

ORIGINAL ARTICLE

CRITERIA FOR ASSESSING ENDOGENOUS INTOXICATION IN PATIENTS WITH MULTIPLE PERITONITIS

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ABSTRACT

The aim: To determine the diagnostic significance of the level of malondialdehyde (MDA) in various biological media for RP for assessing and predicting the course of the disease.

Materials and methods: Our study included The work was based on the results of surgical treatment of 60 patients with RP: according to MPI I - in 17 (28.3%), MPI II - in 23 (38.4%) and MPI III - in 20 (33.3%) patients. Surgical intervention for RP was aimed at sanitation and drainage of the abdominal cavity. The control group included 15 practically healthy people, whose blood and urine biochemical parameters served as the norm. According to the clinical course of the disease, the patients were divided depend on admission, The secondary product of lipid peroxidation - MDA was studied in blood serum, peritoneal exudate and urine in patients with RP, depending on the severity of the pathological process according to the Mannheim peritoneal index (MPI) - I severity (I), II severity (II), III severity (III). The work was based on the results of surgical treatment of 60 patients with RP: according to MPI I - in 17 (28.3%), MPI II - in 23 (38.4%) and MPI III - in 20 (33.3%) patients.

Results: Analyses of results showed that the average value of MDA in various biomedical of recovered (n = 18) and subsequently died (n = 5) patients with MPI II are given in Table. 2. As can be seen from the presented data, the average value of MDA in blood serum and peritoneal exudate in patients with a lethal outcome is significantly higher than in those who have recovered. This fact indicates a more pronounced endogenous intoxication in patients who died from RP.

Conclusions: The content of MDA in the blood serum before surgery in patients with a lethal outcome was 190% (p <0.001). The level of MDA in urine in patients according to MPI II who subsequently died before surgery was 110% (p <0.001), and in those who recovered by 300% (p <0.001) it was higher than the norm. exudate taken during the operation averaged 4.14 ± 0.33 nmol / ml, then in the recovered - 2.89 ± 0.08 nmol / ml. A high level of MDA in the blood serum, peritoneal exudate with a decrease in the elimination of MDA in the urine in the postoperative period are prognostically unfavorable signs in patients, indicating the continuation of endogenous intoxication and a possible death.

KEY WORDS: endogenous intoxication, generalized peritonitis, malondialdehyde (MDA), inflammation

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INTRODUCTION

Treatment of patients with generalized peritonitis (RP) continues to be one of the most pressing problems of abdominal surgery. According to observations, in 20 - 30% of all cases associated with acute surgical pathology of the abdominal organs, peritonitis develops [1,2]. Mortality in RP in Europe reaches from 9.79 to 84% and averages 38.6-45%, which indicates the absence of a single algorithm for the treatment of this complication [3,4]. Along with the systemic inflammatory response and hypoxia, one of the leading places in the development of disorders in the homeostasis system in RP is occupied by disorders of free radical processes and the development of endotoxemia, which are the main causes of metabolic disorders [5,6].

Increased attention to the problem of RP is due to the accompanying serious complications: extremely severe endotoxemia, the development of abdominal sepsis, multiple organ failure and pyoinflammatory complications [7,8]. Along with the systemic inflammatory response and hypoxia, one of the leading places in the development of disorders in the homeostasis system in RP is occupied by disorders of free radical processes and the development of endotoxemia,

which are the main causes of metabolic disorders [9,10].

In the implementation of metabolic processes, lipid peroxidation (LPO) plays a leading role [11,12]. LPO processes as a necessary metabolic link proceed normally in a healthy organism, however, under certain conditions (trauma, inflammation, ischemia, hypoxia, etc.), a sharp intensification of lipid peroxidation occurs with the formation of an excess amount of free radicals, which leads to the development of oxidative stress, and LPO becomes a universal mechanism of damage to both a single molecule and cells at the level of membranes and organ tissue [13-15]. An increase in the intensity of LPO processes plays a triggering role in the development of multiple organ failure [16,17]. To neutralize excess lipid peroxidation and maintain the LPO processes at a stationary level in the body, there is an antioxidant defense system (AOD), which normally provides a balance between LPO and AOD [18-20]. Violations of the antioxidant status of the body with a sharp intensification of lipid peroxidation and AOD deficiency reduce the detoxification of the body and lead to the development of poisoning by the type of oxidative distress [21].

Table I. Comparative assessment of MDA parameters in blood serum, peritoneal exudate and urine ($M \pm m$, min-max (in nmol / ml).

Test material	Index	Research time, day					Norm value
		Before operation	1	3	5	7	
Blood serum	I	6,31±0,25 4,5-7,9	8,58±0,23 5,6-9,6	6,17±0,18 5,2-8,3	5,68±0,18 4,7-7,5	5,3±0,18 4,3-7,4	3,79±0,5 3,4-4,1
	II	9,77±0,34 6,8-11,9	10,73±0,36 7,7-13,9	9,1±0,31 6,8-12,1	8,23±0,32 6,2-11,5	7,26±0,3 5,7-11,1	
	III	13,08±0,42 9,5-16,5	15,58±0,47 10,6-18,8	12,01±0,5 8,5-15	11,24±0,52 7,5-14,4	10,55±0,44 7,1-13	
Abdominal exudate	I	2,45±0,07 2,1-3,1	2,88±0,88 2,4-3,5	2,19±0,08 1,6-2,8	2,11±0,08 1,6-2,7	-	
	II	3,16±0,14 2,2-4,81	3,99±0,18 2,6-6	3,32±0,12 2,4-4,81	3,06±0,11 2,2-4,25	2,81±0,11 2,2-3,87	
	III	4,43±0,22 3,1-6,1	5,05±0,25 3,5-6,91	4,34±0,19 3,5-6	4,13±0,15 3,5-5,6	3,72±0,09 2,9-4,1	
Urine	I	0,043±0,003 0,015-0,065	0,051±0,04 0,02-0,07	0,048±0,03 0,02-0,065	0,042±0,03 0,015-0,06	0,033±0,02 0,02-0,05	0,2±0,02 0,01-0,03
	II	0,072±0,005 0,038-0,11	0,112±0,08 0,043-0,16	0,098±0,07 0,03-0,13	0,084±0,07 0,02-0,12	0,057±0,05 0,02-0,1	
	III	0,107±0,009 0,04-0,18	0,152±0,04 0,05-0,23	0,136±0,01 0,07-0,2	0,111±0,01 0,06-0,18	0,105±0,09 0,05-0,155	

Table II. The average value of MDA in various test materials in patients with RP according to MPI II, ($M \pm m$, min-max (in nmol / ml)

Outcome of the disease	Research material	Research time, day				
		Before operation	1	3	5	7
Favourable (n-18)	Blood serum	9,42±0,39 6,8-11,9	10,32±0,39 7,7-12,8	8,93±0,34 6,8-12,1	8,08±0,35 0,2-11,5	7,11±0,31 5,7-11,1
	Abdominal exudate	2,89±0,08 2,2-3,5	3,59±0,09 2,6-4,1	3,14±0,08 2,4-3,6	2,93±0,08 2,2-3,5	2,7±0,09 2,2-3,3
	Urine	0,8±0,004 0,05-0,11	0,13±0,004 0,09-0,16	0,109±0,005 0,07-0,13	0,094±0,005 0,06-0,12	0,06±0,005 0,04-0,1
Unfavourable (n-15)	Blood serum	n = 5 11,04±0,30 10-11,6	n = 5 12,24±0,5 10,9-13,9	n = 3 10,07±0,46 9,3-10,9	n = 3 9,17±0,46 8,4-10	n = 2 8,2; 9,1
	Abdominal exudate	n = 5 4,14±0,33 3,17-4,81	n = 5 5,41±0,27 4,61-6	n = 3 4,35±0,32 3,73-4,81	n = 3 3,84±0,37 3,11-4,25	n = 2 3,7; 3,87
	Urine	n = 5 0,043±0,2 0,038-0,051	n = 5 0,048±0,03 0,043-0,06	n = 3 0,037±0,003 0,03-0,04	n = 3 0,025±0,003 0,02-0,03	n = 2 0,02; 0,027

In our opinion, the study of lipid peroxidation processes in peritoneal exudate, blood serum and urine is of great importance [22].

There are practically no works in the literature that provide comparative assessments of the levels of lipid peroxidation metabolites in blood serum, peritoneal exudate and urine.

THE AIM

The aim of the work was to determine the diagnostic significance of the level of malondialdehyde (MDA) in various biological media for RP for assessing and predicting the course of the disease.

MATERIALS AND METHODS

All patients had been admitted to the SI «Zaycev V. T. Institute of General and Urgent surgery of National Academy of Medical Sciences of Ukraine», Kharkiv, Ukraine for surgical treatment for generalized peritonitis (RP) underwent standard clinical and laboratory tests. Patients who were treated at the Department of Surgical Infections.

According to the clinical course of the disease, according to severity the patients, according the level of MDA were divided into the groups. The secondary product of lipid peroxidation - MDA was studied in blood serum, peritoneal exudate and urine in patients with RP, depending

on the severity of the pathological process according to the Mannheim peritoneal index (MPI) - I severity (I), II severity (II), III severity (III).

The work was based on the results of surgical treatment of 60 patients with RP: according to MPI I - in 17 (28.3%), MPI II - in 23 (38.4%) and MPI III - in 20 (33.3%) patients. ... Surgical intervention for RP was aimed at sanitation and drainage of the abdominal cavity. The control group included 15 practically healthy people, whose blood and urine biochemical parameters served as the norm. The concentration of MDA in all three biological media was determined by the method of L.I. Andreeva et al. It is necessary to find a foreign method before the operation, during the operation in the taken exudate, on the 1st, 3rd, 5th and 7th days after the operation.

The authors declare that all procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008 (5), as well as the national law. Informed consent to participate in the study was discussed and signed by all study participants. Meeting of the Bioethics Commission (protocol №1 06.09.2021) of the State Institution "Zaycev V.T. Institute of General and Urgent Surgery of the National Academy of Medical Sciences of Ukraine".

There was not found a significant difference in the number of patients, average age, gender composition, or body mass index (BMI) found between OA groups ($p > 0.05$).

Ethics review. All patients signed a voluntary informed consent for the examination and treatment, as well as publication of anonymized personal medical information for academic purposes.

Statistical analysis. Determine the diagnostic significance of the level of malondialdehyde (MDA) in various biological media for RP for assessing and predicting the course of the disease using non-parametric statistical techniques (analysis of two-dimensional frequency distributions based on the chi-squared criterion and relative risk) in free-access software for statistical calculations and MS Excel spreadsheet processor. The differences between the main and control groups are statistically significant ($p < 0.05$).

RESULTS

The level of MDA in peritoneal exudate, blood serum and urine directly depended on the severity of RP according to the MPI. It was found that in patients with MPI I in the blood serum, the concentration of MDA was 66.5% ($p < 0.001$), in urine - 2.1 times ($p < 0.001$) more than in healthy people. In peritoneal exudates obtained during the operation, the concentration of MDA was 2.45 ± 0.07 nmol / ml.

The results of the study as a whole are presented in Table I.

In patients with MPI II, the MDA level in the blood serum was 2.6 ($p < 0.001$), in the urine - 3.6 times ($p < 0.001$), according to MPI III - 3.5 ($p < 0.001$) and 5.3 times ($p < 0.001$), respectively, higher than the normal value. In the peritoneal exudate taken during the operation, the content of this metabolite was 3.16 ± 0.14 according to MPI II, and 4.43 ± 0.022 nmol / ml according to MPI III.

The average value of MDA in various biomedical of recovered ($n = 18$) and subsequently died ($n = 5$) patients with MPI II are given in Table II. As can be seen from the presented data, the average value of MDA in blood serum and peritoneal exudate in patients with a lethal outcome is significantly higher than in those who have recovered. This fact indicates a more pronounced endogenous intoxication in patients who died from RP. So, if in patients with a fatal outcome the average value of MDA in peritoneal exudate taken during the operation averaged 4.14 ± 0.33 nmol / ml, then in those who recovered it was 2.89 ± 0.08 nmol / ml. The content of MDA in blood serum before surgery in patients with a lethal outcome was 2.9 times ($p < 0.001$), and in recovered patients - 2.5 times ($p < 0.001$) more than in healthy people.

The level of MDA in urine in patients according to MPI II who subsequently died before surgery was 2.1 times ($p < 0.001$), and in those who recovered it was 4 times higher ($p < 0.001$) compared to the norm. The average MDA value of blood serum and peritoneal exudate on the 3rd and 3rd day of the postoperative period in recovered patients and patients with lethal outcome increased. Subsequently, the value of MDA in peritoneal exudate and blood serum in recovered patients significantly differed, having a clear tendency to decrease.

During the entire postoperative period, there was a higher level of MDA in the urine with a maximum value on day 3 and up to a level of 0.130 ± 0.004 nmol / ml in recovered patients. The consistently high level of MDA in the urine was accompanied by a natural decrease in the MDA content in the blood serum in these patients. In patients with a lethal outcome throughout the entire postoperative period of observation, the level of MDA in the blood serum and exudate remained high. Against this background, the level of MDA in the urine was lower than in the recovered patients. Thus, a weakly expressed tendency towards a decrease in the level of MDA in peritoneal exudate and blood serum is accompanied by a progressive decrease in the elimination of this metabolite in the urine in patients with a fatal outcome.

In patients with MPI III, in general, the maximum values of the MDA level in the peritoneal exudate and blood serum were recorded. At the same time, an increase in the intoxication of MDA values in the exudate was observed from 4.43 ± 0.22 nmol / ml on the day of surgery to a maximum of 5.05 ± 0.25 nmol / ml on the first day after surgery. In the blood serum before the operation, the MDA level was 13.08 ± 0.42 nmol / ml with a maximum value on the 3rd and 3rd day of the postoperative period. In these patients, there was a distinct tendency towards a decrease in the level of MDA in the peritoneal exudate and blood serum with increased elimination of MDA in the urine.

DISCUSSION

Many pathophysiological events develop due to generalized peritonitis. Free oxygen radicals caused by inflammation damage the cell membrane. Free oxygen radicals increase

lipid peroxidation. The final product of lipid peroxidation, malondialdehyde (MDA) indirectly shows the amount of free oxygen radicals [23].

It should be noted, the comparative analysis of the researches showed that the study of MDA in peritoneal exudate, blood serum and urine in the postoperative period in patients with RP is one of the objective criteria for assessing endogenous intoxication [24]. The relatively rapid resolution of the phenomena of peritonitis in patients was accompanied by a regular drop in the level of MDA in the exudate and serum with enhanced elimination of this metabolite in the urine. A high level of MDA in the blood serum and peritoneal exudate with a decrease in the elimination of MDA in the urine in the postoperative period are prognostically unfavorable signs in patients, indicating the continuation of endogenous intoxication and possible death [25].

Intraabdominal complications, infections, microorganisms and toxins in abdominal cavity due to generation of inflammatory response in the peritoneum is defined as the accumulation of purulent exudate [26]. This inflammatory response may be local or generalized on the surface of the peritoneum. At the present time in Ukraine the statistics of mortality of generalized peritonitis are very high and amounts to 41,3-71,7% whereas postoperative mortality in GP varies in the range of 41,8-72,5% [22]. It is very important to notice that in elderly patients the mortality rate increases to 99%. Mortality in GP in Europe reaches from 9.79 to 84% and averages 38.6-45%, which indicates the absence of a single algorithm for the treatment of this complication [28,29].

Generalized peritonitis is one of the reasons that increase oxidative stress and marks such as lipid peroxidation, an indicator of oxidative stress, is mediated the harmful effects of oxidative stress. There are many ways of mechanisms, are known as antioxidants, against free oxygen radicals occurring in the body. If the concentration of free oxygen radicals released is much more than the antioxidant capacity of the cleaner system, irreversible cell damage occurs. In a healthy cell, there is a balance between the formation and removal of free radicals. Oxidative stress occurs if the balance is disrupted for any reason and more free radicals are formed or the level of antioxidants decreases. This stress causes serious cell damage if prolonged and severe [26,27].

CONCLUSIONS

1. The content of MDA in the blood serum before surgery in patients with a lethal outcome was per 2,9 times more ($p < 0.001$), and in those who recovered - was per 2,5 times ($p < 0.001$) more than in healthy people $3,79 \pm 0,5$ nmol / ml ($p < 0.001$). The level of MDA in urine in patients according to MPI II who subsequently died before surgery was per 2,9 times more ($p < 0.001$), and in those who recovered per 4 times more ($p < 0.005$) it was higher than the norm. exudate taken during the operation averaged 4.14 ± 0.33 nmol / ml, then in the recovered - 2.89 ± 0.08 nmol / ml.

2. Further rapid resolution of the phenomena of peritonitis in patients was accompanied by a regular drop in the level of MDA in the exudate and blood serum with enhanced elimination of this metabolite in the urine.
3. A high level of MDA in the blood serum, peritoneal exudate with a decrease in the elimination of MDA in the urine in the postoperative period are prognostically unfavorable signs in patients, indicating the continuation of endogenous intoxication and a possible death.

STUDY LIMITATIONS

This study contains the research of determination and diagnostic significance of the level of malondialdehyde (MDA) in various biological media for RP for assessing and predicting the course of the disease. Since studying and control these marks we improve results in the post- and preoperative periods and realize the full effect of treatment in patients.

PROSPECTS FOR THE FUTURE RESEARCH

Since the careful study the level of malondialdehyde (MDA) in patients with generalized peritonitis in surgical treatment and conservative treatment patients can notice to improving of surgical results, we plan to develop an algorithm that will reduce the number of postoperative complications.

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Conflict of interest:

The Authors declare no conflict of interest.

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