DIAGNOSTIC AND TREATMENT METHODS

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# EFFECTS OF INTRAOPERATIVE USE OF BETA-ADRENOBLOCKERS IN ENDOSCOPIC RHINOSINUS SURGERY UNDER GENERAL ANESTHESIA

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Functional endoscopic sinus surgery (FESS) provides not only optimal access with a sufficient overview of the surgical field, but also allows to preserve with minimal trauma the functionality of the ostiomeatal complex zone, to provide ventilation and drainage through the natural respiratory tract. To perform FESS procedures it is important to minimize bleeding in the surgical area, since even a small amount of blood can deteriorate the endoscopic view.

**The aim of the study:** to evaluate the effects of beta-blockers as component of general anesthesia in functional endoscopic sinus surgery.

**Materials and methods:** 110 patients were included in a single-center prospective cohort study. FESS procedures were performed under general anesthesia. 3 groups of patients were intraoperatively isolated: without administration of beta-blockers (BB) (control group, C) (n=40); with intravenous metoprolol (M) (n=35) 1-2 mg each until a heart rate of 50-60 beats /min, but no more than 15 mg; with intravenous esmolol (E) (n=35) with loading dose of 0.5 mg/kg during 1 min., then 0.05 – 0.15 mg/kg/min. The same type of general anesthesia was performed in all groups The intraoperative intensity of bleeding (IB), heart rate (HR bpm), noninvasive systolic (SBP), diastolic (DBP) and mean blood pressure (MBP) (mm Hg.), perfusion index (PI) were assessed. The study points were the 10th, 30th and the 60th minute of the procedure.

**Results and discussion:** HR in group C at all points of the study was statistically significantly higher compared to group M and E. MBP significantly differed at the 10th minute of the procedure between the groups, at the 30th minute the levels of MBP were the same in all compared groups, and at the 60th minute in the group M recorded high MBP compared to group E. At the 30th and 60th minutes of the procedure, PI was lower in groups M and E compared to group C. The IB was convincingly lower at all points of the study in groups M and E compared to group C and did not differ between groups M and E. In the prognostic model when assessing factors that may affect the development of intraoperative bleeding the fact of the use of BB in groups M and E leads to a decrease IB at all points of the study. An increase in IB is predicted with an increase in HR and SBP at the 10th and 60th minutes of the procedure.

**Conclusion:** 1. Intraoperative use of beta-blockers in addition to reduction of the heart rate leads to a moderate decrease in mean blood pressure and a decrease in intraoperative bleeding during functional endoscopic sinus surgical procedures under general anesthesia. 2. Metoprolol and esmolol have the same effectiveness for reducing the intensity of bleeding during FESS procedures. 3. The use of esmolol causes a more expressed decrease in heart rate and mean blood pressure compared to metoprolol.

**Short summary.** The effects of beta-blockers as component of general combined anesthesia in functional endoscopic sinus surgery were studied. It was found out that intraoperative use of beta-blockers in addition to decreasing heart rate leads to a moderate decrease in mean blood pressure and a decrease in intraoperative bleeding. Metoprolol and esmolol are equally effective, but the use of esmolol causes a more significant decrease in heart rate and mean blood pressure compared to metoprolol.

**Keywords:** general anesthesia, beta-blockers, metoprolol, esmolol, bleeding control, functional endoscopic sinus surgery, FESS.

**Introduction.** Functional endoscopic sinus surgery (FESS) is the main method of surgical treatment of chronic rhinosinusitis. FESS provides a sufficient overview of the surgical field, minimal injury, preservation of the functionality of the ostiomeatal complex zone, ventilation and drainage through the natural respiratory tract [7]. The conditions for performing these procedures require minimal bleeding in the area of the operation [4]. Control of intraoperative bleeding provides visibility of the surgical field and reduces the risk of complications [3]. Bleeding in the FESS depends on mean blood pressure (MBP) and heart rate (HR) [9, 10, 12, 14]. However, it is known that a decrease in blood pressure by more than 20% from the baseline increases the risk of myocardial ischemia, acute kidney injury and stroke. MBP less than 60-70 mmHg is accompanied by acute myocardial and kidney damage and an increase in 30-day mortality, systolic blood pressure less than 100 mmHg - by myocardial damage and increased mortality, damage is proportional to the depth and duration of hypotension. [5]. Some researchers believe that at a HR of 60 beats/min there is no need to significantly reduce MBP to improve visibility during FESS procedures [4]. Beta-blockers (BB) can be administered to maintain HR at the level of 60-70 bpm [6]. A controlled decrease in HR ensures hemodynamic stability in FESS [8]. According to the national recommendations of the All-Russian Scientific Society of Cardiology from 2011 it is recommended to continue the therapy of BB in patients taking drugs before hospitalization with dose correction until the target heart rate is reached. It is not indicated the routine use of BB, especially in high doses, on the eve of surgery, since the first administration of metoprolol 2-4 hours before the procedure increased the incidence of strokes and overall mortality [6]. Currently, the use of BB to improve visualization is poorly studied in FESS: there are few publications, but there are no studies of the effectiveness of drugs in this group and recommendations for their choice.

**The aim of the study** was to evaluate the effects of beta-blockers as component of general combined anesthesia in functional endoscopic sinus surgery.

**Materials and methods**. 110 patients were included in a single-center prospective cohort study. FESS procedures were performed under general anesthesia in the Otorhinolaryngological clinic of the I.P. Pavlov Institute of Surgery and Emergency Medicine in the period from January 2021 to February 2022. Surgical procedures were performed when conservative treatment of chronic pathology

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of the paranasal sinuses (sinusitis, ethmoiditis, frontitis, sphenoiditis, polyposis of the nose and sinuses) was ineffective. Inclusion criteria: scheduled FESS procedures in patients examined according to the protocol adopted at the clinic. Criteria for non-inclusion: constant usage of BB, grade III obesity (body mass index ≥40), severe lung pathology (severe and uncontrolled bronchial asthma, treatment by stage 4-5; chronic obstructive pulmonary disease of severe degree), ischemic heart disease with signs of angina pectoris, hypertension of stage III on the background of uncontrolled hypertension, signs of decompensation of diseases of the cardiovascular system, pronounced pathology of the kidneys and liver, pathology of the blood coagulation system, taking disaggregants and anticoagulants. Patients were randomized by random numbers into 3 groups: a group without intraoperative administration of BB (control group, C) (n=40); the group with intraoperative intravenous (IV) administration of metoprolol (M) (n=35) and the group with intraoperative IV administration of esmolol (E) (n=35). General anesthesia was performed in all study groups, the same type of premedication was performed on the operating table: IV fentanyl 0.00125–0.004 mg/kg, atropine 0.005 – 0.01 mg/kg, as needed in case of HR <50 bpm. Induction of anesthesia was performed with IV propofol 2.5-3 mg/kg. The classic LMA No. 4-5 was installed after the development of anesthesia, muscle relaxants (rocuronium bromide 0.3-0.6 mg/kg) were injected as needed. Mechanical lung ventilation was carried out by the Dreger Primus (Germany) ventilator in volume control mode with automatic flow control. The leaktightness of the airways was assessed by the indicator of the volume of leakage of the respiratory mixture, the peak inspiratory pressure on and the exhalated respiratory volume. Anesthesia was maintained with desflurane (4-12 vol%) up to a MAC of 0.8-1.4. Additionally, fentanyl was administered at a dose of 50-100 mcg, depending on the stages of the operation. At the beginning of the operation the infiltration anesthesia of the nasal cavity was performed with officinal 3.4 ml solution of articaine hydrochloride with epinephrine hydrochloride 1:100000. Intraoperative monitoring was performed according to the "Harvard Standard". Surgical procedures were performed by one surgeon who assessed at 10, 30 and 60 minutes (study points) of the operation the intensity of intraoperative bleeding (IB) on a 6-point scale (Fromme-Boezaart Score), in which 0 points corresponds to the absence of bleeding in the area of the surgical field and 5 points to severe bleeding with the inability to visualize the surgical field and the continuation of surgical intervention [10]. Simultaneously with the assessment of the visibility of the surgical field the values of HR (bpm), noninvasive systolic (SBP), diastolic (DBP) and mean blood pressure (MBP) (mmHg), perfusion index (PI, %), anesthetic MAC and the concentration of carbon dioxide on exhalation ($PetCO_2$, mmHg). The duration of the operation, anesthesia, time of postoperative recovery (restoration of consciousness), doses of intraoperatively administered drugs were also noted. All patients in the postoperative period were monitored for 2 hours to assess complaints and somatic condition. In C group, BB was not administered intraoperatively, but to reduce the IB the anesthetic MAC was increased, fentanyl was additionally administered, reducing the level of MBP (controlled hypotension). In M group IV metoprolol 1-2 mg was administered to reduce IB until HR of 50-60 bpm was reached. Additional doses were administered up to a total dose of no more than 15 mg with insufficient effect of the initial dose. We tried not to allow a decrease in HR less than 50 bpm. At HR < 50 beats/min metoprolol administration was stopped, and IV atropine 0.005 mg/kg was administered. In E group a loading dose of IV esmolol 0.5 mg/kg was administered in 1 min., then infusion through a syringe pump 0.05 – 0.15 mg/kg/min, with a decrease in HR < 50 bpm, the dose of esmolol was reduced.

Statistical analysis was performed using the StatTech v. 2.8.8 program (developed by Stattech LLC, Russia). Quantitative values are represented using the median (Me) and the lower and upper quartiles (Q1 – Q3). Categorical data were described with absolute values and percentages. Comparison of three or more groups by quantitative indicator was performed using the Kraskel-Wallis criterion, a posteriori comparisons were performed using the Dunn criterion with the Hill correction. Statistical significance

**Table 1**

**Clinical and anthropometric characteristics of patients and intraoperative indicators in groups of comparison**

| Indicators | | Groups of comparison | | | *p* |
|---|---|---|---|---|---|
| | | C | M | E | |
| Gender, n (%) | M | 24 (60.0) | 20 (57.1) | 18 (51.4) | 0.752 |
| | F | 16 (40.0) | 15 (42.9) | 17 (48.6) | |
| Bronchial asthma, n (%) | Not identified | 27 (67.5) | 30 (85.7) | 30 (85.7) | 0.078 |
| | Identified | 13 (32.5) | 5 (14.3) | 5 (14.3) | |
| Allergy, n (%) | Not identified | 32 (80.0) | 31 (88.6) | 30 (85.7) | 0.576 |
| | | 8 (20.0) | 4 (11.4) | 5 (14.3) | |
| Age, year | | 34 (22.0;47.0) | 29 (22.5;47.5) | 34 (27.0;43.5) | 0.697 |
| BMI (kg/m2) | | 23 (21.0;25.5) | 24.4 (21.5;26.7) | 23.4 (22.3;25.2) | 0.293 |
| Time of procedure (min) | | 71 (66;74) | 70 (64;75) | 73 (67;82) | 0.158 |
| Time of recovery (min) | | 14 (12;16) | 12 (10; 13) | 11 (9;13) | <0.001*<br>PE – M < 0.001<br>PE – C < 0.001 |
| Fentanyl (mcg) | | 400 (400.0;550.0) | 300 (250.0;400.0) | 300 (200.0-400.0) | < 0.001*<br>PC – M < 0.001<br>PC – E < 0.001 |

Note. The data is presented in the form of n (%) - the absolute value (the number of percentages of the total) and Me (Q1; Q3) - the median (lower quartile; upper quartile). Comparison groups: C - control, M - metoprolol, E - esmolol. BMI is the body mass index. * - The Kraskel–Wallis criterion.

was determined by the level of p <0.05, confidence intervals – 95%.

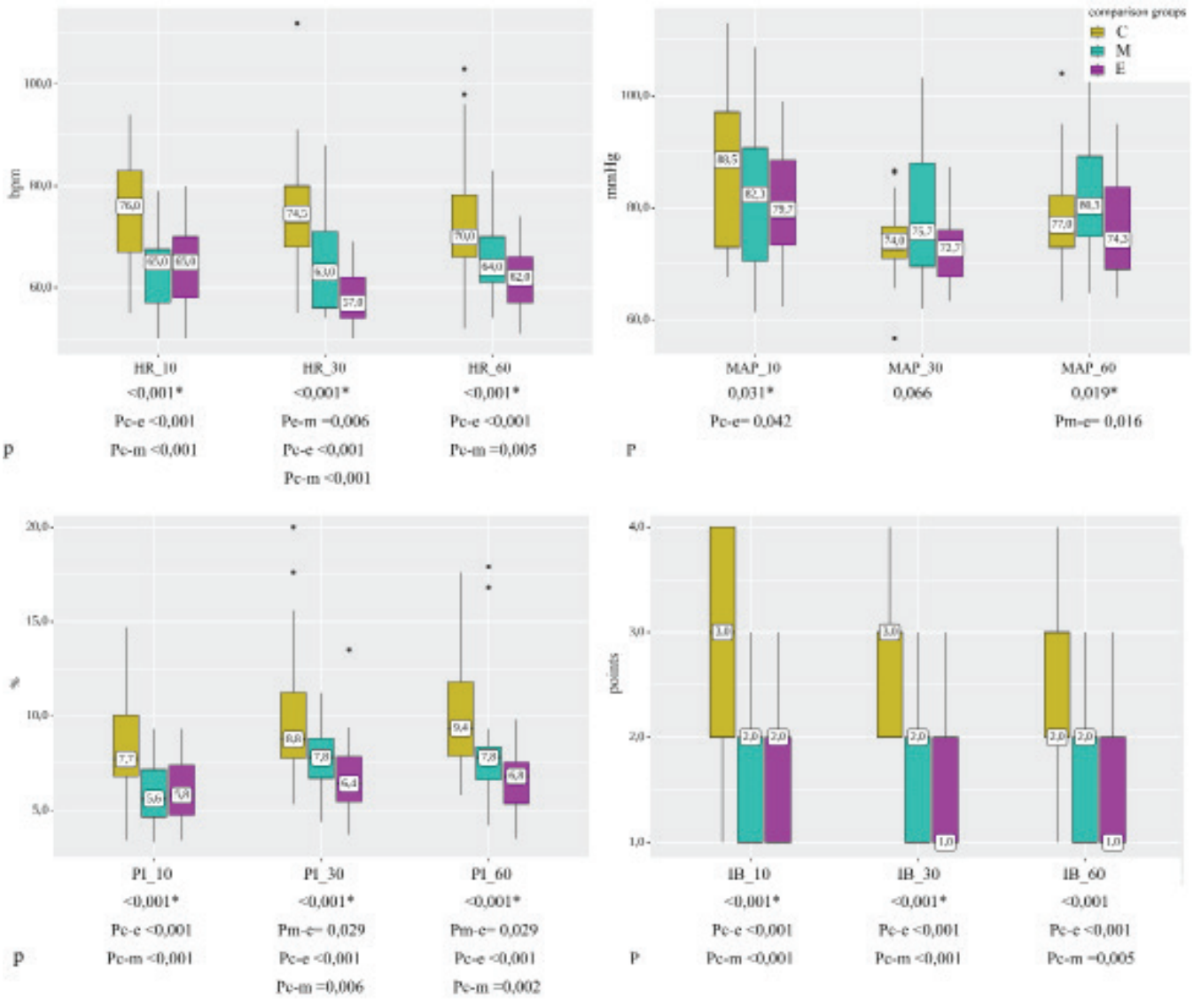
**The results of the study.** Comparison of the study groups revealed no statistically significant differences in anthropometric indicators, concomitant pathology, the groups were homogeneous (Table 1).

The operation time was the same in all study groups, the wake-up time in C group was significantly greater than in M and E groups. The amount of fentanyl required to provide analgesia was significantly higher in C group. The analysis of hemodynamic parameters and the intensity of bleeding at the study points revealed significant differences (Figure).

The HR in C group at the 10th minute of procedure was statistically significantly higher compared to group M and E, there were no differences between M and E groups. At the 30th minute, the HR in C group was significantly higher than in M and E groups, and the HR in E group was significantly lower compared to M group. At the 60th minute of procedure the HR in M and E groups were significantly lower compared to the C group, and the HR in E group was lower compared to M group as well as at the 30th minute of the operation. MBP values significantly differed at the 10th minute of the procedure between C and E groups with a low level of significance. At the 30th minute of the operation MBP levels were the same in all the compared groups and at the 60th minute, high MBP values were recorded in M group compared to E group. There were no significant differences between C and E groups. PI values at the 10th minute of procedure were significantly lower in groups M and E compared to C group. At the 30th and 60th minutes of surgery PI values were lower in groups M and E compared to C group, as well as at the 10th minute, but still significantly they also differed between M and E groups. The IB was convincingly lower at all points of the study in M and E groups compared to C group and did not differ between M and E groups.

To assess the effect of intraoperative hemodynamic parameters (HR, SBP, MBP, PI) and the use of BB on the intensity of intraoperative bleeding a multivariate analysis by linear regression was performed at all points of the study (Table 2).

As a result of multivariate analysis at the 30th minute of the operation it was shown that if the patient belongs to M group, a decrease in IB by 1.437 points




Comparison of heart rate (bpm), MBP (mmHg), PI (%) and IB (points) in C, M and E groups at the study points. Note. Comparison groups: C - control, M- metoprolol, E- esmolol. Heart rate – HR, MBP – mean blood pressure, PI – perfusion index, IB – intensity of bleeding. * - The Kraskel–Wallis criterion.

Table 2

**Results of multivariate analysis of the prognostic model of intraoperative bleeding intensity at the 10th, 30th and 60th minutes of surgery**

| | B | Std. error | t | p |
|---|---|---|---|---|
| Characteristics of the predictive model at the 10th minute of the study | | | | |
| Intercept | -0.452 | 0.628 | -0.719 | 0.474 |
| Group M | -0.902 | 0.179 | -5.050 | < 0.001* |
| Group E | -0.859 | 0.173 | -4.951 | < 0.001* |
| HR 10 | 0.021 | 0.009 | 2.332 | 0.022* |
| SBP 10 | 0.014 | 0.006 | 2.457 | 0.016* |
| Characteristics of the predictive model at the 30th minute of the study | | | | |
| Intercept | 0.649 | 0.690 | 0.941 | 0.349 |
| Group M | -1.437 | 0.163 | -8.839 | < 0.001* |
| Group E | -1.445 | 0.154 | -9.358 | < 0.001* |
| HR 30 | 0.022 | 0.007 | 3.376 | 0.001* |
| Characteristics of the predictive model at the 60th minute of the study | | | | |
| Intercept | -1.586 | 0.711 | -2.230 | 0.028* |
| Group M | -0.477 | 0.174 | -2.747 | 0.007* |
| Group E | -0.424 | 0.178 | -2.386 | 0.019* |
| HR 60 | 0.031 | 0.008 | 3.926 | < 0.001* |
| SBP 60 | 0.014 | 0.006 | 2.353 | 0.020* |

Note. Groups of comparison: M- metoprolol, E – esmolol; HR – heart rate, SBP – systolic blood pressure. * - differences in indicators are statistically significant ($p < 0.05$).

should be expected and to E group by 1.445 points. An increase in IB by 0.022 points is predicted with an increase in SBP. At 1 mmHg the obtained regression model is characterized by a correlation coefficient rxy = 0.728, which corresponds to a high closeness of the connection on the Cheddock scale. The model was statistically significant ($p < 0.001$). The resulting model explains 53.0% of the observed IB variance. Similar results were obtained at the 10th and 60th minutes of the operation (see Table 2). In addition, the probability of an IB raising increased by 0.021 and 0.031 points at the 10th and 60th minutes, respectively, with an increase in HR by 1 bpm.

**Discussion.** The necessary anesthetic care of FESS includes adequate anesthesia, respiratory tract protection, hemostasis control, prevention of postoperative complications, including delayed bleeding [4, 11]. The development of bleeding is determined by several factors: the value of blood pressure, HR and the state of hemostasis [1, 10, 13]. Controlled hypotension is a common method of reducing intraoperative bleeding, however, excessive hypotension can lead to a decrease in blood flow in organs sensitive to fluctuations in perfusion pressure (heart, brain) [13]. It is established that IB depends on MBP and HR [15]. Some researchers believe that with a HR of 60 bpm, there is no need to reduce MBP, since during procedures with controlled hypotension it is not always possible to reduce IB due to peripheral vascular dilation and reflex tachycardia. A decrease in HR reduces the filling of the capillaries of the tissues of the nasal cavity, since venous outflow improves due to an increase in the diastole phase [13, 15]. In our study the use of BB made it possible to reduce IB without a significant decrease in MBP (Fig. 1). The IB in M and E groups was significantly lower at all points of the study, while the MBP values at the 30th and 60th minutes of the operation did not significantly differ from those in C group. The use of BB significantly reduced HR and in E group the effect was more obvious only at the 30th minute of the procedure compared with M group. We believe that this is due to the method of administration of BB with the introduction of a loading dose of esmolol, it is possible to achieve a significant reduction in HR faster without the development of significant bradycardia [2]. The PI values in the control group were significantly higher at all points of the study, since in order to reduce the HR in this group, we increased the concentration of an inhalation anesthetic and additionally administered fentanyl (Table. 1), which led to an increase in peripheral blood flow. We have previously shown that PI >10% is associated with increased tissue bleeding during FESS procedures [1]. Relatively low PI values in E group compared to M group are most likely also associated with a lower need for narcotic analgesics. The decrease in IB in the M and E groups was achieved by a decrease in HR without a significant reduction in MBP. When assessing the factors that may affect the development of bleeding, we found out in the prognostic model that the use of BB in the M and E groups leads to a decrease in IB at all points of the study, but most significantly at the 30th minute of procedure (Table 2). With an increase in HR and SBP an increase in IB is predicted at the 10th and 60th minutes of procedure, which is associated with increased perfusion of peripheral tissues and corresponds to the studies of other authors [8, 13, 14, 15]. In the prognostic model at the 30th minute of surgery the HR losts a significant effect on the IB. Most likely this is due to the stabilization of hemodynamic parameters in all study groups.

**Conclusions.**

1. Intraoperative use of beta-blockers, in addition to reduction of heart rate, leads to a moderate decrease in mean blood pressure and a decrease in intraoperative bleeding during FESS procedures under general anesthesia.
2. Metoprolol and esmolol have the same effectiveness for reducing the intensity of bleeding during FESS procedures.
3. The use of esmolol causes a more significant decrease in heart rate and mean blood pressure compared to metoprolol.

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V.V. Saveliev, V.V. Popov, M.M. Vinokurov

# CHANGES IN THE PHYSICAL AND CHEMICAL PROPERTIES AND FATTY ACID COMPOSITIONS OF THE BLOOD SERUM IN PATIENTS WITH DIFFERENT COMMON PERITONITIS AS ONE OF THE CRITERIA FOR ASSESSING THE SEVERITY OF THE INFECTIOUS-INFLAMMATORY PROCESS

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The **aim** of this study was a clinical assessment of the diagnostic value of determining changes in the fatty acid composition and values of the surface tension of blood serum in patients with peritonitis in the light of assessing the severity of the course of the infectious and inflammatory process. In the course of the study it was found that the most informative indicator of the severity of the course of an infectious-inflammatory process is a sharp and prolonged decrease in the blood serum of patients with CCP in the level of γ-linolenic, dihomo-γ-linolenic fatty acids, as well as a persistent decrease in STC values. The results of the clinical study presented by us allow us to recommend, as a method of choice, to assess the severity of the course of peritonitis with the help of a comprehensive assessment of changes in the fatty acid composition and STC values of blood serum.

**Keywords:** peritonitis, fatty acids, surface tension coefficient.

**Introduction.** Despite the long history of studying peritonitis, various issues of its treatment remain one of the most difficult and not completely resolved problems of abdominal surgery. Given the large number of syndrome complexes developing in response to inflammation in the abdominal cavity, the approach to treatment is multidisciplinary in nature and includes a large set of measures aimed at both eliminating the source of peritonitis and correcting homeostasis disorders. The pathogenesis of peritonitis is a complex dynamic process of progression of pathophysiological disorders [8]. The main role in the pathogenesis of this severe complication is assigned to endogenous intoxication, caused by the accumulation in the body of toxins of microbial origin and metabolic products. It is the control of endotoxemia that often determines the outcome the disease.

In recent years, in the world of medical science, there has been an increasing interest in determining the physiological and biochemical status of a person when monitoring pathological processes developing in tissues, organs, and organ systems [1]. The physiological and biochemical status is determined by the presence at a certain stage and a certain situation of the concentration of biologically active compounds - proteins, fats and carbohydrates, as well as their metabolites [4]. In addition, many physiological and biochemical processes occur at the interface. A very important feature in the physical sense of the structural organization of living systems is a wide variety of dynamically stable and unstable interfaces [12]. These primarily include various

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