

## Short Report

**INFLUENCE OF THIAMIN PREPARATION ON EXPERIMENTAL MYOCARDIAL INFARCTION**

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**Brief**

The purpose of the work was to develop a new approach to myocardial infarction treatment using the preparation of thiamin group elaborated by the Research and Develop Institute of biochemical synthesis of the RAS Ural Branch on the basis of acute myocardial infarction experimental model.

After the MI experimental model development the simulation of the process was performed on 30 intact nondescript male white rats. Two groups of 15 animals were formed: the main group of animals given the preparation "117" intraperitoneally in the dosage of 40 mg/kg daily, and the control one formed of the animals, which intraperitoneally were introduced the normal saline solution of sodium chloride. Taking the animals out of the experiment was carried out on the 1<sup>st</sup>, 5<sup>th</sup> and 7<sup>th</sup> day. Besides visual estimation, the cardiac muscle was examined photo-optically in the left ventricular necrotic zone, near-infarction zone and the zone remote from the lesion.

The research results testified that the administration of the compound "117" forms a more favourable morphofunctional picture in the experimental infarction animals' myocardium in 1-5 days already due to the expansion in the number of hypertrophic muscles located in the circumferential direction from the necrosis of regions; an intensive fibroplastic reaction and vessels' new formation are registered as well.

In spite of the acute MI and postinfarction lethality development rate gradual decline, the myocardial infarction still remains the principal cause of lethality and morbidity [1-6]. The AMI patients have a high risk of the subsequent cardiac malfunctions, the cardiac arrest emergency, cardiac angina, cardiac failure, cerebral crisis, repeated infarction among them [7]; about one third of the patients die throughout a year after the AMI (mainly because of the cardiac arrest emergency), that makes this disease the death rate leading cause [8]. In the Recommendations of the working group of the European Society of Cardiology (2006-2008) and in the National Recommendations based upon the first ones the treatment of ACD (MI among them) is based on the application of thrombin inhibitors (heparin) and antithrombotic agents (aspirin, thienopyridines, glycoprotein thrombotic IIb/IIIa receptors' blockers), which can be combined with beta-blockers, nitrates and calcium antagonists if needed [9-11].

To some extent all these requirements are met by the "117 compound" from the thiamin group ("117 compounds"), elaborated by the Research and Develop Institute of biochemical synthesis of the RAS Ural Branch and possessing anticoagulant and disaggregant properties [12].

In connection with this the purpose of the present research has become the study of the influence of the preparation 117 on the experimental myocardial infarction development.

**Materials, methods of myocardial infarction research in the experiment on white nondescript rats****Methods of research**

After the MI experimental model development the simulation of the process was performed on 30 intact nondescript male white rats. The preoperative anaesthesia was carried out by means of ether-air mixture inhalation. The surgical field was shaven off and treated with the preparation "Ecobreeze". There was no intraoperative lethality registered in the course of myocardial infarction model creating. Taking the animals out of the experiment was carried out by means of decapitation after their preliminary being dropped-off to a narcotic sleep state.

There were two groups of 15 animals formed from the animals with the myocardial infarction experimental model: the main group – made of white rats with average body weight of 248±10 g, which daily were intraperitoneally introduced the preparation "117" (without anaesthesia) in the dosage of 40 mg/kg; and the control one – made of the animals with the average body weight of 241±12 g, which were intraperitoneally introduced the normal saline solution of sodium chloride.

Taking the animals out of the experiment was performed on the 1<sup>st</sup>, 5<sup>th</sup> and 7<sup>th</sup> day. The organ recuperation for the following histo-morphological investigation was carried out with the fixation of the material in formalin.

Besides visual estimation, the cardiac muscle was examined photo-optically in the left ventricular necrotic zone, near-infarction zone and the zone remote from the lesion. The material taken for the photo-optical microscopy and morphometry was fixed in neutral formalin, the myocardium tissue microslides were colored by hematoxylin-eosin.

**Research results**

The acceptability of the "117 compound" by the animals was evaluated as rather satisfactory one: there were no pain reactions and necrobiotic changes in the injection site, operative wound purulence and empyema detected in any case; and only in 20-30 minutes after the injection of the preparation there was a retardation of animals with the sound-and-light irritant reaction inhibition registered, which lasted 40-45 minutes; then there were no behavior differences with

the untreated animals detected. There were no respiratory failure, nutritional liquid intake disturbance registered, as well.

On the first day after the surgery without the preparation administration the infarction zone localized in the left ventricle wall (transmurally in the majority of the cases) was represented by cardiac myocytes with karyolysis, plasmolysis and plasmorrhesis phenomena. A moderate diffuse infiltration by segmental leukocytes without forming a demarcation zone was registered. In the adjacent structures there occurred oedemata, endomysium vessels' repletion phenomena with the formation of sludge-complexes. On the first day of the myocardial infarction with the administration the necrotic zone also localized in the left ventricle wall (subepicardially in most cases) was represented by cardiac myocytes with karyolysis, plasmolysis and plasmorrhesis phenomena. The demarcation zone had not been forming yet. In the infiltrate there appeared lymphocytes (immune-competent cells) in small amounts. The necrotic zone infiltration is minimal.

On the fifth day of the myocardial infarction without the preparation administration the infarction zone was determined as mainly transmural. The necrotized cardiac myocytes were surrounded by a demarcation bank; the granulation tissue formation signs were detected; fibroblasts and hemo-capillary tubes appeared. In the adjacent structures there was detected a spread of the infiltrate through the endomysium. In the same period of the myocardial infarction with the administration the lesion zone was displaced with the granulation tissue represented by fibroblasts, fine collagen fibers and multiple sinusoidal capillaries. The granulation tissue was infiltrated by lymphocytes, macrophages. Polymorphonuclear leukocytes were singular.

On the seventh day of the myocardial infarction without the preparation administration the infarction zone in the left ventricle wall was characterized as a transmural one in 100% of the cases. Histologic signs of the organization stage (the formation of granulation tissue round the necrotic zone with a great amount of fibroblast and macrophages, sinusoidal hemo-capillaries substituting the affected area) at the preserved disintegration of the muscle cells and preserved infiltration of the myocardium by lymphocytes and segmental leukocytes. In some cases a marginal position of leukocytes with leukopedesis signs.

On the seventh day of the myocardial infarction with the administration the necrotic zone was fully substituted by granulation tissue, wherein numerous sinusoidal type hemo-capillaries, fine collagen fibers being formed, intercellular substance, a significant amount of functionally active fibroblasts and macrophages were detected. The cellular structure of the infiltrate is lymphocytic with a small amount of polymorphonuclear leukocytes. In the adjacent areas of the myocardium the signs of interstitial edema re-

tained, the endomysium vessels were belled and sanguine.

#### Discussing

A principal feature of the results got at the 117 preparation application at the experimental myocardial infarction has become the leukocytic reaction inhibition in response to the arising inflammation, that has lead to the restriction of the necrotic zone and earlier emergence of reparative processes. It is interesting that the obtained data align principally with B.G. Yushkov's (1974) findings testified that myocardial infarction in the patients with a higher leukocytosis proceeds more severely, than that in the patients with leuko-inhibitory properties of blood serum. Taking into account the fact that at the development of myocardial infarction there appears a systemic and local inflammatory response [13-15], it seems possible to picture the main mechanism of the 117 preparation action as an anti-inflammatory one due to the change of the fourth phase of inflammation according to A.M. Chernukh [16] from the leukocytic type into lymphocytic one.

#### Conclusions

1. The preparation 117 influences the experimental myocardial infarction course in white non-pedigree rats effectively, restricting the necrotic zone and causing earlier development of reparative processes.
2. The main curative effect of the preparation 117 at the experimental myocardial infarction is conditioned by its anti-inflammatory action.

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