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Assessment of the Cardiac Autonomic Nervous System in Mercury-Exposed Individuals via Post-Exercise Heart Rate Recovery

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Key Words

Mercury · Cardiac autonomic dysfunction · Heart rate recovery · Exercise stress testing

Abstract

Objective: The aim of this study was to assess exercise heart rate recovery (HRR) indices in mercury-exposed individuals when evaluating their cardiac autonomic function. ***Subjects and Methods:*** Twenty-eight mercury-exposed individuals and 28 healthy controls were enrolled. All the subjects underwent exercise testing and transthoracic echocardiography. The HRR indices were calculated by subtracting the first- (HRR1), second- (HRR2) and third-minute (HRR3) heart rates from the maximal heart rate. The two groups were evaluated in terms of exercise test parameters, especially HRR, and a correlation analysis was performed between blood, 24-hour urine and hair mercury levels and the test parameters. ***Results:*** The mercury-exposed and control groups were similar in age (37.2 ± 6.6 vs. 36.9 ± 9.0 years), had an identical gender distribution (16 females and 12 males) and similar left ventricular ejection fractions (65.5 ± 3.1 vs. 65.4 ± 3.1%). The mean HRR1 [25.6 ± 6.5 vs. 30.3 ± 8.2 beats per min (bpm); p = 0.009], HRR2 (43.5 ± 5.3 vs. 47.8 ± 5.5 bpm; p = 0.010) and HRR3 (56.8 ± 5.1 vs. 59.4 ± 6.3 bpm; p = 0.016) values were significantly lower in the mercury-exposed group than in the healthy controls. However, there were no significant correlations between blood, urine and hair mercury levels and exercise test parameters. ***Conclusions:*** Mercury-exposed individuals had lower HRR indices than normal subjects. In these individuals, mercury exposure measurements did not show correlations with the exercise test parameters, but age did show a negative correlation with these parameters. Therefore, cardiac autonomic functions might be involved in cases of mercury exposure.

Introduction

Mercury is considered to be one of the most toxic heavy metals in the world and exposure can occur by various means [1]. Many studies that have researched mercury-related health problems were carried out in study populations mostly exposed through the consumption of mercury-contaminated fish and other seafood [2, 3]. Other sources important for mercury toxicity include occupational exposure, dental amalgam, fluorescent lamps,

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thermometers and batteries [4, 5]. The toxic effects on the central nervous system of mercury are well known [6]; however, epidemiological and experimental studies have recently reported an association between mercury and the cardiovascular system, such as coronary heart disease and myocardial infarction [7, 8], hypertension [9], generalized atherosclerosis and cerebrovascular accident [9, 10].

The cardiac autonomic nervous system (ANS) plays an important role in maintaining cardiovascular functions and is based on a sensitive balance between the parasympathetic and sympathetic systems [11]. There are several tools used for evaluating and also measuring cardiac ANS functions, including heart rate recovery (HRR), heart rate variability (HRV) and baroreflex sensitivity [12]. HRR, after graded exercise, is one of the most commonly used techniques to represent autonomic activity [13, 14]. Sympathetic activity increases during exercise and diminishes during recovery; hence, previously suppressed parasympathetic activity becomes dominant during recovery and reduces the heart rate (HR) [15]. This decline is blunted by a decreased myocardial function and reduced exercise capacity [16, 17]. An abnormal HRR independently predicts increased cardiovascular and all-cause mortality rates [18]. ANS functions have previously been assessed in mercury-exposed individuals using HRV, such as in the study by Lim et al. [12] which showed that mercury might affect the cardiac ANS through parasympathetic dysfunction even at low mercury exposure levels. However, HRR in mercury-exposed individuals has not been evaluated. Therefore, the aim of the present study was to evaluate ANS function using HRR indices in mercury-exposed individuals compared to control subjects.

Subjects and Methods

Study Population

This cross-sectional study was performed at Ankara Occupational Diseases Hospital between March 2014 and March 2015. Initially, 34 mercury-exposed individuals were screened for inclusion into the study protocol. A complete history was taken and a physical examination was performed in all the subjects. Height (in meters) and weight (in kilograms) were measured and used to calculate the body mass index as weight/height squared. The measurement of blood pressure (BP) was performed in each participant using the left arm following approximately 5 min of seated rest. Standardized mercury sphygmomanometers were used. Korotkoff phase I (appearance) and phase V (disappearance) sounds were recorded for systolic BP and diastolic BP, respectively. The exclusion criteria were individuals with diabetes mellitus, hypertension, dyslipidemia, chronic renal failure, chronic liver disease, neurological diseases, known coronary artery or structural heart disease, pulmonary hypertension, rhythm abnormalities, any drug use, particularly those that have effects on the autonomic system (such as antiarrhythmics including beta-blockers and calcium antagonists, tricyclic antidepressants, antipsychotics and diuretics) and smoking. Based on the exclusion criteria, a total of 28 mercury-exposed individuals were found to be suitable and were included in our study. Twenty-eight age- and sex-matched volunteers with no previous history of cardiac disease served as the control group. The mercury-exposed and control population included in the study were all white Turks. In the mercury-exposed group 15 individuals were dentists and the source of mercury was the production and clinical application of dental amalgam. Three individuals were chronically exposed to mercury after a fluorescent light break at home or work. Ten had occupational exposure to mercury in an industrial environment. All the participants were over the age of 18 years. Electrocardiography (ECG), treadmill exercise testing and transthoracic echocardiography were performed in all of the participants. The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all subjects.

Treadmill Exercise Testing

Treadmill exercise testing was conducted in all the individuals using the modified Bruce protocol. Mason-Likar modification of 12-lead ECG [19] was continuously recorded at a paper speed of 25 mm/s. After the participants had all achieved an exercise time of more than 6 min, and a maximum HR (MHR) of at least 85% of the age-predicted MHR response (peak workload), they spent at least 3 min of recovery without a cool-down period in a sitting position. Exercise capacity was measured in metabolic equivalent levels (METs) at peak exercise. The HRR indices were calculated by subtracting the first-, second- and third-minute HR from the MHR obtained during stress testing and were designated as HRR1, HRR2 and HRR3, respectively. Exercise-onset HR change was calculated by subtracting the resting HR from the HR in the first minute of exercise. The HR reserve was determined by the change in HR from rest to peak exercise during the exercise test. An impaired HRR was described as a decrease in HR from peak exercise to 1 min of recovery of <12 beats per min (bpm) [18].

Transthoracic Echocardiography

Standard echocardiographic imaging was performed in the left lateral decubitus position using a commercially available system (Vingmed System Five GE ultrasound, Horten, Norway). Images were obtained using a 2.5- to 3.5-MHz transducer in the parasternal and apical views. Left ventricular end-diastolic and end-systolic diameters were determined with M-mode echocardiography under two-dimensional guidance in the parasternal long-axis view, according to the recommendations of the American Society of Echocardiography [20]. The left ventricular ejection fraction was calculated from the apical four-chamber view, according to the modified Simpson's rule [20]. In the parasternal long-axis views, the maximal left atrium anterior-posterior diameter and right ventricular mid-cavitary diameter in the apical four-chamber view at the end diastole were measured. Pulmonary systolic arterial pressure was estimated using CW Doppler as the peak regurgitation velocity plus an assumed right atrial pressure in relation to the size and respiratory excursion of the inferior cava vein visualized in the subcostal view [20].

Laboratory Analysis

Blood samples from the antecubital vein were taken after an overnight fast of at least 12 h. Whole blood samples were drawn in 10 mm of ethylenediaminetetraacetic acid containing trace elements tubes (BD Vacutainer, Franklin Lakes, N.J., USA). The collected blood was immediately centrifuged at 4,000 rpm for 10 min to separate the plasma from red blood cells. All biochemical parameters were analyzed in the same sample. Each individual was asked to collect 24-hour urine samples and instructed not to collect urine from the first urination after waking up on the morning of the day of collection. The samples were collected in sterile plastic pots during each urination thereafter, including the first urination upon waking the following morning, and then diluted to 1 in 10 with 5% nitric acid solution. Hair samples weighing 0.1 g were cut from the top region of the scalp with surgical scissors, as close as possible to the skin, and then placed in a labelled envelope and stored at room temperature. The blood and hair samples were digested using a microwave-induced acid digestion method. A standard solution of metallic mercury was prepared by a dilution of certified standard solutions (High Purity Standards, Charleston, S.C., USA) and two levels of quality control materials were used (Seronorm, Billingstad, Norway). Mercury levels were determined in the whole blood, 24-hour urine and hair samples using Inductively Coupled Plasma Mass Spectrometry (ICP-MS; 7700 series, Agilent, Tokyo, Japan).

Statistical Analysis

Statistical analyses were performed using SPSS 20 for Windows (SPSS Inc., Chicago, Ill., USA). Numerical variables with a normal distribution are presented as the mean ± standard deviation (SD) and those with a skewed distribution are presented as the median and interquartile range (IQR). Categorical variables are presented as the number and percentage. For numerical variables, an independent sample's t test and Mann-Whitney U test were used for intergroup comparisons. The χ^2 test and Fischer's exact χ^2 test were used for the comparison of categorical variables. The relationship between numerical variables was evaluated using Pearson's or Spearman's correlation tests. Multiple linear regression analysis was used to determine predictors of risk factors thought to be related to first-, second- and third-minute HRR parameters in the mercury-exposed group. Two-tailed p values <0.05 were considered to be statistically significant.

Results

General Characteristics of the Study Population

The baseline characteristics and echocardiographic parameters of our study population are shown in table 1. There was no statistically significant difference between the mercury-exposed and control groups in terms of baseline demographic and clinical characteristics. All mercury-exposed and control group participants had normal values for left ventricular end-diastolic diameter (43.6 ± 3.3 vs. 44.2 ± 2.6 mm; p = 0.64), left ventricular end-systolic diameter (27.7 ± 3.7 vs. 28.1 ± 2.9 mm; p = 0.43), left ventricular ejection fraction (65.5 ± 3.1 vs. 65.4 ± 3.1%; p = 0.96) and systolic arterial pressure (24.0 ± 5.0 vs. 23.3 ± 6.4 mm Hg; p = 0.65). The right ventricular and left atrium diameters were also found to be similar in the two groups. The laboratory and serological data of the two groups are shown in table 2.

Table 1. Demographic characteristics, BP and ECG parameters of the groups

Variable	Mercury-exposure group (n = 28)	Control group (n = 28)	p value
Age, years	37.2±6.6	36.9±9.0	0.49
Female/male	16/12	16/12	0.99
Body mass index	24.3±4.4	26.3±4.0	0.07
SBP, mm Hg	117.3±12.1	116.4±13.0	0.89
DBP, mm Hg	72.4±8.9	69.1±7.8	0.14
End-diastolic diameter, mm	43.6±3.3	44.2±2.6	0.64
End-systolic diameter, mm	27.7±3.7	28.1±2.9	0.43
LVEF, %	65.5±3.1	65.4±3.1	0.96
sPAP, mm Hg	24.0±5.0	23.9±5.2	0.82
Right ventricle diameter, cm	2.56±0.2	2.57±0.2	0.94
Left atrium diameter, mm	31.4±3.7	31.5±3.5	0.95

Numerical variables are expressed as the mean ± SD, unless otherwise indicated. DBP = Diastolic BP at baseline; SBP = systolic BP at baseline; sPAP = systolic pulmonary arterial BP.

In the mercury-exposed group the median mercury exposure time was 12 months (range 2–30, IQR 12). The median blood mercury levels in the mercury-exposed and control groups were 14.8 μg/l (IQR 4.1) vs. 0.9 μg/l (IQR 0.5; p < 0.001), respectively. The median 24-hour urine mercury levels were 51.4 μg/l (IQR 137.2) vs. 1.3 μg/l (IQR 0.6; p < 0.001), respectively, and the median hair mercury levels were 2.1 μg/g (IQR 3.0) vs. 0.2 μg/g (IQR 0.1; p < 0.001), respectively. In the mercury-exposed group, females had a longer mercury exposure time (median 12 months, IQR 7) compared to males (median 6 months, IQR 11) with a statistical significance of p = 0.04. On the other hand, in the mercury-exposed group there were no significant differences between females and males in blood mercury levels (median 13.9 μg/l, IQR 3.1 vs. median 15.5 μg/l, IQR 3.8; p = 0.08), 24-hour urine mercury levels (median 70.3 μg/l, IQR 138.2 vs. median 27.1 μg/l, IQR 109.5; p = 0.24) and hair mercury levels (median 2.4 μg/g, IQR 3.0 vs. median 1.4 μg/g, IQR 3.0; p = 0.28).

Table 2. Laboratory and serologic data of the two groups

Variable	Mercury-exposed group (n = 28)	Control group (n = 28)	p value
Hemoglobin, g/dl	14.3±2.2	14.2±1.0	0.82
White blood cells, /μl	6,793±1,433	7,082±1,455	0.45
Platelet count, /μl	249,200±47,500	247,400±46,800	0.88
Creatinine, mg/dl	0.81±0.12	0.79±0.19	0.77
ESR, mm/h	2 (3)	3 (4)	0.28
ALT, U/l	19.6±6.9	20.4±8.2	0.57
AST, U/l	19.3±6.6	23.2±7.4	0.06
TSH, μIU/ml	1.4 (1.1)	1.2 (0.8)	0.42
Triiodothyronine, pg/ml	2.7±0.3	2.5±0.3	0.06
Thyroxine, ng/dl	1.1±0.1	1.1±0.1	0.48
Blood mercury, μg/l	14.8 (4.1)	0.9 (0.5)	<0.001*
Urine mercury, μg/l	51.4 (137.2)	1.3 (0.6)	<0.001*
Hair mercury, μg/g	2.1 (3)	0.2 (0.1)	<0.001*

Numerical variables are expressed as the mean ± SD or median (IQR); categorical variables are expressed as n (%). * p < 0.05. ESR = Erythrocyte sedimentation rate; ALT = alanine aminotransferase; AST = aspartate aminotransferase; TSH = thyroid-stimulating hormone.

Exercise Test Parameters and HRR Indices

All of the mercury-exposed and control subjects had a normal resting 12-lead ECG. All of the participants completed the exercise stress test without any complications. No rhythm abnormalities or ischemic changes were observed during the ECG stress test in either group. The duration of the treadmill exercise test (8.9 ± 2.7 vs. 9.1 ± 2.4 min; p = 0.77), peak exercise capacity (12.1 ± 2.5 vs. 12.3 ± 2.8 METs; p = 0.77), HR reserve (86.5 ± 18.2 vs. 92.3 ± 16.5 bpm; p = 0.16), baseline HR (78.3 ± 9.4 vs. 75.7 ± 10.0 bpm; p = 0.29), first-minute exercise-onset HR (14.3 ± 2.9 vs. 15.2 ± 2.6 bpm; p = 0.26) and MHR (164.5 ± 14.4 vs. 166.3 ± 11.2 bpm; p = 0.47) were similar in the mercury-exposed and control groups, respectively (table 3). The mean HRR1 (25.6 ± 6.5 vs. 30.3 ± 8.2; p = 0.01), HRR2 (43.5 ± 5.3 vs. 47.8 ± 5.5; p = 0.01) and HRR3 (56.8 ± 5.1 vs. 59.4 ± 6.3; p = 0.01) values were significantly lower in the mercury-exposed group than in the control group (fig. 1).

Table 3. Exercise test parameters and HRR indices of the groups

Variable	Mercury-exposed group (n = 28)	Control group (n = 28)	p value
Duration of exercise test, min	8.9±2.7	9.1±2.4	0.77
Resting HR, bpm	78.3±9.4	75.7±10.0	0.29
MHR, bpm	164.5±14.4	166.3±11.2	0.47
Exercise-onset HR, bpm	14.3±2.9	15.2±2.6	0.26
HR reserve, bpm	86.5±18.2	92.3±16.5	0.16
Maximal SBP, mm Hg	168.6±19.2	166.3±17.1	0.63
Maximal DBP, mm Hg	82.7±7.5	85.1±8.0	0.25
Peak exercise capacity, METs	12.1±2.5	12.3±2.8	0.77
HRR1, bpm	25.6±6.5	30.3±8.2	0.01*
HRR2, bpm	43.5±5.3	47.8±5.5	0.01*
HRR3, bpm	56.8±5.1	59.4±6.3	0.01*

Numerical variables are expressed as the mean ± SD. * p < 0.05. DBP = Diastolic BP; SBP = systolic BP.

Correlation Analysis

The correlation analysis between the exercise test parameters and characteristics of the mercury-exposed group are shown in table 4. There were no significant correlations between any of the echocardiographic measures and laboratory values and exercise test parameters. A negative correlation was found between age and all of the exercise test parameters except HR (maximum HR, HR reserve, HRR1, HRR2 and HRR3). There was also a significant negative correlation between mercury exposure time and maximum HR and HR reserve. Nevertheless, no significant correlation was found between blood, urine or hair mercury levels and any of the exercise test parameters. The multivariate stepwise linear regression model used to determine possible independent predictors that could affect HRR1, HRR2 and HRR3 showed that baseline clinical, echocardiographic and laboratory parame-

Table 4. Correlation analyses between exercise test parameters and some characteristics of the mercury-exposed group

Variable	Baseline HR		Maximum HR		HR reserve		HRR1		HRR2		HRR3	
	r	p	r	p	r	p	r	p	r	p	r	p
Age	0.287	0.139	−0.468*	0.012*	−0.486*	0.009*	−0.474*	0.011*	−0.598*	0.001*	−0.530*	0.004*
Body mass index	0.037	0.853	0.005	0.980	−0.002	0.993	−0.188	0.339	−0.318	0.099	−0.121	0.412
Systolic BP	−0.245	0.209	0.029	0.885	0.155	0.431	0.039	0.846	0.160	0.415	−0.041	0.836
Diastolic BP	−0.111	0.574	0.090	0.647	0.160	0.416	0.055	0.781	−0.016	0.935	−0.145	0.461
Exposure (months)	−0.018	0.929	−0.670*	0.001*	−0.558*	0.002*	−0.311	0.107	−0.179	0.363	−0.267	0.170
Blood mercury	−0.051	0.798	0.112	0.572	0.200	0.306	−0.094	0.634	0.079	0.691	0.031	0.874
Urine mercury	0.047	0.813	−0.137	0.488	−0.131	0.505	−0.291	0.133	0.143	0.469	0.025	0.901
Hair mercury	−0.024	0.903	−0.021	0.914	−0.059	0.764	0.240	0.218	−0.349	0.069	−0.009	0.966

* $p < 0.05$. r = Correlation coefficient.

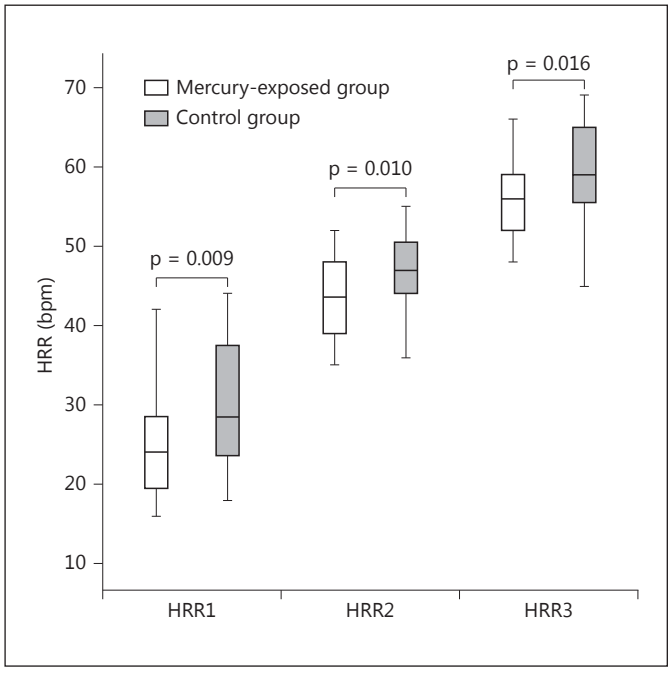

Fig. 1. First-, second- and third-minute HRR values between the mercury-exposed and control groups. There are statistically significant differences between all of the parameters.

ters, including blood, urine and hair mercury levels, were independent predictors of these exercise test parameters. In another analysis, a significant positive correlation was found between exposure time and 24-hour urine mercury levels (r = 0.556, p = 0.002), but there was no correlation with blood mercury levels (r = 0.075, p = 0.70) or hair mercury levels (r = 0.135, p = 0.49).

Discussion

The main finding of the present study was that HRR in the first, second and third minute of the recovery period after maximal exercise testing was lower in mercury-exposed individuals than in healthy controls. While there was no correlation between blood, urine or hair mercury levels and exercise test parameters, in the mercury-exposed group age showed a negative correlation with all of the exercise test parameters except baseline HR. Although many exercise test parameters, including the duration of exercise, baseline and maximum HR, HR reserve and peak exercise capacity, were similar in the two groups and there was no correlation between body mercury levels and any of the exercise test parameters, decreased HRR indices in the mercury-exposed individuals compared to the healthy controls indicate the presence and early blunting of cardiac autonomic dysfunction in this group.

As HR and BP began to decrease at the beginning of the recovery phase, increased sympathetic and decreased parasympathetic activity during exercise was replaced by increased parasympathetic and suppressed sympathetic activity within the recovery phase. This dynamic equilibrium in ANS activity in the exercise/recovery phase provides valuable information about 'cardiac health' in various diseases [21, 22].

In the present study, HRR was evaluated and, being easy to obtain and widely available, is assumed to be a biomarker for autonomic imbalance [23]. We found that HRR indices were blunted in mercury-exposed individuals compared to the control subjects. There have been several studies similar to ours in which the relationship between cardiac ANS function and mercury exposure was

investigated, although HRV was the main method used for the evaluation of autonomic imbalance in these studies. In the study by Valera et al. [24] it was demonstrated that mercury exposure impaired cardiac ANS functions through the use of HRV parameters. Although in that study blood mercury levels were negatively correlated with low-frequency domains, reflecting sympathovagal balance and the standard deviation of the time interval between two consecutive R waves (RR interval) and the coefficient of variation of RR intervals, which mainly reflects parasympathetic activity, we did not find any correlation between HRR indices and body mercury levels. Furthermore, sources of mercury exposure in our study came through both occupational and environmental exposure, and metallic mercury was analyzed in blood, urine and hair samples. In another study from Japan in which cardiac ANS function and HRV were evaluated and the experimental group was exposed to 'methylmercury', the sources of mercury were a seafood-rich diet and mercury levels were measured from blood samples only [25]. Despite the differences in study designs and mercury sources, this interventional study also showed that long-term mercury exposure induced a sympathodominant state similar to our findings. In all these studies, the negative effects of mercury on the sympathovagal balance of the ANS are thought to be responsible for underlying mechanisms. Decreased parasympathetic activity with increased sympathetic activity causes an impairment of HRV parameters by corrupting the sympathovagal balance.

Dynamic parameters seen in exercise, such as HR and BP, depend on a healthy cardiac ANS function. Changes in sympathovagal balance in favor of sympathetic activity during recovery cause an impairment of HRR parameters, which are ANS indicators. However, through which mechanisms does mercury affect the ANS? It has been shown that mercury can cause a sympathovagal imbalance. Although their study involved children, Murata et al. [26] demonstrated that prenatal methylmercury exposure might be associated with reduced parasympathetic activity and a sympathovagal shift. Furthermore, dry umbilical cord tissue methylmercury levels collected from the study population were related negatively to parasympathetic components of cardiac autonomic indicators and positively to sympathovagal indices calculated from the electrocardiographic RR intervals. Similarly, Grandjean et al. [27] suggested that early mercury exposure might have a long-lasting effect on autonomic heart activity. These studies hypothesized that the effects of mercury on cardiac ANS could reflect the brainstem neurotoxicity of mercury. Thus, the neurotoxic effects of mercury may be one of the most important mechanisms of cardiac autonomic dysfunction [28].

In this study the significant correlation between mercury exposure time and 24-hour urine mercury confirmed the previous study of Carman et al. [29] in which a positive correlation between the duration of exposure and urinary mercury levels in mercury-exposed children was reported. The blood mercury level is useful when measured soon after a short-term and high-level exposure, but the level decreases within days of exposure. Estimation of the mercury concentration in urine is the best biomarker of long-term exposure to mercury, and is also an indicator of the bodily burden [30]. Mercury analysis of hair could be useful for assessing chronic exposure because of the abundant sulfhydryl groups in hair, but this remains controversial [30]. Ultimately, urine mercury seems to be one step ahead of blood and hair mercury for the biological monitoring of mercury exposure.

The limitations of this study include the small sample size and the very selected study population. Only HR changes were evaluated, meaning the respiratory exchange ratio, which is the most definitive and objective clinically available measure of the physiological level of effort during exercise, was not included. There was a lack of follow-up of the subjects for cardiovascular outcomes. Therefore, larger studies with the follow-up of end points are required in order to understand the clinical and therapeutic implications of cardiac involvement, as well as the pathogenesis and consequences of autonomic dysfunction in mercury exposure.

Conclusion

In this study, mercury exposure was associated with a blunted recovery of HR after maximal exercise. Mercury-exposed individuals might have cardiac autonomic dysfunction even without overt cardiovascular diseases.

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Disclosure Statement

The authors have no conflicts of interest to declare.

References

1 Tchounwou PB, Yedjou CG, Patlolla AK, et al: Heavy metal toxicity and the environment. EXS 2012;101:133–164.
2 Mozaffarian D: Fish, mercury, selenium and cardiovascular risk: current evidence and unanswered questions. Int J Environ Res Public Health 2009;6:1894–1916.
3 Chan HM, Egeland GM: Fish consumption, mercury exposure, and heart diseases. Nutr Rev 2004;62:68–72.
4 Karakulak UN, Gunduzoz M, Tutkun E, et al: An arrhythmic episode after mercury exposure and successful treatment with chelation therapy: a case report. Anatol J Cardiol 2015;15:589–590.
5 Ye BJ, Kim BG, Jeon MJ, et al: Evaluation of mercury exposure level, clinical diagnosis and treatment for mercury intoxication. Ann Occup Environ Med 2016;28:5.
6 Fernandes Azevedo B, Barros Furieri L, Pecanha FM, et al: Toxic effects of mercury on the cardiovascular and central nervous systems. J Biomed Biotechnol 2012;2012:949048.
7 Guallar E, Sanz-Gallardo MI, van't Veer P, et al: Mercury, fish oils, and the risk of myocardial infarction. N Engl J Med 2002;347:1747–1754.
8 Moszczynski P: Mercury and the risk of coronary heart disease. Przegl Lek 2006;63(suppl 7):84–87.
9 Houston MC: Role of mercury toxicity in hypertension, cardiovascular disease, and stroke. J Clin Hypertens 2011;13:621–627.
10 Salonen JT, Seppanen K, Lakka TA, et al: Mercury accumulation and accelerated progression of carotid atherosclerosis: a population-based prospective 4-year follow-up study in men in eastern Finland. Atherosclerosis 2000;148:265–273.
11 Gordan R, Gwathmey JK, Xie LH: Autonomic and endocrine control of cardiovascular function. World J Cardiol 2015;7:204–214.
12 Okutucu S, Karakulak UN, Kabakci G: Circadian blood pressure pattern and cardiac autonomic functions: different aspects of same pathophysiology. Anatol J Cardiol 2011;11:168–173.
13 Okutucu S, Kabakci G, Deveci OS, et al: Relationship between exercise heart rate recovery and circadian blood pressure pattern. J Clin Hypertens 2010;12:407–413.
14 Gibbons RJ: Abnormal heart-rate recovery after exercise. Lancet 2002;359:1536–1537.
15 Robinson BF, Epstein SE, Beiser GD, et al: Control of heart rate by the autonomic nervous system: studies in man on the interrelation between baroreceptor mechanisms and exercise. Circ Res 1966;19:400–411.
16 Giallauria F, Lucci R, Pietrosante M, et al: Exercise-based cardiac rehabilitation improves heart rate recovery in elderly patients after acute myocardial infarction. J Gerontol A Biol Sci Med Sci 2006;61:713–717.
17 Giallauria F, De Lorenzo A, Pilerci F, et al: Long-term effects of cardiac rehabilitation on end-exercise heart rate recovery after myocardial infarction. Eur J Cardiovasc Prev Rehabil 2006;13:544–550.
18 Cole CR, Blackstone EH, Pashkow FJ, et al: Heart-rate recovery immediately after exercise as a predictor of mortality. N Engl J Med 1999;341:1351–1357.
19 Papouchado M, Walker PR, James MA, et al: Fundamental differences between the standard 12-lead electrocardiograph and the modified (Mason-Likar) exercise lead system. Eur Heart J 1987;8:725–733.
20 Lang RM, Bierig M, Devereux RB, et al: Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18:1440–1463.
21 Karakulak UN, Okutucu S, Sahiner L, et al: Assessment of cardiac autonomic nervous system involvement in systemic sclerosis via exercise heart rate recovery. Med Princ Pract 2015;24:17–22.
22 Sarli B, Dogan Y, Baktir AO, et al: Heart rate recovery is impaired in patients with psoriasis. Med Princ Pract 2013;22:567–570.
23 Ramos RP, Arakaki JS, Barbosa P, et al: Heart rate recovery in pulmonary arterial hypertension: relationship with exercise capacity and prognosis. Am Heart J 2012;163:580–588.
24 Valera B, Dewailly E, Poirier P: Cardiac autonomic activity and blood pressure among Nunavik Inuit adults exposed to environmental mercury: a cross-sectional study. Environ Health 2008;7:29.
25 Yaginuma-Sakurai K, Murata K, Shimada M, et al: Intervention study on cardiac autonomic nervous effects of methylmercury from seafood. Neurotoxicol Teratol 2010;32:240–245.
26 Murata K, Sakamoto M, Nakai K, et al: Subclinical effects of prenatal methylmercury exposure on cardiac autonomic function in Japanese children. Int Arch Occup Environ Health 2006;79:379–386.
27 Grandjean P, Murata K, Budtz-Jorgensen E, et al: Cardiac autonomic activity in methylmercury neurotoxicity: 14-year follow-up of a Faroese birth cohort. J Pediatr 2004;144:169–176.
28 Gribble MO, Cheng A, Berger RD, et al: Mercury exposure and heart rate variability: a systematic review. Cur Environ Health Rep 2015;2:304–314.
29 Carman KB, Tutkun E, Yilmaz H, et al: Acute mercury poisoning among children in two provinces of Turkey. Eur J Pediatr 2013;172:821–827.
30 Park JD, Zheng W: Human exposure and health effects of inorganic and elemental mercury. J Prev Med Public Health 2012;45:344–352.