	0.08	6.2 (−2.4,14.9)	0.16
Hypertension[b]	1.93 (0.66, 5.65)	0.23	4.19 (1.28, 13.76)	0.02

[a] Adjusted for gender, age, body mass index, fish intake, and hypertension (95% CI).

[b] Odds ratio adjusted for gender, age, body mass index, and fish intake. Hypertension defined as systolic BP≥140 or diastolic BP≥90 mm Hg or receiving antihypertensive drugs.

Abbreviations: Hg, mercury; FMD, brachial artery flow mediated dilation; MCAR, middle cerebral artery reactivity to CO_2; BP, blood pressure.