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/m²) 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 atrioventricular 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...
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 hematofluorometer 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 Grabacki [12]. 5-aminolevulinic acid reacted with acetylacetone and formed pyrrole substance, which reacted with dimethylaminobenzoate 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/m²) 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 Chi² test. A value of p<0.05 was considered to be significant.

**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).
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 Ca²⁺ 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-adnergic receptors and cAMP [26]. Increased inotropizm of the heart muscle and raised sympathetic 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...

### Table 2

<table>
<thead>
<tr>
<th></th>
<th>control group</th>
<th>lead exposed group</th>
<th>p level</th>
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<tbody>
<tr>
<td>age (years)</td>
<td>mean ± SEM</td>
<td>median</td>
<td>mean ± SEM</td>
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<tr>
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<td>45.0±1.29</td>
<td>48.0</td>
<td>43.9±0.95</td>
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<td>years of work</td>
<td>21.0±1.47</td>
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<td>BMI (kg/m²)</td>
<td>26.2±0.42</td>
<td>26.4</td>
<td>26.6±0.41</td>
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### Table 3

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<th>control group</th>
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<tr>
<td>blood lead concentration (PbB) mg/dl</td>
<td>mean ± SEM</td>
<td>median</td>
<td>mean ± SEM</td>
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<td>12.2±0.63</td>
<td>12.1</td>
<td>30.4±1.06</td>
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<td>zinc protoporphyrin in blood (ZPP) mg/g Hb</td>
<td>1.52±0.06</td>
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<td>4.25±0.37</td>
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<tr>
<td>uric 5-aminolevulinic acid (ALA) mg/l</td>
<td>3.04±0.18</td>
<td>2.75</td>
<td>4.16±0.23</td>
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### Table 4

<table>
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<th>lead exposed group</th>
<th>p level</th>
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</thead>
<tbody>
<tr>
<td>EF - left ventricular ejection fraction (%)</td>
<td>mean ± SEM</td>
<td>median</td>
<td>mean ± SEM</td>
</tr>
<tr>
<td></td>
<td>53.5±0.56</td>
<td>55.0</td>
<td>51.9±0.43</td>
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<tr>
<td>LVDd - left ventricular enddiastolic diameter (mm)</td>
<td>51.7±0.93</td>
<td>52.0</td>
<td>54.7±0.54</td>
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<td>IVS - interventricular septal (mm)</td>
<td>10.0±0.25</td>
<td>10.0</td>
<td>10.3±0.20</td>
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<td>PW - posterior wall thickness (mm)</td>
<td>10.3±0.21</td>
<td>11.0</td>
<td>10.2±0.17</td>
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<tr>
<td>LAD - left atrium diameter (mm)</td>
<td>32.3±0.74</td>
<td>32.0</td>
<td>33.2±0.51</td>
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<td>AoD - aortic diameter (mm)</td>
<td>29.6±0.67</td>
<td>30.0</td>
<td>30.4±0.49</td>
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<tr>
<td>RVDD - right ventricular enddiastolic diameter (mm)</td>
<td>29.8±0.62</td>
<td>30.0</td>
<td>30.1±0.54</td>
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<td>LVM - left ventricular mass (g)</td>
<td>236±9.71</td>
<td>239</td>
<td>263±7.69</td>
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<tr>
<td>LVMi - left ventricular mass index (g/m²)</td>
<td>125±5.12</td>
<td>122</td>
<td>138±4.10</td>
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increased production of free radicals, it is known that lead induces lipid peroxidation [8, 11, 15], for example O$_2^-$ and 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 inotropism of the heart muscle - is confirmed by ejection efficiency in the interaction between lead and calcium in cardiomyocytes 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 effect of this element till the end of its life. It seems proper to take into account the prevention of the disease, 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 effect of this element till the end of its life.

REFERENCES


