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Glutathione, glutathione-related enzymes, and oxidative stress in individuals with subacute occupational exposure to lead

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ABSTRACT

The aim of the study was to investigate the influence of subacute exposure to lead on the glutathione-related antioxidant defense and oxidative stress parameters in 36 males occupationally exposed to lead for 40 ± 3.2 days.

Blood lead level in the examined population increased significantly by 359% due to lead exposure. Simultaneously, erythrocyte glutathione level decreased by 16%, whereas the activity of glutathione-6-phosphate dehydrogenase in erythrocytes and leukocytes decreased by 28% and 10%, respectively. Similarly, the activity of glutathione-*S*-transferase in erythrocytes decreased by 45%. However, the activity of glutathione reductase in erythrocytes and leukocytes increased by 26% and 6%, respectively, whereas the total oxidant status value in leukocytes increased by 37%.

Subacute exposure to lead results in glutathione pool depletion and accumulation of lipid peroxidation products; however, it does not cause DNA damage. Besides, subacute exposure to lead modifies the activity of glutathione-related enzymes.

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1. Introduction

Lead toxicity is one of the major occupational hazards. Occupational exposure to lead occurs through various sources, such as battery manufacturing and recovery, soldering, lead mining and smelting, lead alloy production, and paint, glass, plastics, printing, and ceramics industries. Inhalation and ingestion are the two main routes of exposure to lead, of which inhalation is the primary route of occupational exposure. After absorption, most of the lead ions bind to the erythrocytes and are distributed to the soft tissues and bones (Barman et al., 2014).

The adverse health effects of chronic occupational lead exposure have been widely studied. It has been established that there is no safe level of such exposure. Lead binds to the thiol groups of proteins resulting in impairment of the activity of many enzymes, including delta-aminolevulinic acid dehydratase and ferrochelatase, necessary for heme synthesis. Besides, it is believed that lead increases the generation of reactive oxygen species (ROS) and depletes the antioxidant defenses, including reduced glutathione (GSH) reserves. GSH serves as one of the most important antioxidants in the human body because it is a tripeptide with a sulfhydryl group, which quenches ROS and acts as a cofactor for the antioxidant enzymes, such as glutathione peroxidase (GPx) and glutathione-*S*-transferase (GST). As a result, a condition of increased oxidative stress occurs in the presence of lead ions in the biological systems (Flora et al., 2012).

Elevated oxidative stress results in the damage to lipids, proteins, and DNA. Oxidative damage to DNA, such as formation of modified DNA bases and sugar moieties, alkali-labile sites, single and double strand breaks, and protein-DNA crosslinks (Dizdaroglu, 2012), may potentially lead to neoplasia. Therefore, the International Agency for Research on Cancer classified inorganic lead compounds as probable human carcinogens (2A group). Consistently, several studies have indicated that an increased incidence of malignant neoplasms of the lung, stomach, and urinary bladder could be associated with the exposure to lead (García-Lestón et al., 2010).

Studies on lead poisoning conducted on humans focus mainly on the chronic exposure. In our previous studies, we showed elevated levels of oxidative stress indicators, decreased GSH level and modified activities of the antioxidant enzymes in workers chronically exposed to lead (Kasperczyk et al., 2014, 2012). How-

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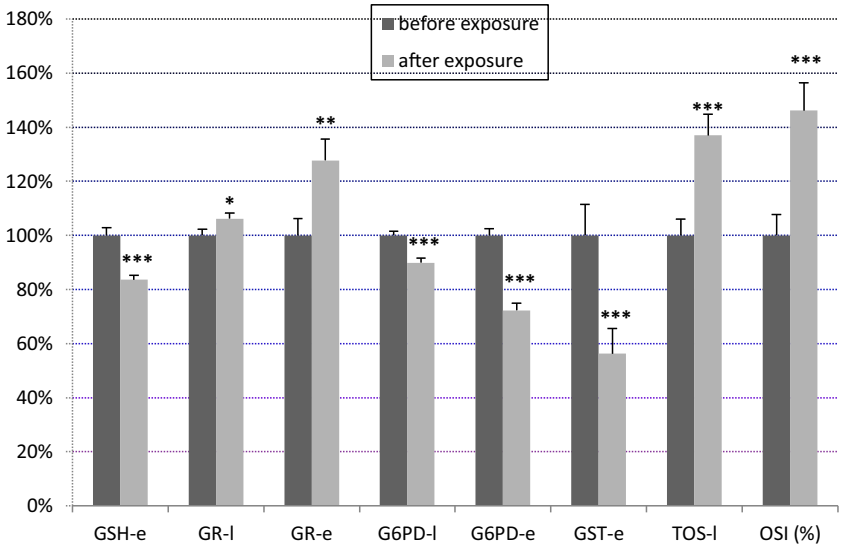

Fig. 1. Relative changes of measured parameters from baseline, normalized to baseline values presented as 100% (mean ± SEM). GSH-e – glutathione level in erythrocytes, GR-l – glutathione reductase activity in leukocytes, GR-e – glutathione reductase activity in erythrocytes, G6PD-l – glucose-6-phosphate dehydrogenase activity in leukocytes, G6PD-e – glucose-6-phosphate dehydrogenase activity in erythrocytes, GST-e – glutathione-*S*-transferase activity in leukocytes, total oxidant status (TOS) in leukocytes, oxidative stress index (OSI) in leukocytes, * - $p < 0.05$, ** - $p < 0.01$, *** - $p < 0.001$ – comparisons between values obtained at the beginning (before) and at the end of the study period (after).

Table 1
Epidemiologic data and lead exposure markers in the group of workers subacutely exposed to lead.

	mean	SD
Lead exposure duration (days)	40	3.2
Age (years)	40.94	13.68
Body mass (kg)	79.67	12.55
Height (cm)	175.50	6.68
BMI (kg/m2)	25.86	3.71
Percentage of smokers (%)	69.4	–

ever, less is known about the negative effects of the short-term exposure to lead because it is quite uncommon. Long-term exposure to lead is associated with its accumulation in bones and development of an adaptive immune response in the individual. Therefore, investigation of lead toxicity due to short-term exposure may bring new information necessary for the better understanding of lead poisoning. In light of this, the aim of the present study was to investigate the influence of subacute exposure to lead on the glutathione-related antioxidant defenses and oxidative stress parameters, including lipid peroxidation and DNA damage.

2. Material and methods

2.1. Study population

The experimental set-up has been approved by the Bioethics Committee of the Medical University of Silesia in Katowice (No. KNW/0022/KB1/108/14).

The examined group consisted of 36 males (aged from 22 to 61 years) who were occupationally exposed to lead for 40 ± 3.2 days. Blood lead level (PbB) served as an exposure marker. Subjects in this group worked in lead-zinc works to perform periodic maintenance of blast furnaces and production lines. Workers were exposed to high doses of lead because they did not adhere to the occupational safety and health precautions and did not properly use the personal protective equipment. One-half of the workers had a history of an occupational exposure to lead (mean PbB = 16.95 ± 5.32 μg/dl), while the other half was only environmentally exposed to lead before the study (mean PbB = 4.16 ± 1.62 μg/dl). In addition, the exposed population was divided into subgroups based on the smoking habits and a median of age (37 years), and body mass index (BMI) (25.6 kg/m^2). None of the examined workers was diagnosed with diabetes, whereas 5% and 3% of them were diagnosed with hypertension and coronary artery disease, respectively.

Table 2
The levels and values of lead, glutathione (GSH), glutathione peroxidase (GPx), glutathione reductase (GR), glucose-6-phosphate dehydrogenase (G6PD), glutathione-*S*-transferase (GST), total antioxidant capacity (TAC), total oxidant status (TOS), oxidative stress index (OSI), malondialdehyde (MDA) before and after subacute exposure to lead; *p*-value – comparison between values obtained after and before exposure to lead using Student's *t*-test or Wilcoxon's test.

	before exposure		after exposure		relative change %	p value
	mean	SD	mean	SD		
PbB (μd/dl)	10.7	7.67	49.1	14.1	359%	<0.001
GSH (mmol/g Hb)	5.56	0.96	4.65	0.513	−16%	<0.001
GPx (IU/g Hb)	55.57	7.69	52.08	10.16	−6%	0.061
GR (IU/g P)	43.37	6.07	46.07	5.22	6%	0.035
GR (IU/g Hb)	2.78	1.05	3.55	1.32	28%	0.004
G6PD (IU/g P)	69.47	6.83	62.47	7.15	−10%	<0.001
G6PD (IU/g Hb)	4.90	0.75	3.54	0.79	−28%	<0.001
GST (IU/g P)	2.99	0.87	3.17	1.01	6%	0.420
GST (IU/g Hb)	0.16	0.11	0.09	0.09	−45%	<0.001
TAC (mmol/g P)	0.33	0.07	0.31	0.05	−7%	0.071
TOS (mmol/g P)	0.81	0.29	1.11	0.38	37%	<0.001
OSI (%)	0.26	0.12	0.38	0.16	47%	<0.001
MDA (μmol/g P)	1.17	0.20	1.15	0.35	−2%	0.737
MDA (nmol/g Hb)	274.16	51.24	262.36	35.95	−4%	0.426

Table 3
The values of the percentage of DNA in the tail and tail length before and after subacute exposure to lead; *p*-value – comparison between values obtained after and before exposure to lead using Student's *t*-test.

	before exposure		after exposure		p value
	mean	SD	mean	SD	
Tail DNA (%)	56.38	8.52	56.09	7.75	0.837
Tail DNA-FPG (%)	67.49	5.51	67.41	5.57	0.574
Tail Length (μm)	45.06	5.19	44.25	6.83	0.514
Tail Length-FPG (μm)	48.56	4.52	49.39	6.83	0.728

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