



STUDYING OXIDATIVE STRESS OF LIPIDS DURING EXPERIMENTAL MYOCARDIAL INFARCTION IN RATS

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Abstract Myocardial infarction is a serious and common disease throughout the world. A method has been developed to simulate myocardial infarction in laboratory animals using minimally invasive approaches such as coronary artery ligation or controlled electrocoagulation.

Comprehensive measures for anesthesiology, microsurgery and resuscitation were introduced, which led to a significant reduction in postoperative mortality in animals from 94.6% to 13.6%. Diagnostic data suggest the possibility of creating a reliable model of myocardial infarction in laboratory animals.

Further improvement and standardization of experimental modeling of myocardial infarction will make it possible to use this model to search for effective treatment methods.

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

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]. 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.

It should be noted that the oxygen produced as a result 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.

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

Уровень МДА также увеличился в МХ- и МС-фракциях печени у крыс после проведения экспериментального инфаркта миокарда (после 3 суток опыта). Количество МДА в МХ-фракции печени при отсутствии окислительного стресса превышало нормальные значения в 6,1 раза. Изучение индуцируемых систем окислительного стресса показало активацию АЗП в 3,1 раза и НЗП в 3,4 раза (Таблица 3).

Интенсивность окислительного стресса в фракции микросом печени усилилась значительно сильнее, чем в МХ-фракции. Это отразилось в увеличении концентрации МДА в перекисях липидов в 28,2 раза, уровне ферментативной НЗП в 4,6 раза и уровне активности АЗП в 9,5 раза (Таблица 4)

Таблица-4

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

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%.

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 necrobiologically 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

References

- asab E. M. et al. COVID-19's immuno-pathology and cardiovascular diseases //Journal of Investigative Medicine. – 2023. – T. 71. – №. 2. – С. 71-80.
- eves K. B. et al. Exosomes and the cardiovascular system: role in cardiovascular health and disease //The Journal of Physiology. – 2023. – T. 601. – №. 22. – С. 4923-
3. Zeng J. et al. Effect of lipid oxidation on quality attributes and control technologies in dried aquatic animal products: A critical review //Critical Reviews in Food Science and Nutrition. – 2023. – С. 1-22.
4. Whitworth G. B., Watson F. L. Translating Ribosome Affinity Purification (TRAP) and Bioinformatic RNA-Seq Analysis in Post-metamorphic *Xenopus laevis* //Axon Regeneration: Methods and Protocols. – New York, NY : Springer US, 2023. – С. 279-310.
5. Acín-Pérez R. et al. Isolation of mitochondria from mouse tissues for functional analysis //Metabolic Reprogramming: Methods and Protocols. – New York, NY : Springer US, 2023. – С. 77-96.
- enjayevich B. A., Baxriddinovna U. G. Experimental giperxolesterolemiyada nitrengik tizim dinamikasi //Новости образования: исследование в XXI веке. – 2023. – Т. 1. – №. 9. – С. 1452-1458.
7. Baykulov A. K., Toshboyev F. N., Akhmadov J. Z. biochemical and physiological changes in parasite parameters in the host-parasite relationship //Modern Scientific Research International Scientific Journal. – 2024. – Т. 2. – №. 1. – С. 257-262.
8. Akhmadov J. Z., Akramov D. K., Baykulov A. K. chemical composition of essential oil *Iagochilus setulosus* //Modern Scientific Research International Scientific Journal. – 2024. – Т. 2. – №. 1. – С. 263-269.
- ayqulov A. K., Raxmonov F. K., Egamberdiyev K. E. Indicators of endogenous intoxication in the model of burn injury in correction with chitosan derivatives //Educational Research in Universal Sciences. – 2022. – Т. 1. – №. 2. – С. 56-63.

10. Baykulov A. K., Norberdiyev S. S. eksperimental giperxolesterolemiyada qondagi gomosistein miqdori bilan endoteliy disfunktsiyasi bog 'iligi //Educational Research in Universal Sciences. – 2023. – Т. 2. – №. 3. – С. 396-402.
11. Bayqulov A. K. et al. experimental giperlipoproteinemiyanı xitosan hosulalari bilan korreksiyasi //Zamonaviy fan va ta'lim yangiliklari xalqaro ilmiy jurnal. – 2024. – Т. 2. – №. 2. – С. 230-240.
12. Байкулов А. К., Убайдуллаева Г. Б., Эшбуриева Б. Р. коррекция экспериментальной гиперлиппротеинемии с производными хитозана //World of Scientific news in Science. – 2024. – Т. 2. – №. 2. – С. 937-947.
13. Советов К. Т., Байкулов А. К. динамика ибс с коррекцией лдг //Modern Scientific Research International Scientific Journal. – 2023. – Т. 1. – №. 9. – С. 47-55.
айкулов А. К., Юсуфов Р. Ф., Рузиев К. А. Зависимость дисфункции эндотелия с содержанием гомоцистеина в крови при экспериментальной гиперхолестеринемии //образование наука и инновационные идеи в мире. – 2023. – Т. 17. – №. 1. – С. 101-107.
айкулов А. К. и др. Воспалительный процесс: от стадии изменений в крови до заживления //International Scientific and Practical Conference World science. – ROST, 2017. – Т. 5. – №. 3. – С. 32-36.
айкулов А. К. и др. Степень эндогенной интоксикации и липопероксидации в динамике термической травмы и лечении производными хитозана //International Scientific and Practical Conference World science. – ROST, 2017. – Т. 5. – №. 3. – С. 28-31.
17. Mohideen K. et al. Assessment of oxidative stress by the estimation of lipid peroxidation marker Malondialdehyde (MDA) in patients with chronic periodontitis: a systematic review and meta-analysis //International Journal of Dentistry. – 2023. – Т. 2023

18. Байкулов А. К., Муртазаева Н. К., Тошбоев Ф. Н. ДИНАМИКА ВЛИЯНИЯ ЛАКТАТДЕГИДРОГЕНАЗЫ ПРИ ЭКСПЕРИМЕНТАЛЬНОМ ИНФАРКТЕ МИОКАРДА //World of Scientific news in Science. – 2024. – Т. 2. – №. 3. – С. 244-251.
- айкулов А. К., Убайдуллаева Г. Б., Эшбуриева Б. Р. Коррекция экспериментальной гиперлиппротеинемии с производными хитозана //World of Scientific news in Science. – 2024. – Т. 2. – №. 2. – С. 937-947.
- enjayevich B. A. et al. EKSPERIMENTAL GIPERHOMOSISTEINEMIYANI OKSIDLOVCHI STRESS HOLATIDA KELTIRIB CHIQRISH //TADQIQOTLAR. UZ. – 2024. – Т. 40. – №. 1. – С. 25-30.
- rmanov R. T., Qarshiev S. M., Baykulov A. K. CHANGES IN THE NITRERGIC SYSTEM DURING EXPERIMENTAL HYPERCHOLESTEROLEMIA //World of Scientific news in Science. – 2024. – Т. 2. – №. 4. – С. 326-339.
22. Akhmadov J. Z., Akramov D. K., Baykulov A. K. Chemical composition of essential oil *lagochilus setulosus* //Modern Scientific Research International Scientific Journal. – 2024. – Т. 2. – №. 1. – С. 263-269.
23. Bayqulov A. K., Raxmonov F. K., Egamberdiyev K. E. Indicators of endogenous intoxication in the model of burn injury in correction with chitosan derivatives //Educational Research in Universal Sciences. – 2022. – Т. 1. – №. 2. – С. 56-63.
24. Baykulov A. K., Norberdiyev S. S. eksperimental giperxolesterolemiyada qondagi gomosistein miqdori bilan endoteliy disfunktsiyasi bog 'liligi //Educational Research in Universal Sciences. – 2023. – Т. 2. – №. 3 SPECIAL. – С. 396-402.
25. Советов К. Т., Байкулов А. К. Динамика ИБС с коррекцией ЛДГ //Modern Scientific Research International Scientific Journal. – 2023. – Т. 1. – №. 9. – С. 47-55.
26. Байкулов А. К., Юсуфов Р. Ф., Рузиев К. А. Зависимость дисфункции эндотелия с содержанием гомоцистеина в крови при экспериментальной

- гиперхолестеринемии //образование наука и инновационные идеи в мире. – 2023. – Т. 17. – №. 1. – С. 101-107.
27. Kenjayevech B. A. et al. Changes of basic intermediates in blood in myocardial infarction //Journal of Positive School Psychology. – 2022. – С. 1775-1781.
28. Байкулов А. К. и др. Показатели системы оксида азота при экспериментальной гиперхолестеринемии //International Scientific and Practical Conference World science. – ROST, 2017. – Т. 4. – №. 12. – С. 5-8.
29. Kenjayevech B. A. et al. TIOKSIKOLOGIK KIMYODA ATOM-ABSORBSION SPEKTROSKOPIYA USULLARI //Yangi O'zbekiston taraqqiyotida tadqiqotlarni o'rni va rivojlanish omillari. – 2024. – Т. 12. – №. 1. – С. 101-106.
30. Kenjayevech B. A. et al. VISMUT ELEMENTINING TOKSIKOLOGIK AHAMIYATI //Yangi O'zbekiston taraqqiyotida tadqiqotlarni o'rni va rivojlanish omillari. – 2024. – Т. 12. – №. 1. – С. 82-86.
31. Kenjayevech B. A. et al. YALLIG'LANISHGA QARSHI NOSTEROID DORI VOSITALARI TOKSIKOLOGIK AHAMIYATI //Ta'limning zamonaviy transformatsiyasi. – 2024. – Т. 12. – №. 2. – С. 38-43.
32. Anvar o'g'li O. A., Kenjayevech B. A. SUD KIMYOSI EKSPERTIZA LABAROTORIYALARDA QÒLLANILADIGAN DASTLABKI EKSPRESS TAXLIL USULLARI //Ta'limning zamonaviy transformatsiyasi. – 2024. – Т. 12. – №. 2. – С. 44-48.
33. Muzaffar o'g'li A. M., Kenjayevech B. A. DORIVOR ÒSIMLIKLAR BILAN ZAHARLANISH HOLATLARI //Ta'limning zamonaviy transformatsiyasi. – 2024. – Т. 12. – №. 2. – С. 58-61.
34. Kenjayevech B. A., Nematjon o'g'li T. D., Rashidovna E. B. SOURCES OF ALKALOIDS AND EFFECTS ON THE BODY //TADQIQOTLAR. UZ. – 2024. – Т. 40. – №. 1. – С. 31-35.