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OXIDATIVE STRESS AND LIPID PEROXIDATION IN EXPERIMENTAL PERITONITIS

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Abstract

Peritonitis is one of the most serious complications of pathology of the abdominal organs, which is characterized by a high mortality rate.

Violation of the natural mechanisms of detoxification (immune, detoxification functions of the liver and kidneys), which occur in acute peritonitis, due to primary damage to their structure and the development of maladaptation mechanisms, accompanied by endogenous intoxication syndrome. One of the characteristic and aggravating manifestations of the syndrome of endogenous intoxication is the activation of lipid peroxidation (LPO).

The aim: study of the dynamics of primary and secondary products of lipid peroxidation in experimental peritonitis.

In the first hour simulated fecal peritonitis development in the rats blood revealed an increase in the level of diene conjugates and malondialdehyde ($p < 0.001$ compared with the results of intact animals. In the second stage was detected more pronounced increase in the level of primary and secondary products of lipid peroxidation ($p < 0.001$) as compared with the data of the same hole in the first stage, and compared with the results of group No. 1. On the 3rd day of simulated peritonitis development in rats there is a marked deterioration of the animal condition, which was manifested in lipid peroxidation progression: the diene conjugates level increased at the significance level $p < 0.001$, and the level of malondialdehyde compared to $p < 0.05$ data from the previous stage of the same group.

Key words: *experimental peritonitis, lipid peroxidation, malonic dialdehyde, diene conjugates*

Introduction

Peritonitis is one of the most serious complications of pathology of the abdominal organs [1, 2], which is characterized by a high mortality rate [3, 4].

Violation of the natural mechanisms of detoxification (immune, detoxification functions of the liver and kidneys), which occur in acute peritonitis, due to primary damage to their structure and the development of maladaptation mechanisms, accompanied by endogenous intoxication syndrome [5, 6]. This syndrome is a complex of pathological conditions of different etiology and severity, but due to the accumulation of endotoxins in biological fluids and tissues [7]. One of the characteristic and aggravating manifestations of the syndrome of endogenous intoxication is the activation of lipid peroxidation (LPO) [8]. LPO is one of the key mechanisms of toxic substances formation. With significant reactivity, lipid peroxidation products interact with nucleic acids, proteins and other cell molecules. This leads to the separation of oxidative phosphorylation, inactivation of enzymes, increased permeability of cell membranes [9]. It is also known that oxidized forms of lipids that accumulate in the blood lead to destructive processes at the molecular (free radical modification of blood lipoproteins),

Given the above, it is important to study the floor against the background of the development of peritonitis for the further development of new effective ways to correct the pathogenetic links of this pathology.

The aim**:** study of the dynamics of primary and secondary products of lipid peroxidation in experimental peritonitis.

Methods

The study was performed on 140 white male rats weighing 180–220 g. The animals were divided into 2 groups:

1 group - 40 intact animals.

Group 2 - 100 rats with simulated fecal peritonitis.

Fecal peritonitis was simulated by introducing a 10% fecal suspension at a dose of 0.5 ml per 100 g of animal weight to the abdominal cavity by the puncture method (Lazarenko VA and others, 2016, patent № 233826).

The analysis of indicators was performed for the first hour after the completion of simulation of peritonitis and the first, third and seventh days of the experiment. The research was conducted in accordance with the "Rules for the performance of work using experimental animals", approved by the Order of the Ministry of Health of Ukraine № 249 from 01.03.2012 and the Law of Ukraine № 3447-IV "On protection of animals from cruelty" (as amended from 15.12.2009 and from 16.10.2012).

Determination of the level of diene conjugates (DC) and malonic dialdehyde (MDA) in the serum was performed by spectrophotometric method. MDA was determined by reaction with thiobarbituric acid.

Before using parametric methods based on the normality of the statistical distribution, the studied series of quantitative data were tested for normality using the Shapiro-Wilk's W test. Due to the normal distribution of digital data in the samples used the parametric Student's t test.

Results

In the group of animals that simulated fecal peritonitis (taking into account the withdrawal from the experiment of 20 animals at each stage), the following dynamics of survival was observed: 1st hour - 98 rats; 1st day - 49 rats; 3rd day - 20 rats; Day 7 - rats with simulated fecal peritonitis without correction did not survive to this stage of the study.

The choice of DC and MDA as markers of the severity of the pathological process is justified by the following. Data on the content of LPO products have diagnostic value in terms of depth, severity and prognosis of the pathological process. In the development of many diseases, lipoperoxidation can be considered as a universal non-specific pathogenetic link [11]. Lipid peroxidation under physiological conditions regulates the functions of organs and cells. A necessary condition for this is a balance between free radicals and the state of the antioxidant system. That is why the activation of lipid peroxidation plays a negative role during the transition from physiological to pathological, while violating regulatory links. Lipid peroxidation itself goes through several stages. It should be noted that each of these stages in endotoxicosis may play different roles in the violation of homeostasis.

In the analysis of diene conjugates, which are the primary products of lipid peroxidation, the following results were obtained in the course of our study (Table 1).

At the first stage (the first hour after the completion of peritonitis modeling), an increase in the level of diene conjugates (p <0.001) was found in the blood of rats compared with the results of intact animals.

In the second stage (the first day of development of simulated peritonitis) revealed a more pronounced increase in the level of primary products of lipid peroxidation (p <0.001 both compared with the data of the same group in the first stage and compared with the results of group №1).

On the third day of development of simulated fecal peritonitis in the group of rats without correction there is a marked deterioration of the animals, which manifested itself in the progression of lipid peroxidation: the level of diene conjugates is increased at the level of significance p <0.001.

Next, consider the dynamics of the level of malonic dialdehyde (secondary product of LPO) against the background of the development of fecal peritonitis (Table 2).

Malonic dialdehyde has characteristic toxic properties, is able to damage nucleic acids, proteins and enzymes and is an indicator of the activity of free radical reactions [12]. Therefore, we can say that excessive accumulation of MDA significantly enhances endotoxemia [13].

In a study of patients with progressive pancreatitis, acute peritonitis, sepsis, ie in critical conditions, an increase in the level of MDA in the blood as the severity of multiorgan failure increased. In the most seriously ill patients, a significant decrease in the levels of antioxidant and proteolytic activities was observed against the background of the maximum increase in the level of MDA [14].

At 1 hour after the completion of modeling peritonitis, an increase in the level of malonic dialdehyde (p <0.001) was found in the blood of rats compared with the results of intact animals.

In the second stage (the first day of development of simulated peritonitis) revealed a more pronounced increase in the level of secondary products of lipid peroxidation (p <0.001 both compared with the data of the same group in the first stage and compared with the results of group №1).

On the third day of development of simulated fecal peritonitis in the group of rats without correction there is a marked deterioration in animals, which manifested itself in the progression of lipid peroxidation: the level of malonic dialdehyde increased at a level of p <0.05 compared with the same group in the previous stage.

The earliest biochemical indicator, which indicates the beginning of the destructive process in the abdominal cavity, and subsequently reflects the dynamics of the pathological process, is an increase in the concentration of LPO products in the blood [15]. The above results of our study indicate a pronounced activation of lipid peroxidation on the background of simulated fecal peritonitis in experimental animals.

Conclusions

1. As a result of our study, a pronounced activation of lipid peroxidation on the background of simulated fecal peritonitis in experimental animals.
2. Already in the first hour of development of the simulated experimental peritonitis in the blood of rats revealed an increase in the level of diene conjugates and malonic dialdehyde (p <0.001) compared with the results of intact animals).
3. The second stage (the first day of development of simulated peritonitis) revealed a more pronounced increase in the level of primary and secondary products of lipid peroxidation (p <0.001 both compared with the data of the same group in the first stage and compared with the results of group №1).
4. On the third day of development of simulated fecal peritonitis in the group of rats without correction there is a marked deterioration of the animals, which manifested itself in the progression of lipid peroxidation: the level of diene conjugates increased at the level of significance p <0.001, and the level of malonic dialdehyde - p <0.05 compared with the previous stage of the same group.

Acknowledgments

The authors declare that there are no conflicts of interest.

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Table 1. The results of the study of the level of diene conjugates in the blood of rats with simulated fecal peritonitis and in intact animals (M ± m)

	1 group	Group 2
1st year	50.41 ± 1.67	68.34 ± 1.98
1st day	50.4 ± 1.98	92.1 ± 1.62
3rd day	50.4 ± 2.27	104.1 ± 1.55
7th day	50.41 ± 1.64	-

Table 2. The results of the study of the content of malonic dialdehyde in the blood of rats with simulated fecal peritonitisand in intact animals (M ± m)

	1 group	Group 2
1st year	5.01 ± 0.67	9.24 ± 0.62
1st day	5.01 ± 0.64	16.82 ± 0.49
3rd day	5.01 ± 0.78	19.11 ± 0.59
7th day	5.01 ± 0.67	-