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ENDOGENIC INTOXICATION IN BLOOD UNDER CONDITIONS OF COMBINATION PATHOLOGY - IMMOBILIZATIONAL STRESS AND ADRENALINE MYOCARDIAL DAMAGE AND CORRECTION OF L-ARGININ

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Abstract

The syndrome of endogenous intoxication, which accompanies pathological processes, is caused by many mechanisms. Erythrocyte index of intoxication (EII) is one of the markers of endogenous intoxication. Medium Molecules (MSM) are products of catabolism of endo- and exogenous proteins.

The aim of the study was to investigate the effect of L-arginine on the level of endogenous intoxication that occurs in the blood of white rats under the influence of acute immobilization stress and adrenal damage to the myocardium.

Material and methods. The experiments were carried out on white male rats of the Vistar line weighing 180-200 g, which were divided into 3 groups of 10 animals (two experimental and one control). MSM₂₅₄ MSM₂₈₀ and EII in blood was determined.

Results. The level of MSM₂₅₄ increased by 1,3 times ($p < 0,05$) and MSM₂₈₀ increased by 1,1 times ($p < 0,05$) compared with the control group. Comparing the analysis of the results of the study of animals in the conditions of IP and APM after the use of the drug L-arginine for 5 days (experimental group 2), it was established that the decrease in the content of MSM₂₅₄ in blood by 0,39 times ($p < 0,05$) and MSM₂₈₀ in blood on 0,31 times ($p < 0,05$), respectively, in comparison with the experimental group number 1 before the treatment. The percentage of endogenous intoxication was also evaluated by the erythrocytic index of intoxication in the blood, which was determined on the 5th day after the simulations of IP and APM in rats prior to treatment. In particular, we have established an increase in EII by 0,99 times ($p < 0,05$) against the control group. In the experimental group 2, which combined IC and APM, and the introduction of L-arginine occurred, on the 5th day the decrease in EII by 0,39 times ($p < 0,05$) compared with the experimental group number 1.

Keywords: endogenous intoxication, middle mass molecules, erythrocytic index of intoxication, immobilization stress, acute adrenaline myocardial damage, L-arginine.

Introduction. The syndrome of endogenous intoxication, which accompanies pathological processes, is caused by many mechanisms. In particular, it is associated with the discoordination of metabolic processes that occur in pathology of different genesis [1]. Erythrocyte index of intoxication (EII) is one of the markers of endogenous intoxication. Taking into account that membranes of ripe erythrocytes are considered as prototype of plasma membranes of all cells of an organism, increase of their permeability (growth EII) can be considered characteristic for cells of an organism, which manifests itself by their cytolysis and release from the cytoplasm of organo- and organ-specific enzymes [2].

Medium mass molecules (MSM) are products of catabolism of endo- and exogenous proteins. Separate fractions of mediumsmolecular peptides have neurotoxic activity, change permeability of membranes, disturb the sodium-potassium balance, amino acid transport processes, withdrawal of creatinine, inhibit glycogenesis, protein biosynthesis, erythropoiesis, tissue respiration, participate in the development of immunosuppression, cause microcirculation and lymphodynamic disorders, have cytotoxic action [3].

For treatment under conditions of combined pathology of IC and APM we have chosen L-arginine. This drug is manufactured by the domestic pharmaceutical industry, possesses membrane-stabilizing, antioxidant, immunomodulating, anti-inflammatory actions [4].

At the present time, it remains unclear whether the level of manifestation of endogenous intoxication syndrome and the peculiarities of its changes before and after treatment with L-arginine [5]. Also challenging is the study of the pathogenesis of immobilization stress (IC) that occurs when adrenal damage to the myocardium (APM), and they both exacerbate both the diagnosis and the therapy of these conditions.

The aim of the study was to investigate the effect of L-arginine on the level of endogenous intoxication that occurs in the blood of white rats under the influence of acute immobilization stress and adrenal damage to the myocardium.

Material and methods of research. The experiments were carried out on white male rats of the Vistar line weighing 180-200 g, which were divided into 3 groups of 10 animals (two experimental and one control). Group number 1 - control group. Animals of the first experimental group were subjected to prolonged immobilization stress (3 h), animals received 0.18% solution of adrenaline hydrochloride at a dose of 1 mg per 1 kg of intramuscular mass (Markova OO 1998) [6], were withdrawn from the experiment on the 5th day before treatment. Animals of the second experimental group were subjected to prolonged immobilization stress (3 h), intraperitoneally injected adrenaline at a dose of 1 mg 1 kg of body weight and withdrawn from the experiment at day 5, L-arginine was injected at a dose of 1.5 mg / kg body weight for 5 days (from the 1st to the 5th day) and were withdrawn from the experiment for the 5th day. Rats of the control group administered 0.9% NaCl at a dose of 1 mg per 1 kg body weight intraperitoneally.

All experimental animals were kept under the standard vivarium of Danylo Halytsky Lviv National Medical University. The research has been carried out with the observance of scientific and practical recommendations on the maintenance and handling of laboratory animals and the provisions of the European Convention on the Protection of Vertebrate Animals, which are used for experimental and scientific purposes. Animals were decapitated under a slight anesthetic induced by sodium thiopental (intraperitoneal injection of 1% solution of 50 mg / kg), and withdrawn from the experiment for the 5th day. The blood plasma was determined by the content of the average density molecules MSM₂₅₄ and MSM₂₈₀ of optic density and the erythrocytic index of intoxication in stress-induced and adrenaline myocardial damage in their combination. These groups were compared to control group rats.

MSM₂₅₄ MSM₂₈₀ in blood was determined by the method of Volchegorsky IA, Dyatlova D.A. (1996) [7]. EII were determined by the method of A. Togobayev. (1988) [8]. Immobilization stress (IC) was modeled by the PD method. Horizontov, O.I. Belousova, M.I. Fetodov (1983) [9]. Adrenal damage to the myocardium (APM) was reproduced by Markova O.O. (1998) [6]. The statistical processing of the data obtained was carried out using the Student's criterion [10].

The results and their discussion. It was established that under the conditions of combined pathology of the IC and APM before treatment, the blood activity of endogenous intoxication indicators increased on the 5th day of the experiment. In particular, the level of MSM₂₅₄ increased by 1,26 times ($p < 0.05$) and MSM₂₈₀ by 1,07 times ($p < 0.05$) compared with the control group. Comparing the analysis of the results of the study of animals in the conditions of IP and APM after the application of the drug L-arginine within 5 days (experimental group 2), it was established that the decrease in the content of MSM₂₅₄ blood by 0,39 times ($p < 0.05$) and MSM₂₈₀ in the blood on 0,31 times ($p < 0,05$), respectively, in comparison with the experimental group №1 before treatment. These, changes in the activity of MSM₂₅₄ and MSM₂₈₀ are shown in Fig. 1 and 2 in detail.

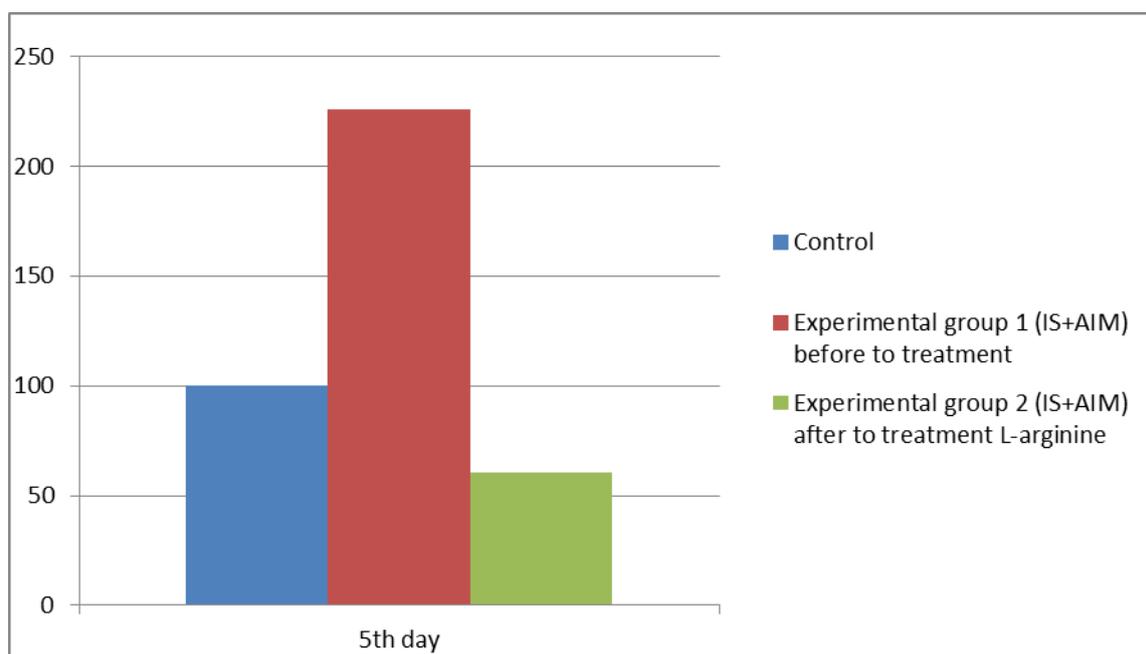


Figure 1. Influence of L-arginine (units of extrusion) before and after treatment on the 5th day of the experiment on the level of MSM₂₅₄ in rat blood with immobilization stress and adrenal damage to the myocardium

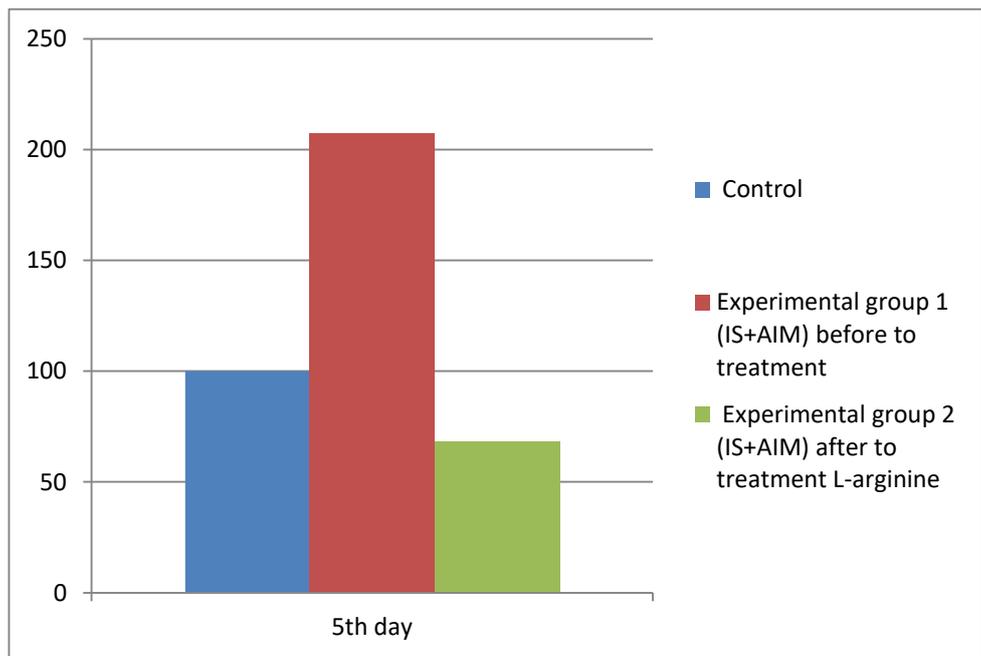


Figure 2. Influence of L-arginine (units of extrusion) before and after treatment on the 5th day of the experiment on the level of MSM₂₈₀ in rat blood with immobilization stress and adrenal damage to the myocardium

The percentage of endogenous intoxication was also evaluated by the content of the erythrocytic index of intoxication in the blood, which was determined at the 5th day after the simulations of the IS and APM in the rats prior to the treatment. In particular, we have established an increase in EII by 99.95% ($p < 0.05$) against the control. In experimental group 2, which combined IS and APM, and administration of L-arginine occurred during the 5th day, which leads to a 39.7% decrease in EII ($p < 0.05$) compared with the experimental group shown in Fig. 3.

Conclusions and perspectives of further research. IC and APM were accompanied by an increase in the levels of MSM₂₅₄, MSM₂₈₀ and EII in the blood at the 5th day of the experiment before treatment. The use of L-arginine for 5 days results in a decrease in MSM₂₅₄ by 0,39 times ($p < 0.05$) and MSM₂₈₀ at 0,31 times ($p < 0.05$), relative to a group of animals with a combined pathology in the experiment (IC + APM) before treatment, indicating the detoxification effect of this drug. The conducted experimental studies showed an increase in concentration on the 5th day of the experiment in blood EII by 99.95% against the intact group of animals before treatment. The use of L-arginine for 5 days reduced EII by 0,39 times ($p < 0,05$), indicating a decrease in intoxication processes in the body's blood system. Therefore, it is expedient to study L-arginine in the future and prospect in the experiment and

clinic for the purpose of correction of metabolic disorders and intoxication under conditions of experimental IC and APM and development of methodical recommendations.

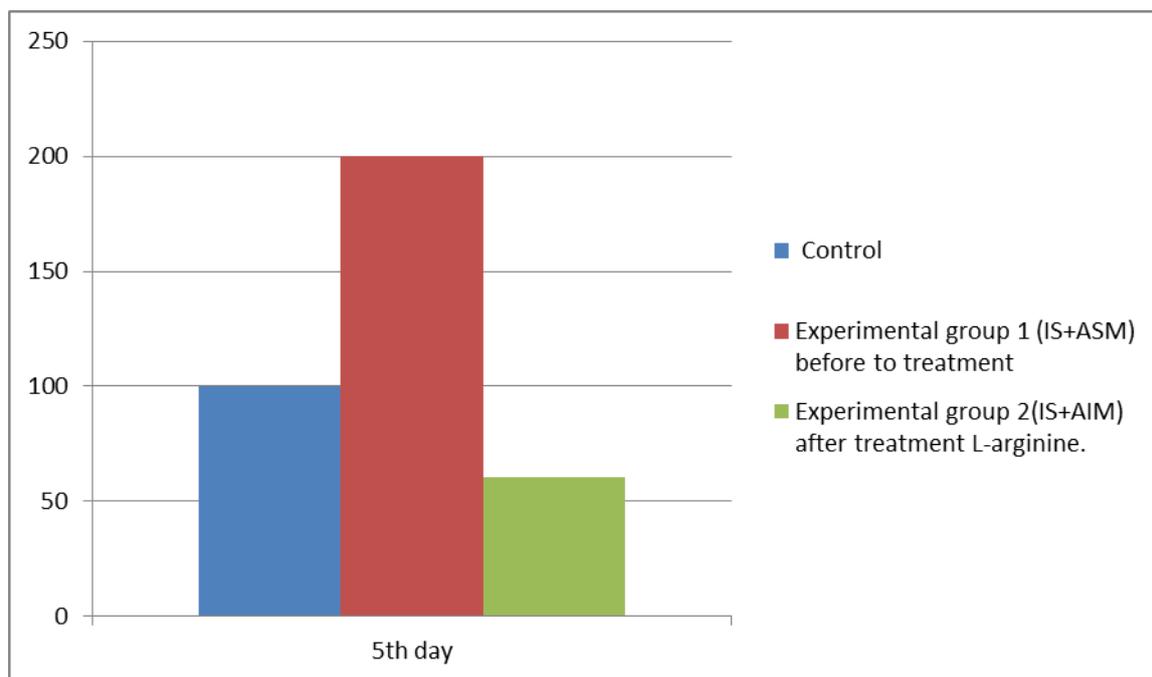


Figure 3. Erythrocyte index of intoxication in rat blood at immobilization stress and adrenal damage to the myocardium and the effect of L-arginine (in %) before and after treatment and the 5th day of the experiment.

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