UDC 616.381-002.1
DOI https://doi.org/10.32782/2226-2008-2025-3-5

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PROBIOTIC SANITATION OF THE ABDOMINAL CAVITY IN THE TREATMENT OF DISSEMINATED PERITONITIS

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The aim of the study was to determine the effectiveness of probiotic sanitation of the abdominal cavity in the treatment of disseminated peritonitis.

Materials and methods. The study included 98 patients with disseminated peritonitis. Patients were divided into 3 groups. Group I (main group) included 31 patients in whom the abdominal cavity was cleaned with a 5% solution of probiotic disinfectant. Group II (comparison group) consisted of 32 patients, in whom the abdominal cavity was cleaned with a solution of the sorbent "Enterosgel". Group III (placebo control group) included 35 patients in whom the abdominal cavity was cleaned with 0.9% NaCl solution. In order to determine the level of intoxication and the dynamics of peritonitis, we determined the functional activity of phagocytic cells of peripheral blood.

Results. Sanitation of the abdominal cavity with probiotic disinfectants in patients of Group I caused a decrease in the manifestations of endogenous intoxication already on the 3rd day of the study. These trends contributed to the optimization of the functional activity of neutrophil granulocytes and their bactericidal properties. A tendency to restore the function of monocytes was established. In patients of Group II, a positive dynamic of the studied indicators was noted on day 7 of the study. While in patients of Group III, these changes did not have a clearly pronounced positive dynamic throughout the study.

Conclusions. The study showed that the use of probiotic disinfectants for the sanitation of the abdominal cavity is an effective treatment for disseminated peritonitis, which significantly improves the treatment outcomes of such patients.

Keywords: peritonitis, abdominal sepsis, endogenous intoxication, antibiotic resistance, probiotics.

УДК 616.381-002.1

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ПРОБІОТИЧНА САНАЦІЯ ЧЕРЕВНОЇ ПОРОЖНИНИ У ЛІКУВАННІ РОЗПОВСЮДЖЕНОГО ПЕРИТОНІТУ

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Дослідження включило 98 пацієнтів з розповсюдженим перитонітом, які були розподілені на 3 групи. В групу І (основну) увійшов 31 пацієнт, якому санацію черевної порожнини проводили 5% розчином пробіотичного дезінфектанту, групу ІІ (групу порівняння) становили 32 пацієнти, санацію проводили розчином сорбенту «Ентеросгель». В групу ІІІ (плацебо-контроль) увійшли 35 пацієнтів, яким санацію проводили 0,9% розчином NaCl. Визначали функціональну активність фагоцитуючих клітин. У хворих групи І зниження проявів ендогенної інтоксикації виявили вже на 3-тю добу дослідження. У хворих групи ІІ позитивна динаміка досліджуваних показників відзначалася на 7-му добу дослідження. Тоді як у хворих групи ІІІ такі зміни не мали чітко вираженої позитивної динаміки.

Ключові слова: перитоніт, абдомінальний сепсис, ендогенна інтоксикація, антибіотикорезистентність, пробіотики.

Introduction

The treatment of peritonitis and abdominal sepsis consists in several aspects: early targeted therapy and volume resuscitation, control of the source of infection, and antibiotic therapy. Surgical treatment of the source is a mandatory treatment for every patient with secondary or ongoing peritonitis and has both therapeutic and diagnostic value. New diagnostic tools, such as biomarker assays and PCR methods for microbial detection, will accelerate the detection of complications after surgical treatment and allow for the rapid initiation of individualized antimicrobial therapy [1].

Proper source control is essential for the management of intra-abdominal infection (IAI). In this setting, appropriate source control is paramount to the treatment of most patients with IAI and can improve outcomes. In addition, adequate source control can also shorten the course of antibiotic therapy. The impact of source control is not related to the use of appropriate antibiotics. Several studies have shown

that both are independent predictors of mortality, but there is consensus that without adequate source control, antibiotic therapy may have little or no effect [2].

The problem remains in antibiotic resistance of microorganisms, which is increasing every year and poses a great threat worldwide. It can be weakened by the use of probiotic disinfectants, which at the same time can have a positive effect on the treatment of peritonitis. The diverse range of properties of probiotics can solve many problems in medicine [3], as they have antibacterial, antifungal, antiviral and anti-inflammatory effects [4].

A great problem in the treatment of patients with peritonitis, and even more in abdominal sepsis, is an imbalance of the immune system. The first line of defense against an infectious factor is neutrophilic granulocytes (NGs) and monocytes, the cells responsible for innate immunity. Therefore, in our study, we chose to determine the functional activity of these phagocytic cells in the peripheral blood for evaluation of the level of intoxication and the dynamics of peritonitis.

Paradoxically, neutrophils are also one of the main mediators of tissue damage in various human diseases, including sepsis. Under normal conditions, the half-life of neutrophils in the blood circulation is limited to 6–10 hours, after which they undergo spontaneous apoptosis. However, during acute inflammation, the lifespan of neutrophils is significantly extended due to the action of proinflammatory mediators and bacterial membrane components such as endotoxin. This prolonged survival of neutrophils is associated with the accumulation of activated neutrophils, which contributes to persistent inflammation and further damage to body tissues with subsequent organ failure in critically ill patients [5].

Monocytes, which are the first to participate in the immune system's response to an infectious factor, also undergo significant changes in abdominal sepsis. The study of the dynamics of these cells at the beginning of the immune response in the peripheral blood revealed a decrease in their number in lipopolysaccharide-induced acute inflammation in humans. This is due to the migration of monocytes into tissues from the blood, where they differentiate into dendritic cells and macrophages, and also reflects an increase in monocytes in the marginal or migrating pool. Monocytes, in addition to their phagocytic function, play a significant role in the regulation of the immune response. They can mediate apoptosis, modulate cytokine responses, and have calculated interactions with lymphocytes [6–8].

Given the above, this study is relevant and can improve the results of treatment of patients with disseminated peritonitis and abdominal sepsis.

The aim of the study was to determine the effectiveness of probiotic sanitation of the abdominal cavity in the treatment of disseminated peritonitis.

Material and methods

This study included 98 patients with disseminated peritonitis who were operated on and treated in 2023–2024 at the Brovary Multidisciplinary Clinical Hospital, which is the base of the Department of General and Emergency Surgery of the Shupyk National Healthcare University of Ukraine. Peritonitis was caused by the following diseases: acute appendicitis – 13 (13.3%) cases, acute cholecystitis – 8 (8.2%) cases, perforated gastric or duodenal ulcer – 34 (34.7%) cases, tumor perforation – 15 (15.3%) cases, small intestinal obstruction and intestinal perforation – 11 (11.2%) cases, trauma and injuries of the abdominal cavity – in 6 (6.1%) cases, colon perforation of non-tumor genesis – in 11 (11.2%) cases. All patients in the study were operated on with both laparoscopic and open surgical interventions.

The patients were divided into three groups, comparable in age and gender (Table 1), as well as in the presence of comorbidities (Table 2).

The table shows that most of the patients of the study were of the working age, which also contributes to the economic problem of peritonitis.

Comorbidities were detected in 62.2% of the study patients. It can be seen from the above data that the most common diseases of the cardiovascular system were found in patients. Most patients had two or more comorbidities.

Group I (main group) included 31 (31.6%) patients in whom the abdominal cavity was sanitized with a 5% solution of probiotic disinfectant "SVITECO PHS" (Sirion LLC, Ukraine) in sterile 0.9% NaCl solution 3–5-fold, then a probiotic disinfectant spray "AREDERMA" (Sirion LLC, Ukraine) was applied to the surgical wound, and after its closure – a gel with probiotics "SVITECO PPG" (Sirion LLC, Ukraine). Group II (comparison group) consisted of 32 (32.7%) patients in

Table 1

Distribution of patients with peritonitis depending on age and gender

Age, years	Group I, n=31				Group II, n=32				Group III, n=35			
	Men		Women		Men		Women		Men		Women	
	Abs.	%	Abs.	%	Abs.	%	Abs.	%	Abs.	%	Abs.	%
18–20	1	3.2	–	–	1	3.1	1	3.1	–	–	–	–
21–30	3	9.7	1	3.2	4	12.5	1	3.1	2	5.7	–	–
31–40	1	3.2	1	3.2	2	6.3	–	–	3	8.6	1	2.9
41–50	4	12.9	3	9.7	2	6.3	2	6.3	2	5.7	2	5.7
51–60	3	9.7	2	6.5	4	12.5	1	3.1	5	14.3	1	2.9
61–70	1	3.2	3	9.7	1	3.1	2	6.3	5	14.3	3	8.6
71–80	3	9.7	3	9.7	4	12.5	3	9.4	2	5.7	4	11.4
>80	1	3.2	1	3.2	–	–	4	12.5	1	2.9	4	11.4
Total	17	54.8	14	45.2	18	56.3	14	43.7	20	57.1	15	42.9

Table 2

Comorbidities in patients with peritonitis by study groups

Name of the disease	Group I, n=31		Group II, n=32		Group III, n=35	
	Abs.	%	Abs.	%	Abs.	%
Diseases of the cardiovascular system (CHD, ASC, HTN)	12	38.7	10	31.3	15	42.9
Post-thrombophlebitic syndrome of the lower extremities	3	9.7	2	6.3	3	8.6
Diabetes mellitus	4	12.9	5	15.6	4	11.4
Drug addiction	1	3.2	1	3.1	1	2.9
Closed chest injury	1	3.2	1	3.1	3	8.6
Obesity	1	3.2	2	6.3	2	5.7
Gastric ulcer and duodenal ulcer	3	9.7	2	6.3	2	5.7
Chronic pancreatitis	3	9.7	2	6.3	2	5.7
Diseases of the respiratory system	3	9.7	4	12.5	3	8.6
Osteochondrosis, intervertebral protrusions and hernias	2	6.5	1	3.1	–	-
Diseases of the genitourinary system	4	12.9	3	9.4	4	11.4

Notes: CHD – coronary heart disease, ASC – atherosclerotic cardiosclerosis, HTN – hypertension.

whom the abdominal cavity was sanitized with a solution of sorbent "Enterosgel" (KREOMA-PHARM, Ukraine) in sterile 0.9% NaCl solution 3–5-fold with an exposure of the solution for 2–3 minutes, after which it was washed out of the abdominal cavity with 0.9% NaCl 3–5 times. Group III (placebo control) included 35 (35.7%) patients who underwent abdominal cavity sanitation with 0.9% NaCl 3–5 times.

Treatment and examination of patients was carried out in accordance with the Helsinki Declaration of the World Medical Association (Seoul, 2008), orders of the Ministry of Health of Ukraine (No. 281 of November 01, 2000, No. 355 of September 25, 2002, No. 356 of May 22, 2009 as amended by the Order of the Ministry of Health of Ukraine No. 574 of August 05, 2009, No. 1118 of December 21, 2012), and with the permission of the Ethics Committee of the Shupyk National Healthcare University of Ukraine (Protocol No. 8 of November 7, 2022). All patients provided written consent to the processing of their personal data.

In order to determine the level of intoxication and the dynamics of peritonitis we determined the functional activity of phagocytic cells of the peripheral blood. The activity of monocytes and NGs was studied in patients in the NST (nitroblue tetrazolium reduction test) [9]. It was performed in two modifications: spontaneous and induced tests. The spontaneous test is an indicator of the functional activity of the total pool of phagocytic cells in the peripheral blood. *E. coli* antigen was used as a stimulant in the induced test. The test makes it possible to determine the ability of NGs and monocytes to complete phagocytosis. The number of NST-positive cells per 200 intact NGs was determined. The study examined the effect of microbial antigens on the activity of the NG myeloperoxidase enzyme, which is oxygen-dependent. The microscopic study was performed using light-optical microscopes "ZEISS" (Germany) with the data processing system "Axio Imager. A2" data processing system with 5x, 10x, 20x, 40x objective magnification, 1.5 binocular objective, and 10x eyepieces.

Statistical processing of the study results was performed using the Statistical software EZR v. 1.64 (graphical user interface for R statistical software version 4.3.1, R Foundation for Statistical Computing, Vienna, Austria). If the values conformed to the law of normal data distribution, the samples were evaluated using Student's t-test or Fisher's F-test at a significance level of 95% ($\alpha = 0.05$). If the values did not conform to the law of normal distribution of data, nonparametric statistics methods were used – Mann–Whitney U-test and Wilcoxon rank sum test. In all cases of statistical evaluation, $p<0.05$ was considered significant.

Results of research and their discussion

When determining the functional state of peripheral blood NGs on day 1 of the study (Table 3), we found an increase in spontaneous activity 3.56-fold ($p<0.01$) and a significant decrease in induced activity 3.64-fold ($p<0.01$).

A decrease in the activity of myeloperoxidase NGs was determined in relation to the reference values 2.81-fold ($p<0.01$).

The activity of monocytes was reduced 2.85-fold ($p<0.01$) compared to the baseline values. A significant inhibition of monocyte function in response to microbial activation was also determined – 8.05-fold ($p<0.001$) compared to the reference values.

On day 3 of the study, we found a tendency to reduce the spontaneous activity of NG 1.55-fold ($p<0.05$) compared to the baseline values, and in the induced test, an increase was determined 1.42-fold compared to the baseline values ($p<0.05$).

An increase in the activity of neutrophils myeloperoxidase was found to be 2.1-fold higher than the baseline values ($p<0.01$).

Also, on day 3 of the study, a tendency to restore the functional activity of monocytes in both spontaneous and stimulated tests was established – 1.49-fold ($p<0.05$) and 5.43-fold ($p<0.001$), respectively.

On day 7 of the study of patients of Group I, a decrease in the functional activity of NGs relative to the baseline values in the spontaneous test with an increase in the induced test was found: 1.94-fold ($p<0.01$) and 2.67-fold ($p<0.01$), respectively.

Table 3

Indicators of functional activity of peripheral blood phagocytic cells in patients of Group I

Indicators	Units of measurement	Study period, day			Reference values
		1 day	3 days	7 days	
Neutrophilic granulocytes					
Spontaneous test	%	44.5±2.24 *p<0.01	28.7±2.9 *p<0.05 **p<0.05	22.9±1.6 *p<0.05 **p<0.01	12.5±0.26
Induced test	%	4.3±1.1 *p<0.01	6.1±1.0 *p<0.05 **p<0.05	11.5±1.4 *p<0.05 **p<0.01	15.67±1.05
Activity of myeloperoxidase NG	AU	0.75±0.08 *p<0.01	1.58±0.09 *p<0.05 **p<0.01	1.73±0.06 *p<0.05 **p<0.01	2.11±0.15
Monocytes					
Spontaneous test	%	3.96±1.01 *p<0.01	5.9±1.10 *p<0.01 **p<0.05	7.95±0.97 *p<0.05 **p<0.01	11.27±0.67
Induced test	%	1.45±0.65 *p<0.001	7.87±0.87 *p<0.05 **p<0.001	8.94±1.05 *p<0.05 **p<0.001	11.67±0.97

Notes: * – probability of differences relative to the reference values; ** – probability of differences relative to the baseline values.

An increase in the activity of myeloperoxidase 2.31-fold ($p<0.01$) relative to baseline values was determined.

The functional activity of monocytes was characterized by an increase in the spontaneous test 2.0-fold ($p<0.01$) and in the induced test 6.17-fold ($p<0.001$) compared to the baseline values.

When determining the functional state of peripheral blood NGs on day 1 of the study (Table 4) in patients of Group II, we found a significant increase in spontaneous activity in relation to the reference values 3.45-fold ($p<0.01$) and a decrease in induced activity 4.24-fold ($p<0.01$).

A decrease in the activity of myeloperoxidase NGs was determined in relation to the reference values 3.06-fold ($p<0.01$).

The activity of monocytes was 3.76-fold reduced ($p<0.01$) compared to the reference values. Also, a significant inhibition of monocyte function in response to microbial activation was determined in relation to the reference values 9.73-fold ($p<0.001$).

On day 3 of the study, we found a tendency to decrease the spontaneous activity of NG in relation to the baseline values 1.37-fold ($p<0.05$), and increase in the induced test 1.33-fold ($p<0.05$).

An increase in the activity of neutrophil myeloperoxidase was found 1.75-fold ($p<0.01$) compared to baseline values.

Also, on day 3 of the study, a tendency to increase the functional activity of monocytes in both spontaneous and stimulated tests 1.63-fold ($p<0.05$) and 3.60-fold ($p<0.01$), respectively, was established.

On day 7 we determined a decrease in the functional activity of the NGs relative to the baseline values 1.68-fold ($p<0.01$) in the spontaneous test and an increase 2.35-fold

Table 4

Indicators of functional activity of peripheral blood phagocytic cells in patients of Group II

Indicators	Units of measurement	Study period, day			Reference values
		1 day	3 days	7 days	
Neutrophilic granulocytes					
Spontaneous test	%	43.1±1.73 *p<0.01	31.5±2.4 *p<0.01 **p<0.05	25.6±0.9 *p<0.01 **p<0.01	12.5±0.26
Induced test	%	3.7±0.3 *p<0.01	4.93±0.7 *p<0.01 **p<0.05	8.7±0.68 *p<0.01 **p<0.01	15.67±1.05
Activity of myeloperoxidase NG	AU	0.69±0.06 *p<0.01	1.21±0.08 *p<0.05 **p<0.01	1.60±0.14 *p<0.05 **p<0.01	2.11±0.15
Monocytes					
Spontaneous test	%	3.0±0.70 *p<0.01	4.9±0.73 *p<0.01 **p<0.05	6.92±0.89 *p<0.01 **p<0.01	11.27±0.67
Induced test	%	1.20±0.45 *p<0.001	4.32±0.66 *p<0.01 **p<0.01	6.28±0.81 *p<0.01 **p<0.001	11.67±0.97

Notes: * – probability of differences relative to the reference values; ** – probability of differences relative to the baseline values.

(p<0.01) in the induced test. However, these indicators were 2.05-fold higher than the reference values in the spontaneous test (p<0.01) and 1.80-fold lower in the induced test (p<0.01).

A positive dynamic of myeloperoxidase activity was determined relative to the baseline values. The obtained results exceeded the baseline values 2.32-fold (p<0.01), but they were higher than the reference values 1.32-fold (p<0.05).

An increase in the functional activity of monocytes relative to the baseline values was found 2.31-fold (p<0.01) in the spontaneous test and 5.23-fold (p<0.001) in the induced test, but they were lower than the reference values 1.63-fold (p<0.01) and 1.86-fold (p<0.01), respectively.

In determining the functional state of peripheral blood NGs in patients of Group III on day 1 of the study (Table 5), we found an increase in spontaneous activity compared with the reference values 3.46-fold (p<0.01) and a decrease in induced activity 4.24-fold (p<0.001).

A decrease in the activity of myeloperoxidase NGs was determined in relation to the reference values 3.46-fold (p<0.01).

The activity of monocytes was reduced compared to the reference values 3.52-fold (p<0.01). Also, a significant inhibition of monocyte function 7.78-fold (p<0.001) in response to microbial activation was determined compared to the reference values.

On day 3 of the study, we found that the spontaneous activity of NGs remained at the same level, and in the induced test it decreased 1.26-fold (p<0.05) and 5.33-fold (p<0.001) compared to the baseline values and reference values.

A decrease in neutrophil myeloperoxidase activity was observed relative to the baseline values by 1.17-fold (p<0.05) and to the reference values by 4.06-fold (p<0.01).

Also, on day 3, a slight increase in the functional activity of monocytes in both spontaneous and stimulated tests was found relative to baseline values, but they remained significantly reduced relative to the reference values – 2.89-fold (p<0.01) and 6.14-fold (p<0.001), respectively.

On day 7, we identified a tendency to a decrease in the functional activity of NGs relative to the baseline values 1.10-fold (p<0.05) in the spontaneous test and an increase 1.27-fold (p<0.05) in the induced test. However, these values remained significantly different from the reference values.

Myeloperoxidase activity was close to the baseline values and significantly reduced compared to the reference values – 3.40-fold (p<0.01).

The functional activity of monocytes in the spontaneous test corresponded to the baseline values and was significantly reduced compared to the reference values – 3.52-fold (p<0.01). In the induced test, an increase in activity was noted in relation to the baseline values 2.60-fold (p<0.01), but it was lower than the reference values 2.99-fold (p<0.01).

According to Table 5, throughout the study, a significant inhibition of the activity of myeloperoxidase NGs was detected in Group III. This indicates a violation of phagocytosis, namely its oxygen-dependent phase. In this group, the functional activity of monocytes was determined at the stage of decompensation throughout the study.

Studies on phagocyte dysfunction caused by microbial load have shown a decrease in their antimicrobial response due to damage to mitochondrial function. This increases the body's susceptibility to secondary infections [10].

Thus, in patients with peritonitis, we found a significant inhibition of NG and monocyte function. There was a significant activation of NGs, but their functional potential, which was determined by the effect of bacterial antigen *E. coli*, was sharply weakened. These processes can be explained by the nature of spontaneous and stimulated NSTs. The spontaneous test shows the ability of NGs and monocytes to carry out phagocytosis, while the induced test, in turn, reflects the ability of these cells to complete phagocytosis. Therefore, an increase in the spontaneous

Table 5

Indicators of functional activity of peripheral blood phagocytic cells in patients of Group III

Indicators	Units of measurement	Study period, day			Reference values
		1 day	3 days	7 days	
Neutrophilic granulocytes					
Spontaneous test	%	43.3±1.42 *p<0.01	43.5±2.2 *p<0.01 **p>0.05	39.5±3.5 *p<0.01 **p<0.05	12.5±0.26
Induced test	%	3.7±0.6 *p<0.001	2.94±0.8 *p<0.001 **p<0.05	4.7±0.9 *p<0.01 **p<0.05	15.67±1.05
Activity of myeloperoxidase NG	AU	0.61±0.06 *p<0.01	0.52±0.09 *p<0.01 **p<0.05	0.62±0.05 *p<0.01 **p>0.05	2.11±0.15
Monocytes					
Spontaneous test	%	3.2±0.67 *p<0.01	3.9±0.7 *p<0.01 **p>0.05	3.2±0.5 *p<0.01 **p>0.05	11.27±0.67
Induced test	%	1.5±0.7 *p<0.001	1.9±0.2 *p<0.001 **p>0.05	3.9±0.7 *p<0.01 **p<0.01	11.67±0.97

Notes: * – probability of differences relative to the reference values; ** – probability of differences relative to the baseline values.

test indicates a significant load of NGs with antigens of microorganisms, and a decrease in the functional activity of these cells in the induced test reflects their ability to complete phagocytosis in the oxygen-dependent phase.

The results of the study showed that peritonitis develops severe and extremely severe endotoxicosis. At the same time, compounds are formed that have a significant damaging effect on the main effector cells of natural resistance, suppressing the functional state and reducing their metabolic activity. As a result, phagocytic cells become a source of secondary microbial intoxication. The accumulation of toxins of microbial and histiogenic origin in the body of patients with peritonitis causes a significant damaging effect of peripheral blood serum on autologous leukocytes, which in turn reduces their antimicrobial functional potential.

Sanitation of the abdominal cavity with probiotic disinfectants in patients of Group I led to a decrease in the manifestations of endogenous intoxication already on day 3 of the study. These trends contributed to the optimization of the functional activity of NGs and their bactericidal capabilities. A tendency to restore the function of monocytes, the main effector messengers of both innate and adaptive immunity, was established. On day 7, a positive dynamic of the studied parameters was observed.

In patients of Group II, a positive dynamic of the studied parameters was noted on day 7 of the study. Whereas in patients of Group III, these changes did not have a clearly expressed positive dynamic throughout the study.

In the available literature, we did not find data on the use of probiotic disinfectants for the sanitation of the abdominal cavity in case of disseminated peritonitis. This trend is interesting from a surgical point of view, since peritonitis is associated with a variety of microorganisms that are resistant to most antibacterial drugs, and probiotics can provide an alternative to them. Also, probiotic disinfectants have a positive effect on the course of peritonitis and significantly improve the results of its treatment. We have proven their effectiveness in an experimental study [3; 11].

Probiotic disinfectants can significantly reduce antibiotic resistance, improve health protection worldwide, and save significant money [12].

Conclusions

The study has shown that the use of probiotic disinfectants for abdominal cavity sanitation is an effective treatment for disseminated peritonitis, which significantly improves the treatment outcomes of such patients.

Sanitation of the abdominal cavity with probiotic disinfectants in patients of Group I led to a decrease in the manifestations of endogenous intoxication already on day 3 of the study. These trends contributed to the optimization of the functional activity of neutrophilic granulocytes and their bactericidal properties. A tendency to restore the function of monocytes was established. On day 7 of the study, a positive dynamic of the studied indicators was observed. In patients of Group II, a positive dynamic of the studied parameters was noted on day 7 of the study. Whereas in patients of Group III these changes did not have a pronounced positive dynamic throughout the study.

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Надійшла до редакції 13.02.2025 р.
Прийнята до друку 26.06.2025 р.
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