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Impact of General Anesthesia and Antioxidants on Cognitive, Static and Locomotor Functions During Laparoscopic Cholecystectomy

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Summary

Aim of the study: to reduce cognitive impairment during laparoscopic cholecystectomy by perioperative administration of drugs with antihypoxic and antioxidant effects under the control of stabilography.

Materials and methods. We studied the effect of general anesthesia and antioxidants on cognitive, static and locomotor functions during laparoscopic cholecystectomy. We studied 90 patients with acute calculous cholecystitis randomized into three experimental groups (n=30, each group). The control group was composed of 24 healthy individuals. Group 1 patients received no antioxidants, group 2 patients received the combination antioxidant drug (sodium fumarate+sodium chloride+potassium chloride+magnesium chloride) in the postoperative period, and group 3 patients received methylethylpyridinol. The patient groups were comparable in sex, age and type of inflammatory and destructive process in the gallbladder. Surgical intervention was performed under endotracheal anesthesia. Premedication with atropine and promedol was given, and anesthesia induction was carried out with propofol, fentanyl and suxamethonium. Sevoflurane, fentanyl and cisatracurium were employed to maintain anesthesia, analgesia and myorelaxation, respectively. The patients were examined before surgery, 24 and 48 hours after surgery. In the groups of patients who received antioxidant therapy, blood sampling for hematological and biochemical examinations was performed 30 min after the administration of antioxidants. Stabilographic studies and MoCA test (Montreal Scale) were performed before antioxidant administration prior to surgery and after surgery, on days 2 and 3.

Results. Neuropsychological testing revealed postoperative cognitive dysfunction on standard therapy which included impaired attention and concentration, executive function, memory, speech, visual constructional skills, abstract thinking, counting, and orientation (21 points on the MoCA scale versus 28–30 points for normal). We found that the pathogenetic factors of cognitive dysfunction included insufficient antioxidant protection, decreased TNF-α and elevated interleukin-18 levels along with an increased level of C-reactive protein in plasma, which manifested as activation of free-radical oxidation processes and reduced antioxidant system and performance of nonspecific resistance. Perioperative use of the combination antioxidant drug and methylethylpyridinol antioxidants reduced the frequency and severity of postoperative cognitive impairment in patients after laparoscopic cholecystectomy.

Conclusion. The most important pathogenetic factors of cognitive dysfunction after laparoscopic cholecystectomy include activation of free-radical oxidation, reduction of antioxidant defense system performance and lack of nonspecific resistance factors. Adding the combination antioxidant drug or methylethylpyridinol to the standard therapy reduces the intensity of radical oxygen species generation, maintains the antioxidant potential, activates production and secretion of nonspecific resistance factors, preventing the development and reducing the severity of cognitive disorders in the perioperative period. Neuropsychological testing and stabilographic examination allow identifying the risk of cognitive disorders in patients after laparoscopic cholecystectomy and provide a rationale for the use of antioxidant therapy for their prevention.

Keywords: laparoscopic cholecystectomy; cognitive disorders; free-radical oxidation; antioxidant therapy

Conflict of interest. The authors declare no conflict of interest.

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Introduction

Recent years have seen a significant increase in the incidence of cognitive disorders in various diseases, both medical and surgical ones. These disorders are manifested primarily by reduced memory and mental performance, impaired perception, processing and analyzing of information, as well as low ability to remember and retain this information [1–4]. Cognitive disorders hamper rational cognition of the world and the possibility of purposeful interaction with it [5–8]. Cognitive dysfunctions are associated with many diseases such as cerebrovascular [9], mental [10], cardiovascular [11, 12], surgical [13, 14], and infectious [15–17] ones.

The introduction of laparoscopic cholecystectomy into clinical practice has expanded the indications for the use of this method, which is considered to be the «first choice intervention» in the treatment of cholelithiasis [18-20]. Its use is associated with cognitive impairment of varying severity in up to 80% of cases [21]. Mortality in laparoscopic cholecystectomy is almost three times lower than in open cholecystectomy [22, 23]. The causes of mortality after laparoscopic cholecystectomy include myocardial infarction (0.4%), pulmonary embolism (0.3%), acute cardiovascular failure (0.4%) [24]. The nature of condition and surgical technique do not allow to fully implement proper prevention of complications and avoid the sequelae of surgical aggression. Anesthesia, along with surgical aggression, is also associated with increased risk of complications during laparoscopic cholecystectomy [25]. These factors are a major challenge for anesthesiologist requiring search for new approaches to anesthesiological support. Quite often (in 16–44% of cases) during surgical interventions, anesthesiologists make errors of varying severity such as erroneous dosing of drugs, inaccurate filling out of the anesthesia record sheet, or failure to control the changes in performance of vital organs and systems [26]. In addition, there are accumulating data on neurotoxic effects of general anesthesia resulting in the development of postoperative cognitive dysfunction, the pathogenesis of which remains poorly understood [14, 27–29]. There are few reports on the results of monitoring the cognitive functions of patients in the postoperative period, which requires further studies [25, 32].

The aim of the study was to reduce cognitive impairment during laparoscopic cholecystectomy by perioperative administration of drugs with antihypoxic and antioxidant activity under control of stabilography.

Material and Methods

Ninety patients hospitalized in Penza City Clinical Hospital № 6 named after G. A. Zakharin and the 3rd Central Military Clinical Hospital named after A. A. Vishnevsky and underwent laparoscopic surgery for acute cholecystitis with ASA severity I–III. The patients were randomized into 3 equal groups which were comparable by gender, age, types of gallbladder disease and differed only in treatment method. Group 1 patients received no antioxidant therapy during surgery, group 2 patients received a combination antioxidant drug containing sodium fumarate, sodium chloride, potassium chloride and magnesium chloride (Mafusol®) 800 ml intravenously (the volume of infusion was the same for every patient due to minor differences in body weight) during surgery, group 3 patients received antioxidant methylethylpyridinol 10 mg/kg intravenously during surgical treatment. The control group consisted of 24 healthy subjects, comparable in gender and age with the study participants.

The surgical intervention was performed under endotracheal anesthesia. Premedication was done 30 min before the patients were transferred to the operating room using 0.1% atropine 0.5 ml and 2% promedol 1 ml, and induction anesthesia was performed with propofol 2 mg/kg, fentanyl 0.01 mg/kg, and suxamethonium 2 mg/kg. After tracheal intubation, the patients were ventilated using a FabiusDraeger machine with a 1:1 air-oxygen mixture, respiratory volume of 8–10 ml/kg and respiratory rate 16–18 per minute. Anesthesia was maintained by 1.5–2‰ sevoflurane, analgesia by fentanyl 2.5–15.0 μg/kg and cisatracurium besilate was used for neuromuscular blockade.

The patients were examined before surgery, 24 and 48 hours after surgery. In the groups of patients receiving antioxidant therapy, blood sampling for hematological and biochemical tests was performed 30 min after the administration of antioxidants. Stabilographic studies and MoCA test (Montreal scale) before surgery were performed before the administration of antioxidants, while on days 2 and 3 these studies were performed 30 min after the administration of Mafusol® in group 2 patients and methylethylpyridinol in group 3 patients [33].

Blood antioxidant status was studied using the photometric method based on reaction of antioxidants (present in the sample) with exogenous hydrogen peroxide, using «Biochemmack» (Russia) kits. The serum level of proinflammatory cytokines TNF-α and IL-18 was determined by enzyme immunoassay using Vector-Best kits. C-reactive protein (CRP) content was studied by immunoturbidimetric method using «Dyakon» kits. Cognitive functions were assessed according to the Montreal scale (MoCA test). The maximum obtainable level on this scale was 30 points. Stabilographic studies were performed on a «ST-150» stabilograph using Stabip software developed by Biosoft-M (Moscow). The patient was standing upright on the stabilometer platform

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Table 1. Effect of laparoscopic cholecystectomy on changes of clinical and laboratory parameters in patients from group 1

Parameter	Value at different periods			
	Before surgery	24 hours after surgery	48 hours after surgery	Control group
Hemodynamic parameters				
Heart rate, beats per minute	87 [85; 89]*	77 [75; 80]#	77 [67; 80]#	70 [60; 80]
SBP, mm Hg	148 [145; 150]*	130 [125; 130]#	125 [120; 130]#	122 [119; 130]
DBP, mm Hg	88 [85; 90]*	78 [75; 80]#	76 [74; 80]#	76 [72; 80]
Blood neutrophil count and free radical status				
Neutrophils, $\times 10^9$/l	5.1 [4.1; 7.3]*	6.0 [4.7; 7.3]*	6.9 [5.8; 9.1]*#	3.5 [2.8; 4.2]
Spontaneous CL, units	2.6 [1.9; 4.9]	4.8 [3.0; 6.5]*#	2.5 [1.4; 4.2]	2.5 [1.4; 2.9]
Differences in CL sums, units	0.46 [–0.41; +1.33]*	–2.00 [–3.00; +0.10]*#	–2.10 [–3.09; +0.12]*#	1.30 [–0.11; +2.05]
BAS,μmol/l	299 [256; 326]	267 [196; 300]*	297 [257; 333]	306 [268; 328]
Inflammatory/proinflammatory markers				
CRP, mg/l	8.0 [3.0; 17.0]*	23.0 [15.0; 65.0]*#	41.0 [27.0; 115.0]*#	3.0 [2.5; 5.5]
TNF-α, pg/ml	2.5 [0.9; 3.3]*	3.1 [3.0; 4.0]*#	2.0 [1.8; 2.5]*	0.5 [0.4; 1.3]
IL-18, pg/ml	88.9 [51.2; 161.9]*	77.5 [45.0; 154.6]*#	68.8 [37.9; 136.5]*#	111.0 [60.0; 121.3]
Montreal scale assessment				
MoCA, points	27.0 [26.0; 28.0]	21.0 [21.0; 22.0]*#	23.0 [22.0; 25.0]*#	28.0 [27.0; 29.0]
Stabilographic parameters				
~X(OE), mm	0.80* [–3.38; 6.16]	0.67* [–4.59; 8.16]	0.93* [–4.41; 6.12]	–2.38 [–6.00; 4.18]
~X (CE), mm	0.54* [–4.78; 6.88]	2.03*# [–5.32; 8.44]	0.89*# [–5.56; 3.87]	–2.63 [–4.40; 3.53]
maxX (OE), mm	14.25* [11.40; 22.00]	15.60* [12.90; 24.10]	17.15*# [12.10; 33.90]	10.25 [9.06; 17.60]
maxX (CE), mm	13.95* [9.95; 17.50]	14.10* [12.00; 17.60]	11.70# [9.52; 16.10]	9.93 [7.40; 16.20]
DX (OE), mm	14.80* [10.40; 24.20]	18.90*# [9.97; 31.20]	16.45* [13.10; 21.90]	8.40 [6.46; 11.70]
DX (CE), mm	16.40* [8.56; 24.60]	17.70* [8.98; 22.90]	12.45# [7.35; 18.60]	10.85 [5.07; 26.05]
FX (OE), Hz	0.20 [0.14; 0.24]	0.16 [0.12; 0.22]	0.19 [0.14; 0.24]	0.20 [0.15; 0.32]
FX (CE), Hz	0.18 [0.16; 0.25]	0.20 [0.12; 0.24]	0.18 [0.14; 0.20]	0.23 [0.15; 0.29]
F60X (OE), Hz	0.50 [0.37; 0.59]	0.51 [0.37; 0.63]	0.47* [0.43; 0.63]	0.62 [0.54; 0.71]
F60X (CE), Hz	0.49 [0.35; 0.65]	0.51 [0.41; 0.57]	0.46* [0.41; 0.63]	0.60 [0.46; 0.77]
~Y (OE), mm	–30.60* [–39.30; –14.30]	–18.95*# [–35.00; –9.08]	–24.50*# [–30.30; –6.93]	–14.80 [–21.90; –9.69]
max Y (OE), mm	31.70* [21.70; 42.20]	32.75* [16.70; 42.30]	24.90*# [16.50; 34.80]	16.15 [13.75; 22.00]
max Y (CE), mm	27.00* [23.00; 36.10]	26.05* [15.50; 39.00]	25.85* [19.20; 35.50]	16.41 [12.25; 18.80]
DY(OE), mm	19.20 [16.60; 36.80]	22.15* [16.10; 36.40]	23.30*# [14.00; 28.80]	16.00 [9.90; 30.05]

Note. * — $P<0.05$ vs the control group; # — $P<0.05$ vs the preoperative values (Mann–Whitney U-test). OE — open eyes; CE — closed eyes; BAS — blood antioxidant status; SBP — systolic blood pressure; DBP — diastolic blood pressure; CL — chemiluminescence; CRP — C-reactive protein; TNF — tumor necrosis factor; IL — interleukin.

under different sensory conditions, with open and closed eyes. The duration of each test was 51.2 seconds. Stabilometry studies were performed according to the Moscow Consensus on the Use of Stabilometry and Biocontrol by Reference Reaction in Practical Medicine and Scientific Research [34].

At the preliminary stage of the study based on the stabilometric parameters in 120 patients during laparoscopic cholecystectomy a regression equation was made to estimate the compensation of antioxidant defense system:

$$P = 95 \times Fy60\% - 70 \times Fx60\% + 4V + W,$$

where P is compensation index of antioxidant protection system, Fy60% and Fx60% are quantiles of spectral power density of oscillations of pressure center frontal and sagittal planes (Hz), V is average speed of pressure center (mm/sec), W is patient weight (kg). Decompensation of the antioxidant system was assessed based on P parameter values: those less than 130 indicated significant level of decompensation, between 130 and 150 — an average decompensation, and those greater than 150 suggested good compensation of the antioxidant protection system.

Statistical analysis of the results was performed using Statistica 6.0 software package and nonparametric statistical methods. The results were considered significant at $P<0.05$. Quantitative parameters were described by median and interquartile range *Me* [LQ; HQ]. Comparative analysis of quantitative characteristics in independent groups was performed using the Kruskal–Wallis method (if $P<0.05$ the groups were considered derived from different general populations or general populations with different medians). In this case, we performed a pairwise comparison of the groups using the Mann–Whitney test. Non-parametric Wald-Wolfowitz test was used where appropriate to reveal cytokine concentrations changes. Spearman's test was used for correlation analysis of the results.

Results

The study of hemodynamic parameters revealed significantly higher HR, systolic (SBP) and diastolic (DBP) pressures in patients who did not receive antioxidant therapy before surgery vs those in the

control group. On day 2 after the surgery, these values decreased and did not differ from those in the healthy subjects (Table 1).

The neutrophil count in the peripheral blood was significantly higher compared to the control group at all stages of the study (Table 1). The highest values of spontaneous chemiluminescence (CL) parameters were observed on day 2 after surgery. The difference in CL sums test was significantly lower than in the control group on day 2 after the operation (Table 1). In view of the increase of CL values exactly on day 2, low values of the difference in CL sums test may indicate reduced activation reserve when neutrophils were exposed to endogenous substances.

The serum CRP level in group 1 patients was significantly higher at all stages of the study compared to similar parameters in healthy subjects (Table 1). The TNF-α level before surgery was higher compared to controls (P=0.04, Wald-Wolfowitz test). On days 2 and 3, TNF-α levels were also significantly higher (P<0,05, Mann–Whitney test). Preoperative and 3-day postoperative concentration values of another proinflammatory cytokine IL-18 were lower compared with controls (P=0.03 and P=0.003, respectively, Wald-Wolfowitz test).

The values of blood antioxidant status (BAS) parameters significantly decreased 24 hours after laparoscopic cholecystectomy and were less than the control values. The preoperative examination revealed a positive correlation (R=0.64; P=0.0001) between the severity of spontaneous CL and CRP level, which could indicate a systemic inflammatory response, and a negative correlation between CL and antioxidant activity (R=–0.69, P=0.0006), which suggests inhibition of antioxidant enzymes with increased free-radical oxidation processes and increased levels of free oxygen radicals.

The use of the MoCA test was the «gold standard» for diagnosing cognitive dysfunction. There was a significant decrease in MoCA test values 24 hours after surgery. Both 24 and 48 hours after surgery, the MoCA test values were significantly lower than those before surgery vs the control group (Table 1).

A significant correlation between the MoCA and BAS values (R=0.46; P=0.03) was revealed 48 hours after surgery. This confirms the involvement of free-radical oxidation products in the pathogenesis of cognitive disorders.

Prior to surgery, there was a significant shift of the center of pressure (COP) vs the control relative to the Y axis in the «open eyes» (OE) and «closed eyes» (CE) positions (Table 1). On day 2, there was a significant shift of ~Y(OE) and ~Y(CE) to the positive direction, resulting in the position of the COP (OE) not differing from the control values, which could indicate a decrease in pain in the patients. We also found significant differences of the stabilographic indices at all stages of the study with the control group: increased values of max Y(OE), max Y(CE), and DX(OE), increased maximum amplitude of COP on the X axis (OE) on days 2 and 3 vs the control group. The described changes may indicate a complex combined impact of acute cholecystitis, surgical trauma and general anesthesia on the patients.

A significant increase in the statokinesiogram area S (OE) 24 hours after surgery was revealed vs the controls (323.0 mm^2) and its value before surgery (230.0 mm^2); 48 hours later, these parameters decreased, but remained higher than prior to the surgery. The S (CE) parameter on day 2 did not differ from the control values, though there was a tendency of its increase both on days 2 and 3 after the surgery. On day 2, a significant correlation between the MoCA values and the statokinesiogram (OE) area (R=–0.48; P=0.02), as well as between MoCA score and Romberg's coefficient (R=0.45; P=0.03) was revealed. The LFS (CE) on day 2 after surgery was significantly lower than the preoperative values and those of the controls. On day 3, there was a correlation between CL and LFS (OE) parameters (R=–0.4; P=0.03), indicating the relationship between these parameters and free-radical oxidation.

Forty-eight hours after surgery, the following values were also found to be significantly higher than those in the control group: maxX (OE); maxY (OE) and (CE) and DX(OE) (Table 1). On day 3 we found a correlation between CL and LFS (OE) values (R=–0.4; P=0.03), indicating an increase in statokinesiogram area and a decrease in LFS with increased free-radical oxidation. Values of total antioxidant activity correlated with values of 60% energy relative to the F60% Y (OE) sagittal area (R=–0.53; P=0.02) and the frequency of oscillations along the Y axis (FY(OE) (R=–0.57; P=0.01). This correlation shows the correspondence of larger values of BAS with lower values of 60% of the energy of the oscillation spectrum and the frequency of oscillations on the Y-axis. Twenty-four hours after surgery, there was a 1.75-fold increase in the number of patients with severe decompensation of antioxidant defense and a 2-fold decrease in the number of patients with moderate decompensation, while the number of patients with P values over 150 remained practically at the same level.

Group 2 patients who received Mafusol® after surgery demonstrated significantly higher HR, SBP and DBP compared to controls (Table 2) and a correlation between HR and CRP level (R=0.69; P=0.0006) in the preoperative period. We detected a higher neutrophil count before surgery, on days 2 and 3 after surgical intervention vs controls. Values of spontaneous chemiluminescence and difference in CL sums test did not differ from control values at all stages of the study [34, 35]. Values of BAS in pa-

Table 2. The effect of Mafusol® (group 2) and methylethylpyridinol (group 3) on hemodynamic parameters in the postoperative period, Me [LQ; HQ].

Parameter	Value at different periods			
	Before surgery	24 hours post surgery	48 hours post surgery	Control group
Heart rate, bpm, G2	87 [85; 88]*	77 [69; 80]*#	78 [75; 80]#	70 [60; 80]
Heart rate, bpm, G3	84 [80; 90]*	77 [70; 80]#	77 [72; 80]#	
Systolic BP, mm Hg, G2	149 [146; 151]*	130 [125; 130]#	125 [120; 130]#	122 [119; 130]
Systolic BP, mm Hg, G3	147 [145; 148]*	130 [130; 135]#	130 [125; 130]#	
Diastolic BP, mm Hg, G2	89 [86; 90]*	75 [70; 80]#	76 [70; 80]#	76 [72; 80]
Diastolic BP, mm Hg, G3	87 [80; 90]*	130 [130; 135]#	76 [72; 80]	

Note. G2 — group 2; G3 — group 3. * — $P<0.05$ vs the control group; # — $P<0.05$ vs the preoperative values (Mann–Whitney *U*-test).

tients treated with Mafusol® did not differ from those in the control group, but nevertheless on day 2 after the surgery a significant decrease of this parameter was found ($P=0.01$).

The serum TNF-α content before surgery, 24 hours and 48 hours after surgery was lower compared to controls ($P=0.03$). The decrease in the concentration of this cytokine in the blood serum may be due to the detoxifying effect of Mafusol®. The IL-18 levels did not differ significantly from the control and postoperative values.

On days 2 and 3 of the postoperative period there was a dramatic increase in serum CRP level vs the control ($P<0.05$). Twenty-four hours after surgery we revealed a correlation between CRP and BAS ($R=–0.39$; $P=0.04$). Correlation analysis also showed a correlation between spontaneous CL and the difference in CL sums before surgery ($R=–0.82$; $P=0.0001$) and 24 hours after surgery ($R=–0.51$; $P=0.02$).

The MoCA scale scores before surgery, 24 and 48 hours after surgery were significantly lower than those of the controls. Meanwhile, the lowest values of the MoCA scale (24.0 points) were registered in the patients 24 hours after laparoscopic surgery. However, the difference in the mean values before and one day after surgery was insignificant, which does not indicate cognitive impairment in group 2 patients.

Stabilography data revealed a significant shift of COP (OE) on the Y axis to the negative direction, a trend to shift of ~Y(OE) to the positive direction on day 2, resulting in the position of COP on Y axis not differing from the values in the control group. We also identified parameters which were different from the control values at all stages of the study. They were max Y(OE), max Y(CE), L (OE), V (OE), Ei (OE). On days 2 and 3, we observed significant increase in maximal COP amplitude on the X (OE) axis compared to the control. On day 2, a negative correlation between the MoCA parameters and the statokinesiogram area ($R=–0.44$; $P=0.03$) was revealed only in the CE position. Significant changes when comparing the *P* parameter values with the control were recorded only prior to surgery. There was a positive correlation between the antioxidant activity compensation and the difference in CL sum in patients 24 hours after surgery ($R=0.52$; $P=0.02$), which, in turn, had a steady negative correlation with the values of spontaneous CL.

Group 3 patients had significantly higher HR, SBP, DBP compared to the control group before the surgery, but there was a decrease of HR and BP on day 2 (Table 2). Thus, although initially in all groups of patients, hemodynamic parameters differed significantly from the ones of healthy controls, during the treatment they «levelled out», which suggests the comparability of the studied groups. In addition, we revealed a higher blood neutrophil count in patients at all stages of the study. Values of differences in CL sums test and luminol-dependent CL did not differ from the control at all stages of study in the group 3 patients. Differences in BAS values vs the controls were observed only before the surgery ($P=0.04$), while no significant differences of this parameter with the control were observed during the study.

The serum TNF-α level at all stages of the study was lower than the control values, which could be due to the antitoxic effect of methylethylpyridinol. The serum CRP level before surgery did not differ from the control but increased on days 2 and 3 after surgery. A negative correlation between CRP and BAS ($R=–0.55$; $P=0.02$) was seen 24 hours after surgery. In addition, a significant negative correlation between spontaneous CL and difference in CL sums was found at all stages of the study: before surgery, $R=–0.78$ ($P=0.001$); 24 hours after surgery, $R=–0.49$ ($P=0.02$); 48 hours after surgery, $R=–0.6$ ($P=0.001$).

A comparative frequency analysis of the patient distribution depending on P parameter grading showed that in Groups 2 and 3 on day 2 after surgery no increase in the number of patients with P level less than 130 was seen, unlike group 1, where the number of such patients increased 1.75 times. In the patients who received antioxidants perioperatively we didn't observe a decrease in the antioxidant defense compensation, unlike those from group 1. The fact that patients had a high compensatory ac-

tivity of the antioxidant system while having a high reactivity reserve of neutrophils can be considered another significant result of the study. In group 3 patients who received methylethylpyridinol after surgery, the postoperative values of antioxidant activity did not differ from those of the control group.

Discussion

Thus, the neuropsychological testing indicated that patients with laparoscopic cholecystectomy who received standard treatment had such postoperative cognitive disorders as impaired attention, executive function, memory, speech, visual and constructive skills, abstract thinking, counting, and orientation. The mean MoCA score one day after surgery was 21 points, differing significantly from both the preoperative score of 27 points (P=0.01) and the mean score of healthy subjects of 28 points (P=0.01). Forty-eight hours after surgery, the mean MoCA score increased to as low as 23 points.

For patients in groups 2 and 3 who received antioxidant therapy, the mean scores on the MoCA scale, even on day 1 after surgery, were 26 and 27, respectively, and did not differ significantly from both the preoperative and healthy subjects scores. This suggests that antioxidant therapy reduces the severity and frequency of cognitive impairment during laparoscopic cholecystectomy.

The results of biochemical and immunological tests indicate that the main pathogenetic factors of cognitive disorders include insufficient antioxidant defense system, decreased TNF-α and increased IL-18 levels along with the increased serum level of C-reactive protein, which manifests in activation of free-radical oxidation, reduced antioxidant system performance and nonspecific resistance of the body. Our results are in line with the previous findings [36].

Conclusion

We found a relationship between stabilographic parameters and indicators of cognitive functions, biochemical parameters characterizing the blood antioxidant status, which offers broad prospects for their use in preoperative preparation of patients, risk assessment of cognitive disorders and decision-making on the prescription of antioxidant therapy.

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