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ENDOGENOUS INTOXICATION IN PATIENTS WITH ACUTE DIFFUSE PERITONITIS AND THE INCIDENCE OF SEPSIS

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Abstract: Goal. Optimization of treatment of endotoxemia and endotoxicosis in patients with acute diffuse peritonitis by early diagnosis of generalization of infection with the development of sepsis and timely correction. Materials and methods: a study of 141 patients with acute diffuse peritonitis of various etiologies was conducted, the patients were divided into 3 groups according to the phases of the prevalence of the process: diffuse, widespread, purulent - fibrous. Results: in patients with group I with acute diffuse peritonitis, generalization of the process with the development of sepsis, it was found that peptide intoxication in patients receiving only infusion-transfusion therapy with forced diuresis turned out to be quite resistant. Hemosorption, in addition to reducing the period of endogenous intoxication, reduced the total amount of liquid media for PL and IL. So, the amount of fluid for PL and IL, in the first 2-3 days in patients of groups II and III, was almost the same, but further, the volume of lavage fluid for group III was lower. Conclusion. In patients with ADP, despite the therapy in the postoperative period, generalization of the process with the development of sepsis occurs in 31.2% of cases, verified clinically by the studied procalcitonin test. With diffuse fibrinous-purulent peritonitis, the frequency of generalization of infection reaches 50%, with serous-fibrinous diffuse peritonitis - 32.2%. with serous peritonitis - 3.9%.

Key words. Endotoxicosis, endotoxemia, sepsis, peritonitis, detoxification.

Introducrion.

The development of intensive care and resuscitation, expanding the limits of recovery, revealed a number of unresolved problems. One of the most difficult problems of intensive care is endogenous intoxication syndrome (EIS). The concept of endotoxicosis (ET) has firmly entered the lexicon of doctors of various specialties and, first of all, anesthesiologists-resuscitators. In order to assess its level, the definition of a whole complex of substances, primarily in blood plasma, is proposed. [7, 13]. According to a number of authors, up to 90% of adverse outcomes in the treatment of surgical diseases, one way or another, are associated with endotoxemia syndrome, or are its consequence, which makes this problem very relevant [10, 14, 5]. The existing criteria for determining the degree of endotoxicosis in surgical sepsis cannot fully satisfy clinicians, because they require large material and time costs associated with expensive equipment, chemical reagents and complex methods for their determination [2, 4, 6, 8]. Metabolic disorders lead to the formation and entry into the bloodstream of a large number of unidentified substances of medium molecular weight, which are currently combined with the terms "medium molecules", medium molecular oligopeptides [3, 1]. Against the background of massive intoxication caused by the accumulation of a wide range of bacterial and endogenous toxins in the body, deep metabolic disorders, damage and dysfunction of almost all body systems develop, i.e.multiple organ failure syndrome [12, 15].If the leading role of endogenous intoxication [EI] in the pathogenesis of common forms of peritonitis can be considered proven, then the question of the sources of intoxication, the deposition of toxins and the issues of their early elimination have not yet been resolved [9, 11], which formed the basis of our study.

Materials and methods of the study.

141 patients of various age groups with signs of endotoxicosis and endogenous intoxication syndrome caused by acute diffuse peritonitis (ADP) of various etiologies - 80 (56.7%) men and 61 (43.3%) women were examined. The most common causes of peritonitis in patients were: perforated stomach ulcer and duodenal ulcer, destructive appendicitis.

In the postoperative period, patients with ADP were retrospectively divided into three groups depending on the severity of the course, the volume of the operation and intensive therapy to study the dynamics of endogenous intoxication.

The I -group consisted of 43 patients with peritonitis of various etiology, phase and prevalence. Diffuse form of peritonitis dominated (53.5%). All patients were operated with the removal of the focus and drainage of the abdominal cavity.

The reactive phase of peritonitis was diagnosed in 21 (48.8%) patients, toxic in 17 (39.5%) and terminal in 5 (11.7%).

Group II consisted of 62 patients. A distinctive feature of these patients was a more severe clinical course due to the significant predominance of common forms of peritonitis with longer periods of its development. The detoxification therapy complex included ITT with stimulation of diuresis, combined with peritoneal and intestinal lavage, and antibacterial therapy.

Phases of peritonitis: reactive - in 8 (12.9%) patients, toxic - in 34 (54.8%) and terminal in 20 (32.3%) patients, i.e. patients with toxic and terminal phases of peritonitis prevailed.

Group III consisted of 36 patients. Their condition was more severe than in group II. The reason was the nature of peritonitis: diffuse purulent and purulent fibrinous, with toxic and terminal phases of the course, a more pronounced picture of hemodynamic disorders and impaired liver and kidney function.

The difference between these groups was only that, due to the dysfunction of organs and systems caused by endotoxicosis, group III patients were also given extracorporeal detoxification using hemosorption as part of complex therapy.

When determining and verifying complications of sepsis in the ADP patients we examined, we followed the recommendation according to the criteria of the SCCM/ ESICM consensus*, according to which "Sepsis is a life-threatening acute organ dysfunction resulting from a violation of the regulation of the response of the macroorganism to infection" [16] (bacterial, viral, fungal).

Results and discussion.

Analyzing patients with ADP of group I (n=43), we diagnosed sepsis in 6 patients (13.9%) of this group who had SIRS (tachycardia, 96.7 ± 5.7, tachypnea - 27.1 ± 2.3 per minute, leukocytosis 14.9 ± 1.2 x 109, pronounced neutrophil shift of the leukoformula with moderate leukopenia).

By the described hemostasiogram indicated the presence of DIC syndrome (stage I) without clinical manifestation (fibrinogen 4.96 ± 0.21 g/ l, PTI 107.4 ± 3.6%, blood clotting time (capillary) - BCT - beginning 16.2 ± 1.7 sec., end 1.9 ± 0.4 min. Fibrinolytic activity of plasma - 1.5 ± 0.2 hours, APTT - 21.6 ± 2.2 seconds, PDF - 7.7 ± 0.4 mg / l).

The above, along with the focus of infection (peritonitis), SIRS indicated the presence of dysfunction in the blood coagulation system in the examined group of patients, which was the fact of the diagnosis of sepsis in this group of patients, there were violations of protein-synthesizing, detoxifying liver function and encephalopathy (stage I – II). Generalization of infection was verified by procalcitonin test, increases in procalcitonin were 10 ng/ml.

The dynamics of changes in endotoxemia indicators in patients with peritonitis in the postoperative period can undoubtedly be a prognostic criterion in the diagnosis of developing purulent-infectious complications, a predictor of upcoming complications.

Thus, for patients with peritonitis of generalization of the process with the development of sepsis, we found that peptide intoxication in group I patients who received only infusion–transfusion therapy with forced diuresis turned out to be quite resistant.

We have not obtained a clear dependence of the generalization of the process on the phase of peritonitis, since these 6 patients in whom we found sepsis were distributed according to the phases of the course: in the reactive phase - 1 patient; in the toxic phase - 3 patients; in the terminal phase - 2 patients. In this case, it can be argued that with the aggravation of the phase of the course of ADP, the possibility of generalization of the infectious process with the development of such a dangerous complication as sepsis increases.

Group II included 62 patients, patients with toxic and terminal phases of peritonitis prevailed: reactive - in 8 (12.9%) patients, toxic – in 34 (54.8%) and terminal - in 20 (32.3%) patients.

The detoxification significance of peritoneal and intestinal lavage in peritonitis, their ability to remove MWM, as well as the duration of their use, we studied the dynamics of endotoxemia and endotoxicosis in patients who, in addition to infusion - transfusion therapy (ITT), performed peritoneal and intestinal lavage (PL, IL)

Intestinal lavage was performed from the first day after surgery by four-fold administration of 1500 ml of saline solution with an exposure of 30 minutes through the nutrient lumen of the probe and subsequent active aspiration.

Peritoneal lavage was performed similarly, from the first day after surgery and continued for 4-7 days, depending on the severity of the pathological process, the results of plasma toxicity studies, bacteriological studies of lavage fluid and intestinal motor function. The duration of the PL was 6.2 ± 0.2 days; the total amount of liquid was 7.6 ± 0.4 liters /day.

Therapy of group II patients in the postoperative period included infusion of colloidal and crystalloid solutions with forcing of diuresis, PL and IL.

The duration of intestinal lavage was 5.8 ± 0.4 days with a volume of 3.8 ± 0.3 liters / day. Therapy improved the absolute majority of clinical and biochemical parameters of blood already from 3-5 days of the postoperative period.

It should be noted that, despite the prevalence in group II of patients with diffuse forms of peritonitis, somewhat prolonged periods of surgical interventions, more pronounced initial intoxication, the terms of plasma toxicity reduction were slightly reduced, which was confirmed by the dynamics of MWM. This was also indicated by the dynamics of changes in the LII indicator. For clarity of the above, we present Table No. 1.

Table 1

Indicators of MWM dynamics and plasma toxicity by groups of patients with ADP without generalization of infection (M±m)

Indicator	Day of study			
	1 - st	3 - rd	5 - th	7 - th
	I group (n=37)			
MWM, mg/ml	0,416±0,025	0,534±0,019**	0,453±0,014	0,332±0,007*
HLPM, min	11,4±0,5	5,4±0,1***	9,4±0,2*	14,8±0,4*
RC, %	26,4±1,0	33,7±1,1**	30,4±0,8*	22,4±0,7*
BFM, $ohm^{-1}cm^{-2}\cdot10^{8}$	5,6±0,2	7,6±0,2*	5,9±0,1	4,2±0,1*
	II group (n=42)			
MWM, mg/ml	0,488±0,016^	0,545±0,014**	0,429±0,013*	0,310±0,010***^
HLPM, min	9,1±0,5^	5,2±0,2	10,8±0,3*	15,3±0,4**^
RC, %	31,2±0,7^^	36,5±0,9	28,8±0,7	20,3±0,5*^
BFM, $ohm^{-1}cm^{-2}\cdot10^{8}$	7,1±0,2^^	7,8±0,2	5,2±0,1**^	3,4±0,1***^

Note: Significant difference from the indicator of the 1st day: * - P<0.05, ** - P<0.01, *** - P<0.001. ^ - Confidence between the corresponding indicators by groups ^ - p <0.05, ^^ - p <0.01.

MWM is a medium-weight molecule, HLPM is the half-life of paramecia, RC is the respiratory coefficient, BFM is biophospholipid membranes.

A detailed analysis of group II patients in 20 patients revealed the generalization of infection with the development of sepsis, which significantly complicates the postoperative course of the disease. In all these patients, the terms of admission to the hospital and their surgical interventions were within 36 and 49 hours, averaging 46.3± 3.9 hours.

In 18 of these 20 patients with ADP complicated by sepsis, diffuse peritonitis occurred, and in 2 – diffuse.

The verification of sepsis was confirmed by numerous markers of it: anemia, a shift of the leukoformula to the left with toxic granularity of leukocytes, lymphopenia, thrombocytopenia and procalcitonin indices, the average values of which were 11.9± 0.7 ng/ml.

Our studies have clearly shown the high detoxification ability of peritoneal and intestinal lavage due to the good elimination of medium-weight molecules responsible for endotoxemia. This is confirmed by the fact that, despite a more pronounced intoxication with an almost equal volume of infusion - transfusion therapy in the first days of the postoperative period, a more pronounced dynamic of MWM was determined than in group I.

In group III (36 patients), serous fibrinous effusion dominated: it exceeded the indicators of groups I and II by 29.5 and 26.1%, respectively.

Phases of peritonitis: toxic – in 19 (52.8%) and terminal – in 17 (47.2%) patients. Thus, toxic and terminal phases of peritonitis occurred in all patients of this group, while in patients of groups 1 and 2 they were 51.1% and 87.1%.

The condition of group III patients turned out to be the most severe. This also caused a more severe course of the immediate postoperative period, 16 patients needed prolonged ventilation (for 28-96 hours after surgery) due to severe endogenous intoxication, inadequate spontaneous breathing, which was confirmed by decompensated respiratory acidosis, hypoxemia, significant hemodynamic disorders, hepatic–renal insufficiency syndrome, i.e. endotoxicosis with a clear violation of the function of detoxifying organs occurred in group III patients. These severe complications required the use of extracorporeal detoxification methods and, in particular, HS.

Peritoneal and intestinal lavage, active decompression of the gastrointestinal tract and probe feeding of patients practically did not differ from those performed in group II.

Clinical and biochemical blood parameters differed from the previous groups by more pronounced leukocytosis and hemoconcentration, increased levels of nitrogenous slags, serum enzymes, a decrease in total protein and A/G coefficient.

Oliguria was characteristic of group III patients on the first day after surgery. Diuresis fluctuated, amounting to 450-850 ml/day (on average - 654.9 ±27.4 ml/day), and was lower than the indicator of groups I and II by 321.9±11.3 and 297.5±9.2 ml/day, respectively.

The study of plasma toxicity also revealed severe endogenous intoxication.

The analysis showed that on the 1st day after surgery, the concentration of MWM was higher than in groups I and II, by 187.6 and 153.3%, respectively.

The severe condition of patients due to late hospital admission, the prevalence of the pathological process, the phase of peritonitis, impaired kidney and liver function, as well as high rates of endogenous intoxication, ascertained by Lowry's express methods and the paramecium test testified to profound disorders of natural detoxifying systems, which made the inclusion of hemosorption in complex detoxification therapy justified.

Starting from the 5th day, MWM indicators were 98% higher than normal values, but lower than the values of groups I and II by 17.1 and 5.8%.

On the 7th day, the concentration of MWM in group III was 48.8 and 40% lower than in groups I and II.

Hemosorption was performed mainly 8-26 hours after surgery.

Complex therapy improved almost all clinical and biochemical blood parameters by 5 days, and by 7 days they were approaching normal values.

Interesting, in our opinion, was the fact that hemosorption, in addition to reducing the period of endogenous intoxication, reduced the total amount of liquid media for PL and IL. So, the amount of fluid for PL and IL, in the first 2-3 days in patients of groups II and III, was almost the same, but further, the volume of lavage fluid for group III was lower.

Conclusion. In patients with ADP, despite the therapy in the postoperative period, generalization of the process occurs in 31.2% with the development of clinically verified sepsis (multiple organ disorders), studied by the procalcitonin test.

With diffuse fibrinous-purulent peritonitis, the frequency of generalization of infection reaches 50%, with serous-fibrinous diffuse peritonitis - 32.2%. with serous peritonitis - 3.9%, which makes it necessary for early diagnosis and timely correction.

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