INVESTIGATION OF LIPID OXIDATIVE STRESS IN RATS WITH EXPERIMENTALLY INDUCED MYOCARDIAL INFARCTION

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Abstract: Myocardial infarction is a widespread and life-threatening condition affecting populations worldwide. A laboratory model of myocardial infarction has been developed using minimally invasive techniques such as coronary artery ligation or controlled electrocoagulation. The implementation of comprehensive anesthetic, microsurgical, and resuscitative measures significantly reduced postoperative mortality in animals—from 94.6% to 13.6%. Diagnostic findings confirm the feasibility of establishing a reproducible and reliable myocardial infarction model in laboratory animals. Further refinement and standardization of this experimental model will enable its effective use in developing and testing novel therapeutic strategies for myocardial infarction.

Key words: Experimental myocardial infarction, peroxidation, oxidative stress, free radical oxidation, malondialdehyde

Аннотация: Инфаркт миокарда является широко распространённым и опасным для жизни заболеванием, поражающим население во всём мире. В лабораторных условиях была разработана модель инфаркта миокарда с использованием малоинвазивных методов, таких как перевязка коронарной артерии или контролируемая электро-коагуляция. Применение комплексных анестезиологических, микрохирургических и реанимационных мероприятий позволило значительно снизить послеоперационную летальность у животных — с 94,6% до 13,6%. Диагностические результаты подтверждают возможность создания воспроизводимой и надёжной модели инфаркта миокарда у лабораторных животных. Дальнейшее совершенствование и стандартизация данной экспериментальной модели позволит эффективно использовать её для разработки и испытания новых терапевтических стратегий при инфаркте миокарда.

Ключевые слова: экспериментальный инфаркт миокарда, перекисное окисление, оксидативный стресс, свободнорадикальное окисление, малоновый диальдегид.

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Annotatsiya: Miokard infarkti dunyo bo‘ylab keng tarqalgan va hayot uchun xavfli kasallik hisoblanadi. Laboratoriya sharoitida miokard infarktining modeli kam invaziv usullar — koronar arteriyani bog‘lash yoki boshqariladigan elektrokoagulyatsiya yordamida ishlab chiqilgan. Anesteziya, mikrojarrohlik va reanimatsiya tadbirlarining kompleks qo‘llanilishi hayvonlarda operatsiyadan keyingi o‘lim darajasini 94,6% dan 13,6% gacha kamaytirdi. Diagnostik natijalar laboratoriya hayvonlarida miokard infarktining qayta ishlab chiqilishi mumkin bo‘lgan va ishonchli modelini yaratish imkonini tasdiqlaydi. Ushbu eksperimental modelni yanada takomillashtirish va standartlashtirish miokard infarktini davolashning yangi terapevtik strategiyalarini ishlab chiqish va sinovdan o‘tkazishda samarali qo‘llash imkonini beradi.

Kalit so‘zlar: eksperimental miokard infarkti, peroksidlanish, oksidlovchi stress, erkin radikal oksidlanish, malondialdegid.

Introduction.

Pathology of the cardiovascular system holds a prominent position among other diseases. The interest in the study of the pathogenesis of these diseases and the development of biochemical correction methods to eliminate disruptions remains high [1, 6, 7].

Disruption of metabolic processes, impairment of the body's nonspecific defense mechanisms, and a decrease in its regenerative capacities contribute to the processes of free radical oxidation of lipids in the body. Activation of free radicals is accompanied by the formation of highly toxic metabolites, such as acylhydroperoxides, unsaturated aldehydes, and malondialdehyde (MDA), which have the properties of powerful mutagens and cytotoxins [2, 8, 9, 10].

Products of free radical lipid oxidation can suppress the activity of glycolytic and oxidative phosphorylation enzymes, inhibit the synthesis of proteins and nucleic acids, as well as slow down many membrane-related enzymes, leading to significant damage to cells and the body as a whole [3, 11, 12].

Aim. To investigate the level of lipid oxidation in the body during myocardial infarction.

Materials and Methods. Experiments were conducted on male white non-pedigree rats (n=25) weighing 200 grams. Myocardial infarction was induced by ligating the left coronary artery. The animals were euthanized by decapitation on the third day after the onset of myocardial infarction.

After euthanasia, the heart and liver were quickly extracted, weighed, washed with cold 0.15M KCl solution at 0-4°C, and then homogenates were prepared for biochemical analysis.

Heart homogenates were obtained by grinding the organ with a scalpel, followed by cell disruption in a glass homogenizer with a Teflon pestle [4, 13, 14].

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Liver homogenates were prepared by pressing the liver through a mesh with 0.5 mm openings. Liver cells were also disrupted in a glass homogenizer with a Teflon pestle. For isolation, 0.05M KCl was used, dissolved in 50 mL of Tris-HCl buffer (pH=7.4). From the liver homogenates, mitochondrial (Mt) and microsomal (Ms) fractions were isolated [5, 16].

The mitochondrial fraction was obtained by differential centrifugation at 9000g for 20 minutes. The microsomal fraction of the liver was obtained by subsequent centrifugation of the supernatant for 60 minutes at 105,000g.

The amount of malondialdehyde (MDA) in the heart homogenates, as well as in the Ms and Mt fractions of the liver, was determined by the method of Staly I.D. et al., and the activity of superoxide dismutase (SOD) was measured according to the method of Mirs and Friedovich, as modified by Brusov et al. [17].

Results. The investigation of oxidative stress levels in heart homogenates from control animals showed that the concentration of malondialdehyde (MDA) in the tissue was significantly low (Table 1).

Table 1

Concentration of Malondialdehyde (MDA) in Heart and Liver Homogenates of Rats

Organ	MDA (nmol/mg protein minut)			ADP/HDP
	SP	ADP	HDP	
Heart	1,65±0,02	3,33±0,11	6,71±0,17	0,49±0,03
Mitochondrial fraction of the liver	8,1±0,11	88,3±0,73	$64,5^{+}$-0,39	1,36±0,11
Microsomal fraction of the liver	1,43±0,06	11,2±0,09	31,4±0,29	0,35±0,01

In control rats, significant levels of lipid peroxidation (LPO) products were detected in both the mitochondria and microsomes of the liver, likely due to the presence of electron transport chains in these organelles and the formation of reactive oxygen species. In the mitochondria, where the primary oxygen-dependent metabolism occurs, the most aggressive of all free radicals—superoxide anion (O^{2-}) - is formed. Therefore, mitochondria exhibit a high level of ascorbate-dependent lipid oxidation (ADLO) and NADH-dependent lipid oxidation (NDLO) compared to other organelles. It is suggested that the predominance of ascorbate-dependent lipid oxidation in mitochondria over NADH-dependent oxidation may be attributed to the intensity of the alternative non-enzymatic pathway for free radical production.

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It should be noted that the oxygen produced because of these reactions is immediately neutralized by the antioxidant defense enzymes - superoxide dismutase (SOD) and catalase.

The microsomal fraction of the liver is characterized by less intense lipid oxidation compared to the mitochondrial fraction, which can be explained by the use of oxygen in biosynthetic processes, where it is integrated into the molecule of the oxidized substrate under the influence of specific oxygenases.

Thus, when analyzing the level of LPO in heart homogenates, as well as in the mitochondrial (Mt) and microsomal (Ms) fractions of the liver, it can be concluded that these tissues exhibit a certain level of free radical lipid oxidation (FRLO), which is determined by their structural characteristics and functional activity. The slowing down of the LPO reaction rates is due to the efficient antioxidant defense system.

The study of LPO activation in rats with experimental myocardial infarction showed a significant increase in its intensity (on the third day after occlusion of the left coronary artery). The level of MDA in heart tissue homogenates was increased 5 times compared to the control during spontaneous peritonitis. The increase in MDA concentration from ascorbate-dependent and NADH-dependent LPO was 5.1 and 14.7 times, respectively (Table 2).

Table -2

Concentration of Malondialdehyde (MDA) on the 3rd Day of the Experiment

Series of Experiments	MDA (nmol/mg protein minut)			ADP/HDP
	SP	ADP	NDP	
Control	1,65± 0,02	3,33± 0,11	6,71±0,17	0,49± 0,03
3 days post myocardial infarction (M.I.)	7,42±0,04	20,64± 0,14	82,53± 0,02	0,25± 0,02

A sharp increase in the activation of lipid peroxidation (LPO) in cardiac tissue three days after the induction of coronary occlusion myocardial infarction indicates pronounced processes of membrane disruption in cardiac cells and their possible death. This is explained by the fact that excessive peroxidation leads to deformation of the membrane lipoprotein complex, increased permeability to protons and water, inhibition of membrane "pores," and ultimately to cytolysis and destruction of cells.

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Table -3

Содержание МДА в МХ-фракции печени на 3 сутки экспериментального инфаркта миокарда

Series of Experiments	MDA (nmol/mg protein minut)			ADP/HDP
	SP	ADP	NDP	
Control	8,1⁺-0,11	88,3⁺-0,73	64,5⁺-0,39	1,36⁺-0,11
3 days post myocardial infarction (M.I.)	59,9⁺-1,73	326,71⁺-3,77	283,8⁺-7,3	1,53⁺-0,08

MDA levels also increased in the MX and MS liver fractions of rats after experimental myocardial infarction (after 3 days of the experiment). In the absence of oxidative stress, MDA levels in the MX liver fraction exceeded normal values by 6.1 times. A study of inducible oxidative stress systems revealed activation of WGA by 3.1 times and NZP by 3.4 times (Table 3).

The intensity of oxidative stress in the liver microsomal fraction increased significantly more than in the MX fraction. This was reflected in a 28.2-fold increase in MDA concentrations in lipid peroxides, a 4.6-fold increase in enzymatic NZP, and a 9.5-fold increase in WGA activity (Table 4).

Table -4

MDA content in the liver MS fraction on day 3 of experimental myocardial infarction.

Series of Experiments	MDA (nmol/mg protein minut)			ADP/HDP
	SP	SP	SP	
Control	1,43⁺-0,06	11,2⁺-0,09	31,4⁺-0,29	0,35⁺-0,01
3 days post myocardial infarction (M.I.)	28,8⁺-1,02	71,68⁺-3,77	85,26⁺-1,14	0,35⁺-0,01

In the microsomal (Ms) fraction of the liver, an increase in the ratio of aldehyde dehydrogenase activity to nonspecific peroxidase activity was observed, with a factor of 2.05. This likely indicates an increase in non-enzymatic oxidative stress due to the weakening of antioxidant protection in the microsomes. This rise in aldehyde dehydrogenase activity was accompanied by a decrease in superoxide dismutase activity in the Ms fraction of the experimental group rats, which amounted to 73.1%. In the mitochondrial (Mt) fraction, superoxide dismutase activity decreased by 31.5%.

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Conclusion. The deficiency of antioxidants leads to the breakdown of the body's compensatory mechanisms. In the early stages of experimental myocardial infarction (3 days), the intensification of free radical processes in cardiac tissue is likely due to the massive death of necrobiotically altered cells. The increase in oxidative stress in the mitochondrial (Mt) and microsomal (Ms) fractions of the liver was probably associated with the absorption of products from cell destruction.

The analysis of the results of our study serves as a basis for searching for agents with protective properties against increased oxidative stress. The use of antioxidants may help reduce the intensity of oxidative stress in the body and restore disrupted metabolism

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