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FUNCTION OF HEART MUSCLE IN PEOPLE CHRONICALLY EXPOSED TO LEAD

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Abstract: Rhythm and conductivity disturbances in heart muscle, change in autonomic system function and raised arterial blood pressure have been described in workers exposed to lead. They may be accompanied by changes in echocardiography test and accordingly we undertook this investigation. The study population included employees of zinc and lead steelworks in the south of Poland that were divided into 2 groups: exposed to lead compounds (n=88) and the reference group - administration workers (n=55) with normal levels of lead concentration in blood (PbB) and zinc protoporphyrin in blood. Left ventricular enddiastolic dimension (LVDd), interventricular septal and posterior wall thickness, right ventricular diastolic, left atrium diameter, aortic diameter and left ventricular ejection fraction (EF) in echocardiograms were performed. Left ventricular mass LVM (g) and left ventricular mass index LVMI (g/m^2) was calculated. In the group exposed to lead, EF decreased by 3%, increased LVDd by 6%, and raised LVM by 11% and LVMI by 10%. There was a positive relation between PbB and LVDd (R=0.18) and between PbB and LVM (R=0.14). Decreased EF, enlargement of the left ventricle and raised left ventricle mass in research undertaken, may be a result of raised arterial blood tension.

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INTRODUCTION

Most epidemiological and experimental researches describe the negative influence of lead (Pb) on the circulatory system. This fact is connected with lipids peroxidation, changed contents of lipid acids, lipoprotein modification, interaction with different metals, increased inactivation of nitric oxide (NO), raised concentration of cholesterol in blood plasma, induction of arteriosclerotic changes in blood vessels and raised arterial blood pressure [2, 11, 13, 16, 18, 20, 27, 28].

Lead may impair and disturb conductivity in heart muscle and also cause disturbances in depolarization in electrocardiography tests (ECG) [6, 19, 23, 25]. In a Normative Aging Study [6] in a subgroup of people in which higher concentrations of lead in blood and bones were detected, scientists noted prolonged QRS complex. Also, disturbances in intracellular conductivity in people over 65 were noted, as well as even more often atrio-ventricular block in people over 65. Those disturbances appeared in low values of lead in blood (concentration of lead in blood (PbB) - average amount in whole population

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5.8 µg/dl), which were within normal limits. In researches concerning occupational exposure to lead, ECG disturbances were more frequently noticed.

In 23% of workers with protracted contact with lead compounds, abnormal ECG records, mainly depolarization disturbances were observed [19]. Furthermore, raised artery tension with ischemic changes were indicated, as well as heart rhythm disturbances [22, 23]. These results may suggest a raised risk of heart ischemic disease. Also, disturbances of the autonomic system measured by heart rate variability analysis (HRV) have been described in workers exposed to lead (mean PbB=41.0 µg/dl) [10].

To date, no researches estimating heart muscle function in people protractedly exposed to lead activity have been undertaken. As rhythm and conductivity disturbances may be accompanied by changes in echocardiography test, we accordingly undertook this investigation.

MATERIALS AND METHODS

The study population included employees of zinc and lead steelworks in the south of Poland. The people were divided into 2 groups: one of people occupationally exposed to lead compounds (n=88) and the reference group (n=55). In order to define the degree of exposure to lead compounds, lead concentration in blood (PbB), zinc protoporphyrin in the blood (ZPP) and 5-aminolevulinic acid concentration in urine (ALA) were indicated. The reference group consisted of administrative workers in whose blood no raised concentrations of PbB and ZPP and ALA in urine were detected. Data about age, height, body mass, period of time in steelworks, arterial hypertension, coronary heart disease and heart attack in the past were taken.

Analysis of lead in blood (PbB) was carried out by graphite furnace atomic absorption spectrophotometry using Unicam 929 and 939OZ Atomic Absorption Spectrometers with GF90 and GF90Z Graphite Furnaces. Data are shown in µg/dl. Concentration of zinc protoporphyrin in the blood (ZPP) was measured directly using Aviv Biomedical hematofluorometr model 206. The light was filtered by means of an interference filter transmitting at 415 nm. The excitation light focused on a drop of blood. The emitted light passed through a narrow band interference filter which transmitted at 596 nm. The instrument measured the ratio of fluorescent substance (ZPP) to the absorption of the light in the sample (hemoglobin) displayed as µg ZPP/g hemoglobin (µg/g Hb). Urine was collected at the same time. 5-aminolevulinic acid (ALA) was estimated in urine samples by the method of Grabecki [12]. 5-aminolevulinic acid reacted with acetylacetone and formed pyrrole substance, which reacted with dimethylaminobenzoese aldehyde. The coloured complex was measured spectrophotometrically at 553 nm. The results were expressed as mg/dl.

Echocardiograms were performed using a Hewlett-Packard Sonos 2000 with a 3.5MHz transducer. M-mode echocardiographic measurements of the left ventricle were obtained in the parasternal long axis guided by 2D echocardiography, with a cross-sectional axis below the mitral valve at the level of the posterior tendinous chord. According to the recommendations of the American Society of Echocardiography, the following measurements were performed: left ventricular enddiastolic dimension (LVDd) (mm), interventricular septal (IVS) (mm) and posterior wall thickness (PW) (mm), right ventricular diastolic (RVDd) (mm), left atrium diameter LAD (mm) and aortic diameter AoD (mm). Left ventricular ejection fraction (EF) (%) was measured according to Simpson. An average of the measurements obtained during 3 consecutive cardiac cycles was taken for statistical analysis. Left ventricular mass LVM (g) and left ventricular mass index LVMI (LVM corrected for body surface area measured in g/m^2) was calculated [21].

Statistical analysis was performed with Statistic 6.0 PL software. Statistical methods included mean, median and standard error of mean (SEM). Shapiro-Wilk's test was used to verify normality and Levene's test to verify homogeneity of variances. Statistical comparisons were made by t-test, t-test with separate variance estimates or Mann-Whitney U test. Spearman non-parametric correlation was calculated. Discrete variables were compared using Chi^2 test. A value of $p<0.05$ was considered to be significant.

Table 1. Epidemiological data - rate of the arterial hypertension, coronary heart disease and heart attack in the past in control and lead exposed group.

	control group	lead exposed group	p level
number	55	88	
arterial hypertension	9 (16%)	23 (26%)	0.172
coronary heart disease	5 (9%)	10 (11%)	0.666
heart attack	1 (2%)	4 (4%)	0.388

RESULTS

There were no differences in epidemiological data – rate of the arterial hypertension, coronary heart disease and heart attack in the past (Tab. 1) and in age, years of work at the lead steelworks and BMI (Tab. 2). The blood lead level was significantly higher ($p<0.001$) in the lead exposed group by about 150% ($p<0.001$), ZPP was significantly higher by about 180% ($p<0.001$) and ALA was significantly higher by about 37% when compared to the control (Tab. 3). In the group exposed to lead, decreased EF of 3% when compared to the control group was noted, simultaneously increased LVDd dimension of 6% and raised heart muscle mass of 11% (left ventricular mass index was higher by 10%). Other echocardiography parameters did not differ from the control group. Spearman correlation showed that there was a positive relation between PbB and LVDd dimension ($R=0.18$ $p=0.031$) and between PbB and LVM ($R=0.14$ $p=0.086$).

Table 2. Age, years of work in lead steelworks (time of exposure to lead) and body mass index (BMI) in control and lead exposed group.

	control group		lead exposed group		p level
	mean ± SEM	median	mean ± SEM	median	
age (years)	45.0±1.29	48.0	43.9±0.95	45.5	0.473
years of work	21.0±1.47	25.0	21.2±1.02	22.5	0.916
BMI (kg/m^2)	26.2±0.42	26.4	26.6±0.41	26.0	0.515

Table 3. Blood lead level (PbB), zinc protoporphyrin in the blood (ZPP) and urine d-aminolevulinic acid (ALA) concentration in control and lead exposed group.

	control group		lead exposed group		p level
	mean ± SEM	median	mean ± SEM	median	
blood lead concentration (PbB) mg/dl	12.2±0.63	12.1	30.4±1.06	29.2	<0.001
zinc protoporphyrin in blood (ZPP) mg/g Hb	1.52±0.06	1.50	4.25±0.37	3.00	<0.001
uric 5-aminolevulinic acid (ALA) mg/l	3.04±0.18	2.75	4.16±0.23	3.80	<0.001

Table 4. Echocardiographic parameters in control and lead exposed group.

	control group		lead exposed group		p level
	mean ± SEM	median	mean ± SEM	median	
EF - left ventricular ejection fraction (%)	53.5±0.56	55.0	51.9±0.43	54.0	0.013
LVDd - left ventricular enddiastolic diameter (mm)	51.7±0.93	52.0	54.7±0.54	55.0	0.005
IVS - interventricular septal (mm)	10.0±0.25	10.0	10.3±0.20	11.0	0.449
PW - posterior wall thickness (mm)	10.3±0.21	11.0	10.2±0.17	10.0	0.790
LAD - left atrium diameter (mm)	32.3±0.74	32.0	33.2±0.51	33.0	0.326
AoD - aortic diameter (mm)	29.6±0.67	30.0	30.4±0.49	30.0	0.405
RVDd - right ventricular enddiastolic diameter (mm)	29.8±0.62	30.0	30.1±0.54	30.0	0.820
LVM - left ventricular mass (g)	236±9.71	239	263±7.69	251	0.031
LVMI - left ventricular mass index (g/m^2)	125±5.12	122	138±4.10	128	0.047

DISCUSSION

The disadvantageous influence of lead on heart muscle may be connected with raised concentration of catecholamines in blood, interaction with calcium ions, disturbances in ATP production in cardiomiocytes, and raised the arterial blood tension [1, 22, 26].

Many researches have revealed that lead may significantly raise the arterial blood tension [11, 20]. Self-observation in the population of workers occupationally exposed to lead compounds indicated that exposure even to low doses of lead may raise arterial blood tension [17]. Experiments on different laboratory animals showed that lead activity depends on dose, though both low and high doses may raise the arterial blood tension [24]. Decreased ejection fraction EF, enlargement of the left ventricle and raised left ventricle mass in research undertaken, may be a result of raised arterial blood tension.

Lead may disturb renin-angiotensin system, activate the sympathetic system, change the homeostasis of electrolytes and induce free radicals production that lead to arterial hypertension [1, 5, 20, 26].

Experiments on rats, which were supplemented with lead acetate in different doses, indicated increased production of catecholamines [1, 26]. Increased stimulation of alpha-2-adrenoreceptors, beta- and dopaminergic receptors in heart and blood vessels were observed. In rats with the arterial hypertension induced by lead, raised cAMP and Ca^{2+} taking part in the constriction process in miocytes of the blood vessels [1], and a decreased amount of beta-adrenergic receptors in the blood vessels as the answer to raised amount of catecholamines was observed [3, 4, 26]. In kidney, there was observed an increased amount of beta-adrenergic receptors and cAMP [26]. Increased inotropizm of the heart muscle and raised symphatic activity were also noted [5]. In experiments on rats poisoned with lead during the foetal period, there was proved increased sensitivity of the heart muscle to the arthmogenic influence of adrenaline and noradrenaline, as well as an inhibiting influence on baroreceptors in the heart [14].

There also exists the possibility of direct influence of lead on the smooth muscle of blood vessels by neurohormonal stimulation, which affects increased contractility and internal membrane growth [2, 22]. Depending on the dose and the time of exposure, lead affects in different ways the growth process of the smooth muscle in blood vessels and may selectively lower the concentration of angiotensin II receptor [2]. The arterial hypertension caused by lead compounds may also be bound with

increased production of free radicals, it is known that lead induces lipid peroxidation [8, 11, 15], for example $O_2^{\cdot -}$ and $^{\cdot}OH$ [11, 15], which may directly raise the arterial blood tension, or indirectly by increased amount of Ca^{2+} in endothelial cells [9] or NO inactivation [7].

The above-mentioned factors - increased concentration of catecholamines and intensified contractility of the smooth muscle of blood vessels, increased inotropizm of the heart muscle - is confirmed by ejection efficiency in people exposed to lead. Handicapped contractility of the heart muscle may also be a result of the interaction between lead and calcium in cardiomiocytes and decreased production of ATP [1]. A rise of arterial blood tension under lead influence may be followed by the overgrowth of heart muscle and enlarged heart dimensions.

This is the reason why frequent controls of the arterial blood tension in people exposed to lead and observation towards the marks of heart muscle insufficiency are so important. Approximately 95% of lead gathers in bones, most of it irreversibly. The releasing process of this metal from bones is active even if the exposure is finished, which is why no prevention can be taken, and the organism is protractedly exposed to the biological activity of this element till the end of its life. It seems proper to treat such patients with medicines neutralising the toxic influence of lead, for example, from the antioxidants group [13], such as vitamin E, acetylcysteine, captopril or, in the case of arterial hypertension, the inhibitors of the adrenergetic system [1, 26].

REFERENCES

1. Carmignani M, Volpe AR, Boscolo P, Qiao N, Di-Gioacchino M, Grilli A, Felaco M: Catcholamine and nitric oxide systems as targets of chronic lead exposure in inducing selective functional impairment. *Life Sci* 2000, **68**, 401-415.
2. Carsia RV, Forman D, Hock CE, Nagele RG, McIlroy PJ: Lead alters growth and reduces angiotensin II receptor density of rat aortic smooth muscle cells. *Proc Soc Exp Biol Med* 1995, **210**, 180-190.
3. Chang HR, Chen SS, Tsao DA, Cheng JT, Ho CK, Yu HS: Change of cardiac beta-adrenoceptors in lead-exposed rats. *Toxicology* 1997, **123**, 27-32.
4. Chang HR, Chen SS, Tsao DA, Cheng JT, Ho CK, Yu HS: Reduced vascular beta-adrenergic receptors and catecholamine response in rats with lead induced hypertension. *Arch Toxicol* 1997, **71**, 778-781.
5. Chang HR, Tsao DA, Yu HS, Ho CK: The change of beta-adrenergic system after cessation of lead exposure. *Toxicology* 2005, **207**, 73-80.
6. Cheng Y, Schwartz J, Vokonas PS, Weiss ST, Aro A, Hu H: Electrocardiographic conduction disturbances in association with low-level lead exposure (the Normative Aging Study). *Am J Cardiol* 1998, **82**, 594-599.
7. Dalloz F, Maupoil V, Lecour S, Briot F, Rochette L: *In vitro* studies of interactions of NO. donor drugs with superoxide and hydroxyl radicals. *Mol Cell Biochem* 1997, **177**, 193-200.
8. Ding Y, Gonick HC, Vaziri ND: Lead promotes hydroxyl radical generation and lipid peroxidation in cultured aortic endothelial cells. *Am J Hypertens* 2000, **13**, 552-555.
9. Dreher D, Junod AF: Differential effects of superoxide, hydrogen peroxide, and hydroxyl radical on intracellular calcium in human endothelial cells. *J Cell Physiol* 1995, **162**, 147-153.
10. Gajek J, Zysko D, Chlebda E: Heart rate variability in workers chronically exposed to lead. *Kardiol Pol* 2004, **61**, 21-30.
11. Gonick HC, Ding Y, Bondy SC, Ni Z, Vaziri ND: Lead-induced hypertension: interplay of nitric oxide and reactive oxygen species. *Hypertension* 1997, **30**, 1487-1492.
12. Grabecki J, Haduch T, Urbanowicz H: Die einfachen Bestimmungsmethoden der delta-Aminolavulinsaure im Harn. [Simple determination methods of delta-aminolevulinic acid in urine]. *Int Arch Arbeitsmed* 1967, **23**, 226-240.
13. Gurer H, Ercal N: Can antioxidants be beneficial in the treatment of lead poisoning? *Free Radic Biol Med* 2000, **29**, 927-945.
14. Hejtmancik M, Williams BJ: Time and level of perinatal lead exposure for development of norepinephrine cardiotoxicity. *Res Commun Chem Pathol Pharmacol* 1979, **24**, 367-376.
15. Kasperczyk S, Birkner E, Kasperczyk A, Kasperczyk J: Lipids, lipid peroxidation and 7-ketocholesterol in workers exposed to lead. *Hum Exp Toxicol* 2005, **24(6)**, 287-295.
16. Kasperczyk S, Birkner E, Kasperczyk A, Zalejska-Fiolka J: The activity of superoxide dismutase and catalase in people protractedly exposed to lead compounds. *Ann Agric Environ Med* 2004, **11**, 291-296.
17. Kasperczyk S, Dziwisz M, Kasperczyk A, Birkner E: Wpływ ołowiu na występowanie nadciśnienia tętniczego. [Influence of lead exposure on arterial hypertension]. *Wiad Lek* 2002, **55**, 230-234.
18. Kasperczyk S, Kasperczyk A, Ostałowska A, Dziwisz M, Birkner E: Activity of glutathione peroxidase, glutathione reductase and lipid peroxidation in erythrocytes in workers exposed to lead. *Biol Trace Elem Res* 2004, **102**, 61-72.
19. Konstantinova M: Ballistocardiographic and electrocardiographic changes in men working with lead. *Bibl Cardiol* 1975, **(33)**, 101-104.
20. Korrick SA, Hunter DJ, Rotnitzky A, Hu H, Speizer FE: Lead and hypertension in a sample of middle-aged women. *Am J Public Health* 1999, **89**, 330-335.
21. Levy D, Savage DD, Garrison RJ, Anderson KM, Kannel WB, Castelli WP: Echocardiographic criteria for left ventricular hypertrophy: the Framingham Heart Study. *Am J Cardiol* 1987, **59**, 956-960.
22. Ni Z, Hou S, Barton CH, Vaziri ND: Lead exposure raises superoxide and hydrogen peroxide in human endothelial and vascular smooth muscle cells. *Kidney Int* 2004, 66, 2329-2336.
23. Pfister E, Bockelmann I, Ferl T: Vegetative function diagnosis for early detection of lead intoxication. *Int Arch Occup Environ Health* 1996, **69**, 14-20.
24. Skoczyńska A, Stojek E, Gorecka H, Wojakowska A: Serum vasoactive agents in lead-treated rats. *Int J Occup Med Environ Health* 2003, **16**, 169-177.
25. Sroczyński J, Biskupek K, Piotrowski J, Rudzki H: Wpływ ołowiu występującego na stanowisku pracy wspólnie z cynkiem i kadmem na niektóre wskaźniki układu krążenia u pracowników przemysłu metalurgicznego. *Med Pr* 1990, **41**, 152-158.
26. Tsao DA, Yu HS, Cheng JT, Ho CK, Chang HR: The change of beta-adrenergic system in lead-induced hypertension. *Toxicol Appl Pharmacol* 2000, **164**, 127-133.
27. Vaziri ND, Ding Y: Effect of lead on nitric oxide synthase expression in coronary endothelial cells: role of superoxide. *Hypertension* 2001, **37**, 223-226.
28. Ye XB, Fu H, Zhu JL, Ni WM, Lu YW, Kuang XY, Yang SL, Shu BX: A study on oxidative stress in lead-exposed workers. *J Toxicol Environ Health A* 1999, **57**, 161-172.