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EFFECT OF L-ARGININE ON LEAD INDUCED OXIDATIVE STRESS IN THE BLOOD OF RATS WITH DIFFERENT RESISTANCE TO HYPOXIA*

Halyna Tkachenko[1], Nataliya Kurhalyuk[2], Liliya Khabrovska[1], Piotr Kamiński[3]

[1]Department of Hygiene and Toxicology, Danylo Halytskiy Lviv National Medical University, Lviv, Ukraine; [2]Department of Animals Physiology, Institute of Biology and Environment Protection, Pomeranian University, Słupsk, Poland; [3]Department of Ecology and Environmental Protection, Nicholas Copernicus University, Collegium Medicum in Bydgoszcz, Bydgoszcz, Poland

Key words: lead, L-arginine, antioxidants, oxidative stress, resistance to hypoxia, blood

The aim of the study was to estimate beneficial effects of L-arginine, a nitric oxide precursor, on antioxidant enzymes activity (superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, ceruloplasmine), the lipid peroxidation processes level and parameters of membrane erythrocytes resistance before and after lead intoxication in rats with different resistance to hypoxia. Our results suggest that the antioxidant system enzymes activity and lipid peroxidation processes level in animals which differ in sensitiveness to hypoxia, are higher in animals with low resistance to hypoxia in the control group. We have shown that the amino acid, L-arginine, is an efficient antioxidant capable of reducing the level of lipid peroxidation processes in blood of lead-preexposed rats. L-arginine treatment under lead intoxication caused alteration in antioxidant enzymes activity due to increasing the enzymes activity of glutathione system, especially in animals with low resistance to hypoxia. The influence of L-arginine under lead intoxication was investigated to ascertain whether this amino acid possesses antioxidant properties before lead injection (preventive effect) and whether L-arginine has therapeutic effects by treatment after lead intoxication. We have shown a significant protective effect of L-arginine under treatment with a preventive effect before lead intoxication. These studies suggest that L-arginine may be a useful drug in treatment under lead intoxication.

INTRODUCTION

Lead is a ubiquitous environmental and industrial pollutant with wide toxic manifestations of physiological, biochemical, and behavioral dysfunctions [Goyer, 1996; Ruff *et al*., 1996]. Lead can cause human health problems when it enters the food chain through plants and contamination of air, dust, and soil. It has been detected in almost all phases of environmental and biological systems. Recent studies suggest lead's potential for inducing oxidative stress and evidence is accumulating in support of its role in oxidative stress as one of important mechanisms of toxic effects [Ercal *et al.*, 1996; Gurer *et al.*, 1998; Gurer & Ercal, 2000]. Increase in lipid peroxidation in tissues has been implicated in lead-induced organ damage and dysfunction including central and peripheral nervous system, haemopoietic and cardiovascular system, kidneys, liver and reproductive system [Hsu & Guo, 2002]. These findings reported a possible involvement of oxidative stress in pathophysiology of lead toxicity. Some known biochemical mechanisms of lead toxicity let us hypothesize that some of lead's effects on the component of antioxidant defense system that occur first by lead, might cause an impairment in the prooxidant/antioxidant balance of cell, resulting in oxidative damage [Gurer & Ercal, 2000].

Blood or its constituents are the best indicators of the present internal exposure of an individual to lead. The problem of prevention and therapeutic intervention in lead intoxication may be approached in different ways: (1) chelation of lead due to a lead mobilizer capable of reducing intracellular absorption of lead [Tandon *et al.*, 2002], and (2) free radical scavenging by antioxidants and enzymatic defense system *via* rebalancing the impaired prooxidant/antioxidant ratio [Gurer & Ercal, 2000; Hsu & Guo, 2002]. An ideal treatment for lead intoxication should combine both chelating and antioxidant actions.

In the present study, we have studied amino acid L-arginine, a nitric oxide precursor, capable of reducing the level of lipid peroxidation processes in blood of lead-exposed rats. L-arginine is classified as "semi-essential" or "conditionally essential" amino acid as it is extracted from the diet as a supplement to synthesis in mammals and humans. L-arginine participates in many important and diverse biochemical reactions associated with normal physiology of an organism. Research on the biology of L-arginine widened after the identification of nitric oxide synthase to produce nitric oxide.

It is now clear that nitric oxide is a fundamental component of basal metabolism and cellular function and it is implicated in numerous pathophysiological fields including aging, apoptosis, diabetes, exercise, inflammation, ischemic preconditioning, oxidative stress, neurodegenerative pathology, vascular function *etc*. NO modulates various enzymes, ion channels, receptors and proteins by binding to heme, Fe–S

Author's address for correspondence: prof. dr hab. Natalia Kurhalyuk, Department of Animals Physiology, Institute of Biology and Environment Protection, Pomeranian University, ul. Arciszewskiego 22B,76-200 Słupsk, Poland; e-mail: kurhalyuk@pap.edu.pl

clusters, ADP ribosylation and nitrosylation [Bredt & Snyder, 1994; Beckman, 1996; Beckman & Koppenol, 1996; Alderton *et al.*, 2001].

Our laboratory studies previously showed that pharmacological treatment with L-arginine induced protection under stressed condition and model of experimental myocardium dystrophy in rats and in guinea pigs [Kurhalyuk & Tkachenko, 2006]. Our studies have shown that protection induced by L-arginine was mediated by oxidation of α-ketoglutarate and reduced level of lipid peroxidation processes in blood and tissues under stressed conditions [Kurhalyuk, 2003].

The main goal of the present study was to investigate beneficial effects of L-arginine on altered oxidative stress parameters before and after lead treatment in *in vivo* systems and to show that the pharmacological treatment with L-arginine, a nitric oxide precursor, induces protection under lead intoxication in rats with different resistance to hypoxia.

MATERIALS AND METHODS

Animals and experimental design. The study was conducted in conformity with the policies and procedures detailed in the Guide for the Care and Use of Laboratory Animals (Strasburg, 1986). Male white rats (180–220 g) were used in the study. Rats were housed at a constant temperature of 20±2ºC. The animals (n=6 per group) had free access to food and water throughout the experiments. All procedures were done in accordance with guidelines for the care and use of animals in scientific research. Previously animals were divided in two groups: rats with low resistance and high resistance to hypoxia. Resistance of rats to hypoxia was evaluated as survival time (min) in the altitude chamber 11,000 m (170 mm Hg) above sea level. Survival time was measured after achieving the altitude. Cessation of breathing served as the criterion for resistance to hypoxia.

Rats were randomly assigned into four groups. Group I (n=12; rats with both low (n=6) and high resistance (n=6) to hypoxia) served as control and received daily up injection of sterile normal saline solution for 30 days. Group II (lead group, rats with low (n=6) and high resistance (n=6) to hypoxia) received daily 3.6 mg lead nitrate/kg b.w. through an oral route. Group III (L-arginine and Pb group, rats with low (n=6) and high resistance (n=6) to hypoxia) also received daily 3.6 mg lead nitrate/kg b.w. for 30 days and during these days animals were given L-arginine intraperitoneally at a dose of 600 mg/kg b.w. before $Pb(NO_3)_2$ intoxication. Group IV (Pb and L-arginine group, rats with low (n=6) and high resistance (n=6) to hypoxia) was treated like group III, except that it received L-arginine after influence of lead nitrate. Rats were decapitated under ether narcosis. As a coagulant for blood analysis 4% sodium citrate was used.

Chemicals. The following drugs were used: L-arginine hydrochloride (Sigma Aldrich, USA), and lead nitrate. L-arginine hydrochloride was dissolved in isotonic solution and treated intraperitoneally in a dose of 600 mg/kg b.w. Lead nitrate was suspended in distilled water and administered *per os* in a dose of 3.6 mg/kg b.w. All drugs were freshly prepared. The pretreatment time for L-arginine was 30 min before or after administration of lead nitrate respectively. All other reagents used were of analytical reagent grade.

Biochemical assay

Lipid peroxide processes. We measured malondialdehyde (MDA) concentration, an end product indicative of the extent of lipid peroxidation in the blood following the method with 2-thiobarbituric acid [Kamyshnikov, 2004]. Briefly, 0.1 mL of blood was added to 2 mL of distilled water, after which 1 mL of thrichloracetic acid and 1 mL of 2-thiobarbituric acid reagent and the mixture was heated in boiling water bath for 10 min. After cooling the mixture was centrifuged at 1500 × g for 10 min. The μmol of MDA per L of blood was calculated by using 1.56×10^5 mmol/L/cm as extinction coefficient and lipid peroxides level in the blood was expressed in μmol of MDA per L of blood.

Superoxide dismutase (E.C. 1.15.1.1). Superoxide dismutase (SOD) activity in blood was measured using quercetine as a substrate after suitable dilution following the method by Kostyuk *et al.* [1990]. The assay mixture in a total volume of 1 mL consisted of 0.08 mmol/L of EDTA and 0.1 mol/L of sodium phosphate buffer (pH 7.8) in a proportion of 1:1. Briefly, 0.1 mL of 1:1000 blood after dilution was added to 2.3 mL of distilled water, followed by the addition of 1 mL of assay mixture with EDTA and sodium phosphate buffer. The increase in absorbance due to oxidation of quercetine in 0-20 min was recorded at 406 nm using "SPECOL SP 1103 LanOptics" spectrophotometer. In the blank, blood was substituted by equal quantity of distilled water. One unit of SOD activity was defined as the quantity of enzyme that inhibited quercetine oxidation by 50% under given experimental conditions.

Catalase (E.C. 1.11.1.6). Catalase activity was estimated by measuring the breakdown of hydrogen peroxide in the reaction mixture using "SPECOL SP 1103 LanOptics" spectrophotometer at the wave length of 410 nm by the method of Korolyuk *et al.* [1988]. The reaction was started by addition of 0.1 mL of serum to 2 mL of 0.03% of H_2O_2 solution and 1 mL of 4% ammonium molibdate. One unit of catalase activity was defined as the amount of enzyme required to clear 1 μmol of H_20_2/min per L of blood.

Glutathione reductase (E.C. 1.6.4.2). Glutathione reductase activity in the hemolysate was measured according to the method described by Glatzle *et al.* [1974]. Enzyme assay mixture contained 0.2 mL of 7.5 mmol/L oxidized glutathione, 0.1 mL of 1:20 hemolysate, 2.4 mL of 67 mmol/L of sodium phosphate buffer, pH 6.6 and 0.2 mL of 6 mmol/L NADPH. The rate of NADPH oxidation was followed spectrophotometrically at 340 nm. Controls without NADPH were used and the specific activity was expressed as μmol/min per mL of blood.

Glutathione peroxidase (E.C. 1.11.1.9). The activity of glutathione peroxidase in the hemolysate was measured spectrophotometrically as described by Moin [1986]. The assay mixture contained 0.8 mL of 0.1 mol/L Tris-HCl with 6 mmol/L of EDTA and 12 mmol/L of sodium aside, pH 8.9, 0.1 mL of 4.8 mmol/L GSH, 0.2 mL of 1:50 hemolysate, 1 mL of 20 mmol/L t-butylhydroperoxide, and 0.1 mL of 0.01 mol/L 5,5-dithiobis-2-nitrobensoic acid. The rate of GSH reducing was followed spectrophotometrically at 412 nm. Glutathione peroxidase activity was expressed as μmol/min per L of blood.

Ceruloplasmine (E.C. 1.16.3.1). The ceruloplasmine level was measured spectrophotometrically at the wave length of 540 nm as described by Kamyshnikov [2004]. The assay mixture contained 0.1 mL of serum, 8 mL of 0.4 mol/L sodium acetate buffer, pH 5.5, 1 mL of 0.5% p-phenylenediamine. The mixture was heated in boiling water bath to 37°C for 60 min. Before cooling at 4°C for 30 min the mixture was added to 2 mL of 3% sodium fluoride. The ceruloplasmine level in the blood was expressed in mg per L of blood.

Resistance of erythrocytes to a hemolytic reagent

Acid resistance of erythrocytes. The acid resistance of erythrocytes was measured spectrophotometrically following the method with 1 N HCl [Terskov & Hitelzon, 1957]. The method is based on the measuring of dynamics of erythrocytes disintegration under hemolytic reagent action. The time of hemolytic reagent action serves as the measure of erythrocytes resistance. Freshly collected blood samples were centrifuged at 700 × g for 10 min. The sedimented cells were washed with 0.9% NaCl solution. The process was repeated three times. Washed erythrocytes were dissolved with 9-fold volume of 0.9% NaCl solution to prepare 1% erythrocytes solution. The assay mixture contained 10 mL of 1% erythrocytes solution and 0.1 mL of 1 N HCl. The absorbance was read at 540 nm in every 30 sec. after addition of HCl till the end of hemolysis. Difference of absorbance at the beginning and at the end of hemolysis was determined as 100%. Disintegration of erythrocytes (%) for every period of time was expressed in curve.

Osmotic resistance of erythrocytes. The osmotic resistance of erythrocytes was measured spectrophotometrically at a wave length of 540 nm as described by Kamyshnikov [2004]. The method is based on the determination of differences between osmotic resistance of erythrocytes to a mixture with a different concentration of 0.9% NaCl solution and urea. Absorbance of a mixture containing erythrocytes and 0.3 mol/L urea solution was determined as 100% (standard). The degree of hemolysis in every test tube (%) was calculated in respect of the absorbance of standard. Hemolysis of erythrocytes (%) in every test tube with different urea concentration was expressed in curve.

Peroxide resistance of erythrocytes. The peroxide resistance of erythrocytes was determined spectrophotometrically at 540 nm by monitoring the rate of erythrocytes disintegration with hydrogen peroxide as described by Gzhegotskyi *et al.* [2004]. The mixture contained 0.25 mL of erythrocytes, 0.08 mL of 4 mmol/L phosphate buffer (pH 7.4) with 4 mmol/L sodium aside for catalase activity inhibition, and 0.17 mL of phosphate buffer (pH 7.4) with 30 μmol/L hydrogen peroxide. In the blank, erythrocytes were substituted by phosphate buffer without hydrogen peroxide. Absorbance of a mixture containing erythrocytes and phosphate buffer without hydrogen peroxide was determined as 100%. The peroxide resistance of erythrocytes was expressed in %.

Statistical analysis. The results are expressed as mean ±S.D. Significant differences between the means were measured using a multiple range test at min. $p<0.05$. Data not having a normal distribution were log transformed. Student t-tests with 95% confidence intervals ($\alpha=0.05$) were applied to determine the significance of differences between animals. The individual treatment difference between two groups was assessed by computation of the least significant difference by taking at value for error at the level of 5% significance. The intergroup comparisons were done by computing the least significant differences.

RESULTS AND DISCUSSION

Our results suggest that activity of the antioxidant system and lipid peroxidation processes level in animals differing in sensitiveness to hypoxia, are higher in those with low resistance to hypoxia in the control group (Figure 1, Tables 1 and 2). It can serve as a reserve compensative mechanism under influence of unfavorable factors of environment and is better shown in animals with high resistance to hypoxia. Animals with low resistance to hypoxia are characterised by tension of regulatory mechanisms and decrease of antioxidant system ability, which results in activating of lipid peroxidation processes under lead intoxication. Possibly, such changes in the activity of antioxidant system indicate the presence of system mechanism through the state of hem components in the system of oxygen transport and prooxidant/antioxidant balance of lipid peroxidation level.

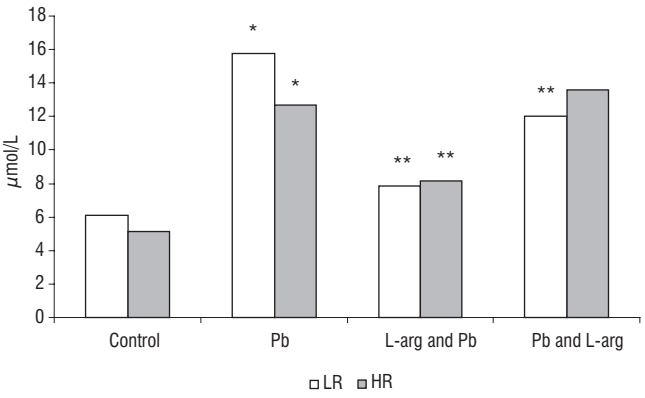

FIGURE 1. Lipid peroxide level (μmol of MDA/L) in blood from lead exposed rats with low (LR) and high (HR) resistance to hypoxia given different L-arginine treatment.
* $p<0.05$ compared with the control group, ** $p<0.05$ compared with the respective value of lead group.

One of the major findings in the present study was that L-arginine decreased the lipid peroxidation processes level in blood of rats with different resistance to hypoxia compared with that of the group with lead toxicity. This result indicated that L-arginine prevented cell damage in blood under experimental lead intoxication.

We measured malondialdehyde concentration, an end product indicative of the extent of lipid peroxidation, in the blood of rats with low and high resistant to hypoxia (Figure 1). The lipid peroxide level in blood from rats of lead group was significantly higher than the respective control value. Treatment with L-arginine significantly lowered the MDA level, especially in rats with low resistance to hypoxia. Therefore, L-arginine may have a beneficial prophylactic effect under lead intoxication. In the blood of rats with high resistance to hypoxia in group with injection of L-arginine after

TABLE 1. Antioxidant enzymes in blood of lead exposed rats with low resistance to hypoxia under treatment with L-arginine.

Antioxidant enzymes	Control	Pb	L-arginine and Pb	Pb and L-arginine
Superoxide dismutase (U/min·mL)	371.11±25.37	265.64±15.69*	172.83±11.32**	315.2±29.28
Catalase (μmol/min·L)	5.75±0.22	15.10±0.95*	7.34±0.33**	11.57±0.31**
Glutathione reductase (μmol/min·mL)	52.18±4.87	22.45±3.29*	61.49±4.15**	51.12±4.64**
Glutathione peroxidase (μmol/min·L)	58.22±5.78	44.54±2.55*	69.26±5.34**	41.91±4.07
Ceruloplasmine (mg/L)	266.29±18.11	177.33±15.53*	148.89±11.57	168.14±12.98

* $p<0.05$ compared with the control group, ** $p<0.05$ compared with the respective value of lead group.

TABLE 2. Antioxidant enzymes in blood of lead exposed rats with high resistance to hypoxia under treatment with L-arginine.

Antioxidant enzymes	Control	Pb	L-arginine and Pb	Pb and L-arginine
Superoxide dismutase (U/min·mL)	249.67±20.71	288.62±24.12	336.61±26.54	245.41±20.75
Catalase (μmol/min·L)	4.82±0.73	12.24±1.17*	7.80±0.56**	13.03±0.45
Glutathione reductase (μmol/min·mL)	64.24±4.52	28.78±3.84*	55.84±4.96**	58.71±4.24**
Glutathione peroxidase (μmol/min·L)	90.81±5.21	48.72±5.89*	75.43±4.49**	48.19±4.74
Ceruloplasmine (mg/L)	184.48±14.40	194.39±18.35	147.58±12.15**	117.83±10.46**

* $p<0.05$ compared with the control group, ** $p<0.05$ compared with the respective value of lead group.

lead intoxication, the therapeutic effect of L-arginine did not reach statistical significance. Injection of L-arginine before lead intoxication significantly reduced values of the lipid peroxide level in blood of rats either with low or with high resistance to hypoxia, indicating better protective efficiency of the treatment with L-arginine.

The oxidative stress is one of the important mechanisms of toxic effects of lead [Gurer *et al.*, 1998]. The oxidative stress has also been implicated to contribute to lead-associated tissue injury in many organs [Adonaylo & Oteiza, 1999]. Several studies have focused on the possible toxic effects of lead on membrane components and identified a correlation between these effects and lead-induced oxidative damage [Yiin & Lin, 1994]. These data suggest that altered lipid composition of membranes may results in altered membrane integrity, permeability, and function. These would increase the susceptibility to lipid peroxidation.

Several studies suggest alteration in antioxidant enzyme activity, and changes in the concentration of some antioxidant molecules, such as glutathione in lead-exposed animals [McGowan & Donaldson, 1986; Hsu, 1981] and others [Sugawara *et al.*, 1991; Chiba *et al.*, 1996]. Therefore, the next stage of our investigation was the measurement of antioxidant enzymes activity. Tables 1 and 2 shows the activity of superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, and ceruloplasmine level in blood from rats with low and high resistance to hypoxia. Enzymatic activity tends to changes according with L-arginine dose and lead toxicity. These factors can modify these changes according to individual responses to hypoxia and L-arginine treatment. We can conclude that lead intoxication caused the decreasing of superoxide dismutase, glutathione reductase and glutathione peroxidase activities and celuloplasmine level in the group of rats with low resistance to hypoxia. In the group of lead-exposed rats under these conditions the activity of catalase is coursed reversely. We can also state that in lead-exposed rats with high resistance to hypoxia significant changes occurs in calatase, glutathione reductase, and glutathione peroxidase activity. Glutathione reductase and peroxidase decreased twice compared with the control group. Apart from these, catalase activity increases significantly more than twice as high. Dismutase and ceruloplasmine activity does no significant changes under these conditions.

Another mechanism involving lead-induced oxidative stress is antioxidant defense system of cells. For instance, superoxide dismutase plays an important role in protecting cells against toxic effects of O_2^- by catalyzing its dismutation reactions. In our research, a non-significant increase of superoxide dismutase activity (15.6%) in blood of rats with high resistance to hypoxia and decrease (28.4%) in rats with low resistance to hypoxia were recorded in lead-treated rats as compared with the control group. It must be emphasized that no significant changes have been noted in our studies in superoxide dismutase activity in the blood of rats with high resistance of L-arginine treatment groups. Moreover, the treatment with L-arginine before lead intoxication during 4 weeks of our experiment decreased superoxide dismutase activity in blood of rats with low resistance. These results were compared with lead group. These changes in superoxide dismutase activity were correlated with increased activity of glutathione reductase in blood of rats either with high resistance (94%) or low resistance to hypoxia (173.9%). The activity was comparable to that in lead-exposed rats, given no treatment.

Superoxide dismutase, catalase, and glutathione peroxidase are metalloproteins and accomplish their antioxidant function by enzymatically detoxifying peroxides, H_2O_2 and O_2^-, respectively. Since these antioxidant enzymes are a potential target for lead toxicity [Gelman *et al.*, 1978]. It must be mentioned that catalase is a major antioxidant enzyme having hem as the prosthetic group. Lead is known to reduce the absorption of iron in the gastrointestinal tract and to inhibit the hem biosynthesis. Decreased catalase activity observed in lead-exposed animals was attributed to the interference of lead by both processes [Sandhir *et al.*, 1994; Sandhir & Gill, 1995]. Moreover, Tandon *et al.* [2002] suggested that catalase activity increased in lead-exposed animals.

As it results from our research, the increase in catalase activity in blood was recorded in lead treated rats as compared with controls: by 162.6% for rats with low resistance and by 153.9% for rats with high resistance to hypoxia. Treatment with L-arginine before lead intoxication decreased the catalase activity in blood from rats with different resistance to hypoxia by 51.4% and 36.3% respectively compared with lead group. Decrease of catalase activity was correlated with enhanced activity of glutathione peroxidase in blood under treatment with L-arginine before lead intoxication. Ceruloplasmine level in blood from rats with low resistance to hypoxia of lead group was significantly lower than the respective control value. Treatment with L-arginine before the lead intoxication decreased the ceruloplasmine level in blood of rats with high resistance to hypoxia (Tables 1 and 2). Decreased ceruloplasmine level in blood is probably linked with the enhancement of glutathione peroxidase and reductase activities under L-arginine treatment before lead intoxication.

As referenced data suggest, the generation of reactive oxygen species such as superoxide anions, hydrogen peroxides, and hydroxyl radicals or products of lipid peroxidation (lipid hydroperoxides, lipid aldehydes) has been implicated in lead toxicity [Adonaylo & Oteiza, 1999]. Therefore, compounds with antioxidant properties probably may have a beneficial effect on therapy or/and prophylactic in lead intoxication.

According to these results, blood is the best indicator of present internal exposure of an individual to lead. Ribarov & Benov [1981] investigated the relation between hemolytic action of heavy metals and lipid peroxidation. Considering their finding that lead-induced hemolysis is associated with peroxidation of erythrocyte membranes, and the assumption that Pb^{2+} can not initiate peroxidation by direct action on the membrane lipids they investigated a possible indirect mechanism for initiation of lipid peroxidation by lead [Ribarov *et al.*, 1981, 1982]. According to general opinion, Pb^{2+} may induce generation of reactive oxygen species by interaction with oxyhemoglobin, leading to peroxidative damage of erythrocyte membranes. That is why the next stage of our investigation was the measurement of resistance of erythrocytes to hemolytic reagent in blood of rats with low and high resistance to hypoxia (Figures 2–4). It was shown that amino acid, L-arginine, is an efficient antioxidant capable of increasing the resistance of erythrocytes to a hemolytic reagent especially in animals with low resistance to hypoxia. Treatment with L-arginine before the lead intoxication decreased the percent of hemolysis in the blood compared with lead group (Figures 2–4).

As we know from the literature, the physiological targets of NO falls into three broad categories. (1) Reactions with molecular oxygen and superoxide anions. The reaction with superoxide anions generates peroxynitrite, a highly reactive free-radical that mediates oxidative injury of cellular components. (2) Reactions with transition metals, such as hem iron or iron-sulfur centers to form metal-NO addition products. This allows for modulation of enzyme activity, as occurs with guanylate cyclase which is stimulated to produce cyclic, or for buffering of NO by the iron-containing proteins myoglobin and hemoglobin. (3) Reactions with reduced protein thiol

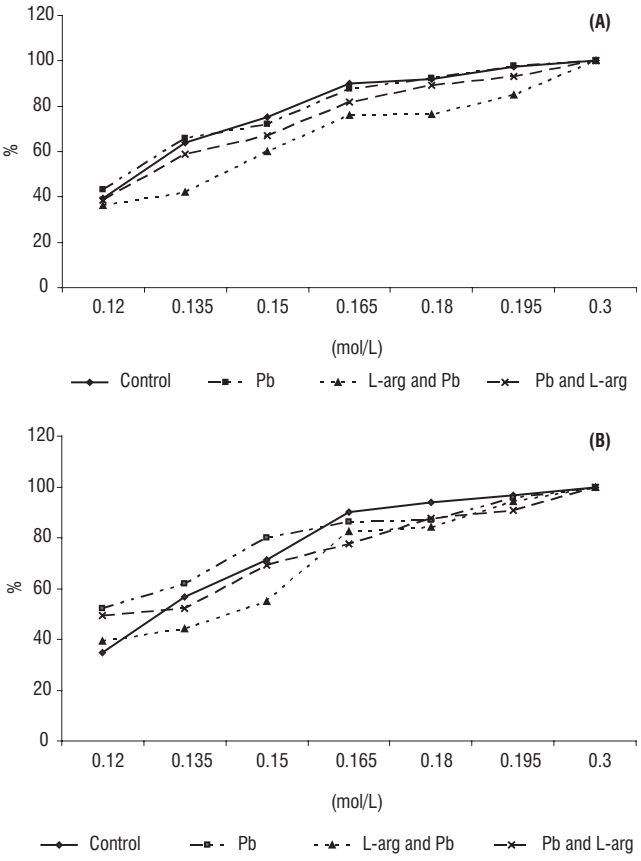

FIGURE 3. Osmotic resistance of erythrocytes of rats with low (A) and high resistant to hypoxia (B) given L-arginine treatment under lead intoxication.

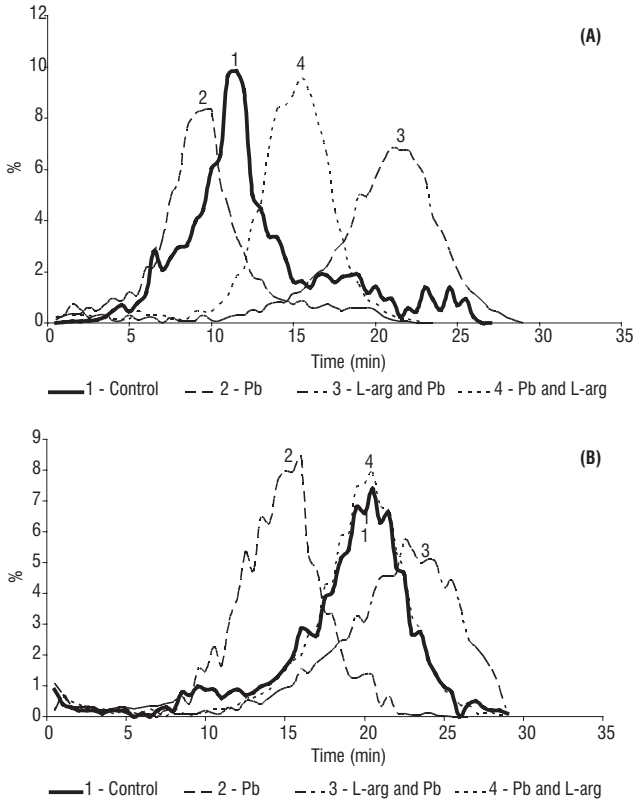

FIGURE 2. Acid resistance of erythrocytes of rats with low (A) and high resistance to hypoxia (B) given L-arginine treatment under lead intoxication.

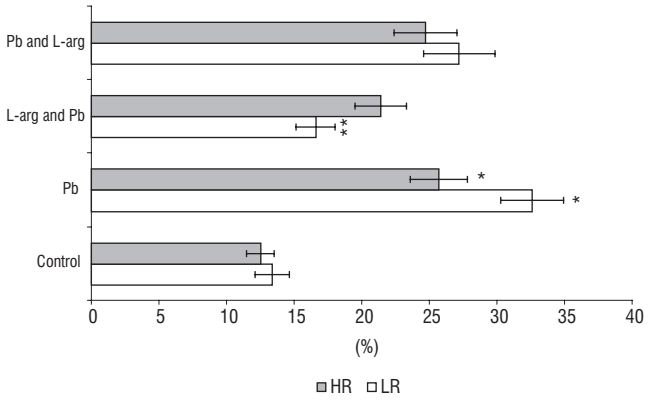

FIGURE 4. Peroxide resistance of erythrocytes of rats with low (LR) and high resistance to hypoxia (HR) given L-arginine treatment under lead intoxication.

* $p<0.05$ compared with the control group, ** $p<0.05$ compared with the respective value of lead group.

groups (RSH or RS^-) to form RS-NO groups. This provides another mechanism by which NO influences protein function as well as means by which glutathione can buffer NO [Moncada *et al.*, 1991; Bredt & Snyder, 1994; Nathan, 1994; Beckman & Koppenol, 1996; Beckman, 1996].

CONCLUSIONS

Summarizing our results, we have shown that the amino acid, L-arginine, is an efficient antioxidant capable of reducing the level of lipid peroxidation processes in blood of lead-preexposed rats. In the present study, the treatment with L-arginine under lead intoxication caused alteration in antioxidant enzyme activity due to increasing the activity of glutathione system, especially in animals with low resistance to hypoxia. The influence of L-arginine, the precursor of NO metabolism, in lead poisoning, was investigated to ascertain whether this amino acid possess antioxidant properties before lead injection (preventive effect) and whether L-arginine has therapeutic effects by treatment after lead intoxication. We have shown a significant protective effect of L-arginine under treatment with a preventive effect before lead intoxication. These studies suggest that L-arginine may be a useful drug in treatment under lead intoxication.

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WPŁYW L-ARGININY NA STRES OKSYDACYJNY WYWOŁANY OŁOWIEM WE KRWI SZCZURÓW Z RÓŻNĄ ODPORNOŚCIĄ NA NIEDOTLENIENIE

Halyna Tkachenko[1], Nataliya Kurhalyuk[2], Liliya Khabrovska[1], Piotr Kamiński[3]

[1]Department of Hygiene and Toxicology, Danylo Halytskiy Lviv National Medical University, Lviv, Ukraine; [2]Katedra Fizjologii Ziwerząt, Instytut Biologii I Ochrony Środowiska, Uniwersytet Pomorski, Słupsk, Polska; [3]Katedra Ekologii i Ochrony Środowiska, Uniwersytet im. Mikołaja Kopernika, Collegium Medicum w Bydgoszy, Polska

Zamierzeniem pracy było określenie korzystnych efektów działania L-argininy, prekursora tlenku azotu, na aktywność enzymów antyoksydacyjnych (dysmutazy ponadtlenkowej, katalazy, glutationreduktazy, glutationperoksydazy, ceruloplazminy), intensywność procesów peroksydacji lipidów i parametry odporności błony erytrocytów, przed i po intoksykacji ołowiem, u szczurów z różną odpornością na niedotlenienie. Nasze wyniki sugerują, że aktywność enzymów antyoksydacyjnych i poziom procesów lipoperoksydacji, u zwierząt różniących się wrażliwością na niedotlenienie, są wyższe u osobników z niską odpornością na niedotlenienie w grupie kontrolnej. Wykazaliśmy, że aminokwas L-arginina jest efektywnym antyoksydantem, zdolnym do zmniejszania intensywności procesów lipoperoksydacji we krwi szczurów eksponowanych na ołów. Traktowanie L-argininą w warunkach intoksykacji ołowiem powoduje zmianę aktywności enzymów antyoksydacyjnych, spowodowanym wzrostem aktywności enzymów systemu glutationu, w szczególności u zwierząt z niską odpornością na niedotlenienie. Wpływ L-argininy w warunkach intoksykacji ołowiem zbadaliśmy w celu określenia, czy aminokwas ten determinuje właściwości antyoksydacyjne przed intoksykacją ołowiem (efekt prewencyjny) oraz, czy L-arginina wykazuje efekty terapeutyczne w wyniku jej oddziaływania po intoksykacji ołowiem. Wykazaliśmy znaczący rezultat ochronny L-argininy w warunkach działania efektu prewencyjnego przed intoksykacją ołowiem. Nasze badania sugerują, że L-arginina może być użytecznym lekiem w warunkach intoksykacji ołowiem.