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THE STATE OF FREE-RADICAL OXIDATION OF LIPIDS IN EXPERIMENTAL MYOCARDIAL INFARCTION IN RATS.

Baykulov Azim[1*], Djalilov Mustafo[1], Eshimov Dusmurat[2], Yusupova Saodat[3], Kim Oksana[1], Sovetov Karokul[1]

[1]*Department of Biochemistry, Samarkand State Medical Institute, Uzbekistan, Samarkand*

[2]*Department of of Animal Physiology, Biochemistry and Pathological Physiology, Samarkand Institute of Veterinary Medicine*

[3]*Department of Medical chemistry, Samarkand State Medical Institute, Uzbekistan, Samarkand*

***Corresponding author**

Baykulov Azim, Ph.D.

Address: Department of Biochemistry, Samarkand State Medical Institute, A. Temur Str 18, Uzbekistan, Samarkand

Phone number (+99891) 5460369,

E-mail: azimbaykulov81@mail.ru

ORCID ID: 0000-0002-1139-1436

Abstract. Lipid peroxidation products are capable of inhibiting the activity of enzymes of glycolysis and oxidative phosphorylation, inhibiting the synthesis of protein and nucleic acids, inhibiting many membrane-bound enzymes and thus exerting a pronounced damaging effect on cells and the body as a whole. It is of particular interest to study the intensity of lipid peroxidation in the body during myocardial infarction, which was the price of this study.

Key word: Lipid peroxidation, malondialdehyde, metabolic processes, of free-radical oxidation, Mitochondrial (MC) and microsomal (MS) fractions, (MP)-medium peptide, (ADP)- ascorbate dependent peroxidation, (NDP)NADPH dependent peroxidation.

Introduction. Diseases of the cardiovascular system occupy a leading position in disability and mortality of working age in the world and in Russia as well. Most frequent a form of this pathology is ischemic heart disease. Long-term research of the Center for Preventive Medicine notes the contributing role of the socio-economic crisis. The most important features of the pathophysiology of ischemic heart disease include dysfunction endothelium of the coronary arteries, in the genesis of which LPO plays a role, oxidatively modified LDL, which disrupt NO metabolism. Pathology of the cardiovascular system takes a leading place among other diseases. The interest in the study of the pathogenetic mechanisms of these diseases and the development of methods for the biochemical correction of the arising disorders continues unabated [1, 5, 7].

Disorganization of metabolic processes, violation of the state of nonspecific defense of the body and a decrease in its regenerative capabilities are the initiators of free-radical oxidation of lipids in the body [3, 6,8].

LPO activation is accompanied by the accumulation of highly toxic metabolites, which are formed during the reaction of acyl hydroperoxides, unsaturated aldehydes and malondialdehyde [MDA], are powerful mutagens and have pronounced cytotoxicity. LPO products are able to suppress the activity of enzymes of glycolysis and oxidative phosphorylation, inhibit the synthesis of protein and nucleic acids, inhibit many membrane-bound enzymes, and thus have a pronounced damaging effect on cells and the body as a whole [2, 4].

Therefore, it is of particular interest to study the ability of lipid peroxidation in the body during myocardial infarction.

Therefore, it is of particular interest to study the intensity of lipid peroxidation in the body during myocardial infarction, which was the task of this study.

Material and research methods. The experiments were carried out on white outbred male rats [n = 25] weighing 200g. Myocardial infarction was induced by alloying the left coronary artery. The animals were slaughtered by decapitation on day 3 from the beginning of the experimental myocardial infarction.

After the animals were slaughtered, the heart and liver were quickly removed, weighed, washed with cold 0,15M [0-4^{0}C] KCl solution, and then homogenates were prepared for biochemical research.

Heart homogenates were prepared by crushing the organ with a scalpel, followed by destruction of heart cells in a glass homogenizer with a Teflon pestle.

Liver homogenates were prepared by forcing the liver with a press through a lattice with 0,5 mm holes. Thereafter, liver cells were also destroyed in a glass homogenizer with a Teflon pestle. The isolation medium consisted of 0,05 M KCl dissolved in 50 ml of Tris HCl buffer (pH = 7,4). Mitochondrial (MC) and microsomal (MS) fractions were isolated from liver homogenisates.

The mitochondrial fraction was obtained by differential centrifugation at 9000 revolutions per 20 minutes.

The microsomal liver fraction was obtained by repeated centrifugation of the supernatant for 60 minutes at 105000 Hz.

In heart homogenisates, MS and MX fractions of the liver, the amount of MDA was determined by the method of Stalnaya I.D. et al., the activity of superoxide dismutase (SOD) by the method of Mirsa P.H., Fridovich S. in the modification of O.S. Brusova et al.

Research results

The study of the LPO intensity in the heart homogenates of control animals showed that the MDA content in the tissue was at a significantly low level.

The intensity of lipid peroxidation in the MC and MS fractions of the liver in control rats was at a high level, which is evidently due to the presence of electron transport chains in mitochondria and microsomes and the generation of reactive oxygen species in them. At the same time, in the mitochondria, where the main consumption of oxygen in the body occurs, the formation of the most aggressive of all free radicals, the superoxide anion O_2^-, occurs. In this regard,

mitochondria are distinguished by a high level of SP, WGP, and WIP compared to other organelles. The predominance of WGA in mitochondria over NZP is apparently due to the high intensity of the nonenzymatic pathway of free radical formation.

Note that the O_2 formed in the course of these reactions is immediately rendered harmless by the action of the AO enzymes for the protection of SOD and catalase.

The microsomal fraction of the liver is characterized by a lower intensity of lipid peroxidation compared to the mitochondrial fraction, which is associated with the use of oxygen in it for plastic purposes, when it is incorporated into the molecule of the oxidized substrate under the action of specific oxygenases.

Thus, analyzing the intensity of lipid peroxidation in heart homogenates, MC- and MS-fractions of the liver, it can be concluded that these tissues are characterized by a certain level of SROL, determined by the structural features and performed by the structural features and functions. At the same time, the rate of LPO reactions is stationary-low due to the action of a powerful antioxidant defense system.

A study of the intensity of LPO in rats with experimental myocardial infarction revealed its significant activation. (3 days after alloying of the left coronary artery).

The content of MDA in homogenates of heart tissue was increased 5-fold compared to the control at SP. An increase in the level of MDA with WRA and WIP was observed 5.1 and 14.7 times, respectively (Tab. 1).

A sharp activation of LPO in the heart tissue on the 3rd day after the reproduction of coronary occlusive myocardial infarction indicates pronounced membrane-destructive processes in the cells of the heart tissue, as well as their possible death. This is due to the fact that the process of excessive peroxidation is accompanied by deformation of the membrane lipoprotein complex, increased permeability to protons and water, inhibition of "pores" in membranes, and as a result, cytolysis and cell destruction.

An increase in the concentration of MDA was also observed in the MC- and MS-fractions of the liver of rats after the reproduction of experimental myocardial infarction (3 days of the experiment). So its amount in the MX-fraction of the liver with non-induced LPO exceeded normal values by 6.1 times. The study of induced LPO systems revealed activation of WGA by 3.1 times, and WRP by 3.4 times (Tab. 2).

The LPO intensity in the liver microsome fraction was increased to a greater extent than in the MX fraction. This was manifested by an increase in the concentration of MDA pr SP by 28.2 times, with enzymatic WIP by 4.6 times, and with WGA by 9.5 times.

The content of MDA in the MS-fraction of the liver on the 3rd day of experimental myocardial infarction (Tab. 3).

In the MS fraction of the liver, a 2.05-fold increase in the WGA / WIP coefficient was found. This may indicate an increase in non-enzymatic lipid peroxidation as a result of a weakening of antioxidant protection in microsomes. In this case, WGA activation was accompanied by a decrease in SOD activity in the MS fraction; in rats of the experimental group, SOD activity decreased by 73.1%. In the MX-fraction, the SOD activity decreased by 31.5% (Tab. 4).

Conclusion. Antioxidant deficiency leads to disruption of the body's compensatory capabilities. In the early stages of experimental myocardial infarction (3 days), the intensification of free radical processes in the cardiac tissue is possibly due to massive death of necrobiotic altered cells. The increase in LPO in the MC and MS fractions of the liver was probably associated with the absorption of cell cleavage products.

The analysis of the results of our research serves as the basis for the search for agents that have protective properties during LPO activation. Perhaps the use of antioxidants will reduce the intensity of lipid peroxidation in the body and normalize metabolic disorders.

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Application

Table 1

MDA content in rat heart and liver homogenates.

Organ	MDA (n mol/mg proteins min)			ADP/NDP
	MP	ADP	NDP	
Heart	1,65^{+} 0,02	3,33^{+} 0,11	6,71^{+} 0,17	0,49^{+}0,03
MC-fraction of liver	8,1^{+}0,11	88,3^{+}0,73	64,5^{+} 0,39	1,36^{+}0,11
MC- fraction of liver	1,43^{+}0,06	11,2^{+}0,09	31,4^{+}0,29	0,35^{+}0,01

Table 2

MDA content in rat heart and liver homogenates.

Series of experiments	MDA (n mol/mg proteins min)			ADP/NDP
	MP	ADP	NDP	
Control	1,65^{+} 0,02	3,33^{+} 0,11	6,71^{+} 0,17	0,49^{+}0,03
3 days	7,42^{+} 0,04	20,64^{+} 0,14	82,53^{+} 0,02	0,25^{+}0,02

Table 3

MDA content in MX-fraction

Series of experiments	MDA (n mol/mg proteins min)			ADP/NDP
	MP	ADP	NDP	
Control	8,1^{+}0,11	88,3^{+}0,73	64,5^{+} 0,39	1,36^{+}0,11
3 days	59,9^{+}1,73	326,71^{+}3,77	283,8^{+} 7,3	1,53^{+}0,08

Table 4

MDA content in MS-fraction

Series of experiments	MDA (n mol/mg proteins min)			ADP/NDP
	MP	ADP	NDP	
Control	1,43^{+}0,06	11,2^{+}0,09	31,4^{+}0,29	0,35^{+}0,01
3 days	28,8^{+}1,02	71,68^{+}3,77	85,26^{+}1,14	0,35^{+}0,01