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Review Article

Investigating lipid oxidative stress in rats during experimental myocardial infarction

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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. Interest in studying the pathogenesis of these diseases and developing methods of biochemical correction to address disorders remains high [1, 5]. Disruption of metabolic processes, the body's nonspecific defenses, and a decrease in its regenerative abilities contribute to the occurrence of free radical lipid oxidation processes in the body. The activation of free radicals leads to the formation of highly toxic metabolites, such as acylhydroperoxides, unsaturated aldehydes, and malondialdehyde (MDA), which possess mutagenic and cytotoxic properties [2, 6, 7, 8]. Products of free radical lipid oxidation can suppress the activity of glycolytic enzymes and oxidative phosphorylation, inhibit protein and nucleic acid synthesis, and hinder many membrane-bound enzymes, resulting in significant damage to cells and the body as a whole [3, 9, 10, 11].

Aim

The aim of this study is to investigate the level of lipid oxidation in the body during myocardial infarction.

Materials and Methods

The experiments were conducted on white outbred male rats (n=25) weighing 200 grams. Myocardial infarction was induced by ligation of the left coronary artery. The animals were euthanized by decapitation on the 3rd day following the initiation of the myocardial infarction experiment. Subsequently, the heart and liver were swiftly removed, weighed, washed with a cold 0.15M KCl solution at 0-4°C, and homogenates were prepared for biochemical analysis. Heart homogenates were obtained by mincing the organ with a scalpel, followed by the disruption of heart cells in a glass homogenizer with a Teflon pestle [4, 12, 13]. Liver homogenates were obtained by pressing the liver through a grid with 0.5 mm holes and further disrupted in a glass homogenizer with a Teflon pestle [5, 14, 15]. For isolation, 0.05M KCl dissolved in 50ml of Tris-HCl buffer (pH=7.4) was used. Mitochondrial (MC) and microsomal (MS) fractions were isolated from liver homogenates. The mitochondrial fraction was obtained by differential centrifugation at 9000g for 20 minutes, while the liver microsomal fraction was obtained by subsequent centrifugation of the supernatant for 60 minutes at 105000g. In heart homogenates and MS- and MX-fractions of the liver, the amount of MDA was determined using the method of Steel I.D. and others, along with the activity of superoxide dismutase (SOD) according to the method of Mears, Fridovich modified by Brusov, etc [16, 17].

Results

A study of the level of oxidative stress in heart homogenates from control animals showed that the concentration of malonic dialdehyde (MDA) in the tissue was significantly low (Table 1).

In control rats, a significant content of lipid peroxidation (LPO) products was detected in both mitochondria and liver microsomes, likely due to the presence of electron transport chains in these organelles and the formation

of reactive oxygen species. In mitochondria, where the main oxygen-dependent metabolism in the body occurs, the most aggressive of all free radicals, the superoxide anion O2-, is formed. Therefore, mitochondria are distinguished by high levels of ascorbate-dependent lipid oxidation (ADL) and NADH-dependent lipid oxidation (NDL) compared to other organelles. It is assumed that the predominance of ascorbate-dependent lipid oxidation in mitochondria over NADH-dependent may be due to the intensity of the alternative non-enzymatic pathway for the formation of free radicals. Note that the oxygen formed as a result of these reactions is immediately neutralized under the influence of antioxidant defense enzymes - superoxide dismutase (SOD) and catalase. The microsomal fraction of the liver is characterized by less intense lipid oxidation compared to mitochondria, which is explained by the use of oxygen in plastic processes when it is integrated into the molecule of the oxidized substrate under the influence of specific oxygenases.

Organ	MDA (nmol/mg proteins min)			ADL/NDL
	SP	ADL	NDL	
Heart	1,65±0,02	3,33±0,11	6,71±0,17	0,49±0,03
MX fraction of the liver	8,1±0,11	88,3±0,73	64,5+- 0,39	1,36±0,11
MS fraction of liver	1,43±0,06	11,2±0,09	31,4±0,29	0,35±0,01

Table 1: Concentration of malondialdehyde (MDA) in rat heart and liver homogenates.

Thus, when analyzing the level of lipid peroxidation in heart homogenates, as well as in mitochondrial (MC) and microsomal (MS) fractions of the liver, we can conclude that these tissues exhibit a certain level of free radical lipid oxidation (FROL), which is determined by their structural characteristics and functional activity. The slowdown in the rate of LPO reactions is due to an effective antioxidant defense system. A study of LPO activation in rats with experimental myocardial infarction showed a significant increase in its intensity (on the 3rd day after occlusion of the left coronary artery). The level of MDA content in cardiac tissue homogenates was increased 5 fold compared to the control during spontaneous peritonitis. The increase in MDA concentration during ascorbate- and NADH-dependent lipid peroxidation was 5.1 and 14.7 fold, respectively (Table 2).

Series of experiments	MDA (nmol/mg proteins min)			ADL/NDL
	SP	ADL	NDL	
Control	1,65±0,02	3,33±0,11	6,71±0,17	0,49±0,03
3 days I.M.	7,42±0,04	20,64±0,14	82,53±0,02	0,25±0,02

Table 2: Concentration of malondialdehyde (MDA) on the 3rd day of the experiment.

A sharp increase in LPO activation in cardiac tissue 3 days after inducing coronary-occlusive myocardial infarction indicates pronounced processes of membrane destruction in cardiac tissue 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 cell destruction. The level of MDA also increased in the MC and MS fractions of the liver in rats after experimental myocardial infarction (after 3 days of the experiment).

The amount of MDA in the MC fraction of the liver in the absence of oxidative stress exceeded normal values by 6.1 fold. A study of inducible oxidative stress systems showed activation of ADL by 3.1 and NDL by 3.4 fold (Table 3).

Series of experiments	MDA (nmol/mg proteins min)			ADL/NDL
	SP	ADL	NDL	
Control	8,1±0,11	88,3±0,73	64,5±0,39	1,36±0,11
3 days I.M.	59,9±1,73	326,71±3,77	283,8±7,3	1,53±0,08

Table 3: MDA content in the MC fraction of the liver on day 3 of experimental myocardial infarction.

It seems like there was a significant increase in oxidative stress in the liver microsomal fraction compared to the MC fraction. This increase was evident in the higher concentrations of MDA in lipid peroxides, ADL enzyme levels, and NDL activity. The information presented in Table 4 shows that MDA increased 28.2-fold, while ADL showed a 4.6-fold increase and NDL activity increased 9.5-fold. These results highlight the significant difference in oxidative stress levels observed between the two fractions.

In the liver MS fraction, there was a 2.05-fold increase in the ratio of aldehyde dehydrogenase activity to the activity of nonspecific peroxidase. This likely suggests an increase in non-enzymatic oxidative stress because of impaired antioxidant defenses in microsomes. The increase in aldehyde dehydrogenase activity coincided with a significant 73.1% decrease in superoxide dismutase activity in the MS fraction of rats of the experimental group. In addition, superoxide dismutase activity in the MC fraction decreased by 31.5%.

Series of experiments	MDA (nmol/mg proteins min)			ADL/NDL
	SP	ADL	NDL	
Control	1,43±0,06	11,2±0,09	31,4±0,29	0,35±0,01
3 days I.M	28,8±1,02	71,68±3,77	85,26±1,14	0,35±0,01

Table 4: MDA content in the MS fraction of the liver on day 3 of experimental myocardial infarction.

Conclusion. A deficiency of antioxidants leads to the destruction of the body's compensatory mechanisms. In the initial periods of experimental myocardial infarction (3 days), an increase in free radical processes in cardiac tissue may be due to the massive death of necrobiotic altered cells. The increase in oxidative stress in the MC and MS fractions of the liver was probably associated with the absorption of cell destruction products. Analysis of the results of our study serves as the basis for the search for agents that have protective properties against increased oxidative stress. Perhaps the use of antioxidants will help reduce the intensity of oxidative stress in the body and restore impaired metabolism.

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