THE EFFECT OF BILE DECOMPRESSION ON PRO- AND ANTIOXIDANT MARKERS IN THE COMPLICATIONS OF GALLSTONES ASSOCIATED WITH CHOLESTATIC JAUNDICE

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THE EFFECT OF BILE DECOMPRESSION ON PRO- AND ANTIOXIDANT MARKERS IN THE COMPLICATIONS OF GALLSTONES ASSOCIATED WITH CHOLESTATIC JAUNDICE (Abstract): Argumentation of optimal terms for a staged surgical approach in the benign complications of gallstones associated with cholestatic jaundice by assessing the effect of biliary decompression on pro- and antioxidant markers. Material and methods: Prospective study, selected 105 patients with complicated gallstones and associated cholestatic jaundice, divided into three homogeneous subgroups, dependent on evolutionary complication. Control group - 35 patients with uncomplicated gallstones. All patients in the study group followed the staged treatment protocol in obstructive jaundice, with the primary prerogative - internal biliary decompression by endoscopic papillosphincterotomy. Pro- and antioxidant markers were assessed at hospitalization, on the 1st and 4th day after decompression. Results: Malonic dialdehyde at hospitalization marked in all subgroups with statistically significant results compared to the control group: I - 12.11±0.64 mol/l [p<0.001 (t=10.7)], II - 11.12±0.53 mol/l [p<0.001 (t=10.9)]; III - 13.16±0.44 mol/l [p<0.001 (t=16.5)]. The activity of the antioxidant system evaluated by superoxide dismutase values [p<0.001 (t=6.4); (t=4.1); (t=5.7)] and catalase [p<0.001 (t=6.7); (t=5.6); (t=7.6)] shows a decrease in all subgroups compared to the control group. On the 1st day after drainage, malonic dialdehyde values did not show statistical significance compared to the before decompression state [I - p>0.05 (t=0.11); II - p>0.05 (t=0.91)]. An obvious reduction of its activity was found on the 4th after decompression day [I - p<0.001 (t=5.15); II - p<0.01 (t=2.6); III - p<0.001 (t =3.99)]. The return of the antioxidant system in all subgroups to values relatively similar to the control group: superoxide dismutase [I - p<0.05 (t=2.21); II - p<0.05 (t=0.008); III - p<0.05 (t=0.33)] and catalase [I - p<0.05 (t=2.39); II - p<0.05 (t=3.52); III - p<0.01 (t=2.87)] was found more than 4 days after decompression. Conclusions: The study demonstrated the positive influence of biliary decompression in the complications of gallstones associated with cholestatic jaundice for the reduction of a massive lipid oxidation and the creation of conditions for increasing the antioxidant capacity with the restoration of the body's biological balance, which is more pronounced 4-5 days after decompression, serving as criterion for the possibility of definitive resolution of gallstones in these terms. Keywords: COMPLICATIONS OF GALLSTONES, CHOLESTATIC JAUNDICE, OXIDATIVE STRESS, ANTIOXIDANT SYSTEM.
The effect of bile decompression on pro- and antioxidant markers in the complications of gallstones associated with cholestatic jaundice

From the range of surgical pathologies of the organs of the hepato-biliopancreatic region, the most difficult to approach are the diseases associated with mechanical jaundice syndrome, being accompanied by the partial or total stoppage of the bile passage. Biliary lithiasis is one of the pathologies located in this area, with an incidence of 10-15% in the adult population, which frequently evolves with complications associated with cholestatic jaundice (1). Despite the improvement of the population's access to medical assistance, the emergence of new non-invasive and informative methods in the diagnosis of gallstones, the rate of complications associated with cholestatic cholelithiasis in pathology remains high-10-20% cases (1, 2). Studies show choledo-cholithiasis as the main cause of jaundice, but acute biliary pancreatitis, acute cholecystitis, cholangitis, are also mentioned (2, 3). It is known that, over time, obstructive cholestasis causes variable functional disorders in several systems and organs, with the most severe repercussions in the liver (3, 4, 5). Some authors, in studies aimed at suppressing the metabolic activity of the liver in mechanical jaundice, associate the severity of jaundice with blood bilirubin values, which of course is an important marker (2, 4, 5). However, taking into account a single indicator is not enough to evaluate the complex changes that occur when there is an interruption of the bile passage. Recently, papers have appeared that associate liver dysmetabolism in jaundice with the universal mechanism of cell injury - oxidative stress (OS) (6, 7, 8). The notion of oxidative stress, according to the opinion of several researchers, includes all the oxidative damage produced by oxygen free radicals. It is defined as the imbalance between the free radicals - the prooxidant and antioxidant systems, in the conditions where the oxidants are more and have a destructive potential on the human body (6). In other words, oxidative stress is triggered by the imbalance between the amount of reactive oxygen produced in the body and its ability to eliminate it (8). The presence of marked lipid peroxidation, which occurs in endotoxemia associated with cholestasis, is known in the literature (9, 10). Previous studies on the issue report that the suppression of the metabolic activity of the liver present in jaundice contributes to the reduction of the barrier function of the gastrointestinal tract, the inhibition of the immune system and hemostasis mechanisms, appreciating the mechanical jaundice syndrome as a medical-surgical emergency, which requires solving the biliary obstruction as early as possible (6). However, the laborious surgical interventions performed at the peak of the “icterus” to restore the bile flow, demonstrated an evolution with a significant number of postoperative complications, and a mortality of 15-40% (2, 11, 12), thus opening a field larger for staged surgical treatment, which has as its main goal biliary decompression in the first stage and definitive resolution of gallstones in the second stage (5;11). Because it contributes to the reduction of complications through the use of minimvasive methods, the treatment in stages is currently widely used, although the problem of assessing the times of surgical interventions in stages, continues to be a topic of dispute. Also, the accessible literature data do not contain information, which aims to use the deviations of oxidative stress in the assessment of the times of surgical intervention in stages. In this context, we set out to try to argue the optimal
terms for a staged surgical approach in the benign complications of gallstones associated with cholestatic jaundice by assessing the effect of biliary decompression on pro- and antioxidant markers.

**MATERIAL AND METHODS**

The clinical research was carried out within the Clinical Base II of the Department of Surgery no.1 of SUMF “Nicolae Testemițanu”. In order to achieve the goal, 105 patients with complicated gallstones and associated cholestatic jaundice were investigated, followed the staged treatment protocol in obstructive jaundice, with the primary prerogative - internal biliary decompression through endoscopic papillosphincterotomy (PST) with or without removal of the stone. 35 patients with uncomplicated gallstones were included in the control group. Biliary decompression by PST with or without removal of the stone in the study subgroups was performed after confirming the etiological diagnosis and establishing the indications. In subgroups I and II, endoscopic PST was practiced within 24-96 days of hospitalization, in subgroup III, in the case of preserved bile flow - after 4-5 days of conservative treatment. Indication for internal drainage via PST in subgroups was persistent cholestatic jaundice. The age of the patients varied between 51-72 years. Female/male ratio - 3/1. The criteria for including patients in the basic group were: the presence of complications of gallstones associated with cholestatic jaundice, confirmed by positive clinical and paraclinical diagnostic parameters, which met:

- clinical criteria: history of gallstones or biliary colic at the onset, the presence of jaundice during hospitalization;
- biological syndrome: battery of characteristic tests: - elevated values of serum bilirubin on account of the direct fraction, elevated values of alkaline phosphatase, elevated values of leukocytes, serum fibrinogen, serum urea, serum amylase, marked ALAT values and imaging confirmation of gallstones and diameter of main bile duct > 0.8 cm.

Cases that met the stated criteria were included in the study. The research was started after obtaining approval from the Institutional Ethics Committee.

Depending on the evolutionary complications present: the patients from the base group were divided into 3 homogeneous subgroups: I - acute cholecystitis, cholangitis and cholestatic cholemia in gallstones (n=35); II - chronic gallstone disease and cholestatic cholemia (n=35) and III - acute biliary pancreatitis and cholestatic cholemia (n=35).

The comparative evaluation of SO in subgroups was carried out by assessing in the blood serum the correlation between the intensity of peroxidic oxidation of lipids (POL) and the antioxidant potential. The tests were taken during hospitalization, until the start of treatment, on the first day after biliary drainage, over 4 days after drainage. In the case of a preserved bile flow, in subgroup III, the primary testing was performed after 4 days of conservative treatment. The intensity of POL was determined by the values of the final product of lipoperoxidation - malonic dialdehyde (MDA), assessed according to the procedure modified by Gudumac V. et al. (2010) (13). The antioxidant potential was expressed by the values of superoxide dismutase (SOD) and catalase (CAT). SOD activity was estimated according to the procedures modified by Gudumac V., Tagadiuc O et al. (2010) (14). CAT activity
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was determined according to the method modified by Baciu E. and Nastas I. (1996) (15). The data of each case were recorded in a standardized form and processed, using the MS Excel program. The obtained results were compared and the changes in dynamics were related to the values of the parameters of the control group. The statistical analysis was performed. The discrepancy with the margin of error < 5% was considered statistically significant (p < 0.05).

RESULTS
Survey data and results of laboratory parameters in the study subgroups and the control group at hospitalization are presented in table 1. Depending on age and concomitant pathologies, the control group and the study subgroups were selected homogeneously, with an insignificant difference in subgroup I (p c/1 >0.05 (t=1.10); p c/2 <0.05 (t=2.55); p c/3 <0.01 (t=2.84)). The homogeneity of the subgroups is also with insignificant deviations between subgroups I and II ( p 1/2 >0.05 (t=1.64); p 1/3 <0.01 (t=3.31); p 2/3 <0.01 (t=4.55)). The data analysis shows that the association of an inflammatory, progressively painful component presents the patient earlier for hospitalization, reducing the duration of jaundice until hospitalization (p 1/2<0.001(t=3.5); p 1/3<0.001 (t=8.6); p 2/3<0.001(t=9.6)). Statistically significant difference in the levels of biochemical markers of cholestasis: alkaline phosphatase (p<0.001(t=10.6); (t=8.2); (t=7.27)), direct bilirubin (p<0.001 (t=12.3); (t=12.5); (t=14.9)) in all subgroups compared to the control group, reveals the severity of the liver disease, which is correlated with inflammation markers - elevated values of fibrinogen, blood leukocytosis, neutrophils - p<0.001 in subgroups I and III. The assessment at hospitalization of the DAM values as the final product of lipoperoxidation, confirms a marked lipoperoxidation in all subgroups, compared to the control group (p<0.001 (t=10.7); (t=10.9); (t=16.5)). The activity of the antioxidant system evaluated by superoxide dismutase and catalase values shows a decrease in both SOD values (p<0.001(t=6.4); (t=4.1); (t=5.7)) as well as CAT (p<0.001(t=6.7); (t=5.6); (t=7.6)) in all subgroups compared to the control group.

TABLE I.
Survey data and results of laboratory parameters at hospitalization

<table>
<thead>
<tr>
<th>Markers</th>
<th>Control group n=35)</th>
<th>Subgroup I (n=35)</th>
<th>Subgroup II (n=35)</th>
<th>Subgroup III (n=35)</th>
<th>p c/1</th>
<th>p c/2</th>
<th>p c/3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>59.1±1.12</td>
<td>61.4±1.75***</td>
<td>64.2±1.65*</td>
<td>53.1±1.79**</td>
<td>p&gt;0.05</td>
<td>p&lt;0.05</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>t=1.1</td>
<td>t=2.55</td>
<td>t=2.84</td>
</tr>
<tr>
<td>Duration of jaundice</td>
<td>0</td>
<td>3.19±0.19</td>
<td>4.44±0.38</td>
<td>1.48±0.06</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alkaline Phosphatase (U/I)</td>
<td>149.8±12.4</td>
<td>541.4±34.6***</td>
<td>881.14±78.3**</td>
<td>760.0±83.0***</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(t=10.6)</td>
<td>(t=8.2)</td>
<td>(t=7.27)</td>
</tr>
<tr>
<td>Total bilirubin (mmol/l)</td>
<td>12.1±0.79</td>
<td>78.55±5.3***</td>
<td>119.31±8.7***</td>
<td>80.28±4.9***</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(t=12.4)</td>
<td>(t=12.2)</td>
<td>(t=8.7)</td>
</tr>
<tr>
<td>Direct bilirubin (mmol/l)</td>
<td>4.2±0.06</td>
<td>56.2±4.2***</td>
<td>88.2±6.7***</td>
<td>54.8±3.4***</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(t=12.3)</td>
<td>(t=12.5)</td>
<td>(t=14.9)</td>
</tr>
</tbody>
</table>
### Table

<table>
<thead>
<tr>
<th>Markers</th>
<th>Control group n=35</th>
<th>Subgroup I n=35</th>
<th>Subgroup II n=35</th>
<th>Subgroup III n=35</th>
<th>p c/1</th>
<th>p c/2</th>
<th>p c/3</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALAT (U/l)</td>
<td>19.57±0.97</td>
<td>207.1±12.1***</td>
<td>128.7±8.2***</td>
<td>289.62±9.4***</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Blood amylase (U/l)</td>
<td>20.57±1.4</td>
<td>43.1±2.3***</td>
<td>37.9±1.9***</td>
<td>164.9±9.7***</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fibrinogen (U/L)</td>
<td>2.69±0.06</td>
<td>4.21±0.1***</td>
<td>3.52±0.1***</td>
<td>4.43±0.17***</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Blood leukocytes(n)</td>
<td>6.23±0.23</td>
<td>12.12±0.52***</td>
<td>7.51±0.31**</td>
<td>10.24±0.43***</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Neutrophil(n)</td>
<td>3.86±0.22</td>
<td>13.1±0.43***</td>
<td>7.5±0.39***</td>
<td>9.9±0.56***</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Urea (U/l)</td>
<td>6.23±0.21</td>
<td>7.0±0.21*</td>
<td>6.56±0.24***</td>
<td>7.92±0.47***</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Creatinine (U/l)</td>
<td>68.8±1.19</td>
<td>86.58±3.2**</td>
<td>81.0±3.5**</td>
<td>82.17±2.8**</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>DAM (mol/l)</td>
<td>4.62±0.27</td>
<td>12.11±0.64***</td>
<td>11.12±0.53***</td>
<td>13.16±0.44***</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SOD (UC/ml)</td>
<td>1230.74±16.39</td>
<td>1060.91±21.05**</td>
<td>1096.97±27.4**</td>
<td>1057.44±25.2***</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CAT (μmol/s)</td>
<td>15.79±0.33</td>
<td>13.27±0.14***</td>
<td>13.17±0.33***</td>
<td>12.62±0.25***</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Caption *: p<0.05; p<0.01**; p<0.001***; p>0.05**** - compared to the values of the control group

According to the results of the study, depending on the time interval after drainage, biliary decompression differently influenced the activity of the pro- and antioxidant systems. On the first day after endoscopic PST, a decrease in the level of direct bilirubin was found in all subgroups (I - p<0.01 (t=5.4); II - p<0.001 (t=3.3); III - p<0.001 (t=7.6)), but the level of leukocytes and neutrophils in the blood increased (I - p<0.05 (t=3.2); II - p<0.01 (t=1.6); III - p<0.05 (t=5.2)), factor that influenced a massive continuation of lipid peroxidation in all subgroups. The evaluation of the influence of internal biliary decompression on the prooxidant system by assessing the MDA values showed, on the first day after decompression, the maintenance of high values compared to the before decompression parameters in all subgroups. Characteristic for subgroups I and II, the increased values of MDA did not show statistical significance compared to the before decompression state (I - p>0.05 (t=0.11); II - p>0.05 (t=0.91)), characteristic of subgroup III in which the patients were initially subjected to a complex drug treatment, which reduced the degree of endogenous intoxication and contributed to the decrease of before decompression MDA values (p<0.001 (t=8.66)), elevated MDA values after drainage showed statistical significance (p<0.001 (t=6.4)). An obvious reduction in lipid oxidation activity was found on the 4th day after decompression, when MDA values decreased significantly (I - p<0.001 (t=5.15; II - p<0.01 (t=2.6); III - p<0.001 (t=3.99)), but not up to control group values. The influence of time-dependent biliary decompression on MDA values is shown in first figure.
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The analysis of the influence of internal biliary drainage on the systemic antioxidant response in the case of endotoxemia with a marked lipoperoxidation in the complications of gallstones associated with cholestatic jaundice, also reported a variability in the values of SOD and CAT parameters depending on the elapsed time after decompression. Fluctuations in SOD and CAT values are shown in figures 2 and 3.

On the first day after PST, the values of SOD and CAT in groups I and II decreased insignificantly compared to before decompression values but showing a statistically significant decrease compared to the control group SOD (I - p<0.001 (t=4.1); II - p<0.01 (t=4.8)); CAT (I - p<0.001 (t=4.1); II - p<0.01 (t=4.8)), demonstrating the maintenance of an antioxidant response inability in this postoperative stage. In subgroup III, subjected preoperatively to standard complex therapy used in case of acute biliary pancreatitis, with potentiation of the antioxidant system through increased values of SOD (III - p<0.001 (t=4.8)) and CAT (III - p<0.001 (t =7.4)) before decompression, decreased values after drainage of SOD (III - p<0.05 (t=3.04)) and CAT (III - p<0.05 (t=2.19)), according to statistical significance, they showed a better antioxidant response capacity in these patients.

The increase in SOD and CAT values on day 4 after drainage exposes an increased potential of the antioxidant system at this postoperative stage (tab. II).


**Table II.**

**SOD and CAT parameters 4 days after decompression**

<table>
<thead>
<tr>
<th>Markers</th>
<th>Control group (n=35)</th>
<th>Subgroup I (n=35)</th>
<th>Subgroup II (n=35)</th>
<th>Subgroup III (n=35)</th>
<th>p c/1</th>
<th>p c/2</th>
<th>p c/3</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOD (UC/ml)</td>
<td>1230.74±16.39</td>
<td>1178.7±16.77</td>
<td>1230.72±16.26</td>
<td>1237.6±12.2</td>
<td>p&lt;0.05 (t=2.21)</td>
<td>p&lt;0.05 (t=0.0008)</td>
<td>p&lt;0.05 (t=0.33)</td>
</tr>
<tr>
<td>CAT (μmol/s)</td>
<td>15.79±0.33</td>
<td>14.94±0.13</td>
<td>13.99±0.39</td>
<td>14.77±0.13</td>
<td>p&lt;0.05 (t=2.39)</td>
<td>p&lt;0.05 (t=3.52)</td>
<td>p&lt;0.01 (t=2.87)</td>
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</tbody>
</table>

**DISCUSSION**

According to the data accumulated in the literature, cholestatic jaundice, associated with various pathologies, is considered a complex surgical problem, presenting both diagnostic and therapeutic challenges (4, 5, 11). Early biliary decompression is recognized as the optimal method of treatment in avoiding functional and organic alteration of the liver. The ideal for the patient would be to resolve both the cholestatic jaundice and the etiological factor triggering cholestasis at the same time, an argument supported by some authors (17). However, practice has shown that these interventions are more often associated with complications and a slow postoperative evolution (16, 18). Staged treatment with the primary prerogative of biliary de-
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Compression is currently recognized and widely used in solving pathologies associated with cholestatic jaundice (4, 11, 19). However, the issue of operating times is presented controversially in the literature. Some authors, taking into account the high cost of diagnosis and treatment of these patients, claim that the definitive resolution of gallstones after decompression must be performed in the first 24-48 hours (18, 20). Others, focusing on the hepatic homeostatic disturbances, characteristic of lithiasis cholestasis, prefer for “late” cholecystectomy, in repeated hospitalization (4, 11, 19), which according to studies can lead to a recurrence of complications (18, 20). The continuous study of the complex pathophysiological mechanism characteristic of the evolution of cholestatic jaundice requires solving the problem depending on the biological balance of the patient (11, 19).

It is known that the permeability of the biliary tree and the uncompromised drainage of bile into the intestine are important for a homeostatic balance of the body. Substances normally excreted in the bile, in the case of biliary obstructions, accumulate in the blood system and, together with the bile salts also accumulated, have systemic toxic effects, clinically manifested by prolonged infectious complications, coagulopathy, hypovolemia and endotoxemia, which can ultimately lead to organ failure (2, 4, 21). Among the factors capable of modifying the normal functioning of biological membranes are reactive oxygen species, capable of inducing the phenomenon of lipoperoxidation, which contributes to the destruction of membrane lipid structures, consequently increasing the permeability of membranes with an unbalanced transport of ions (7, 9, 21). The attack of oxygen free radicals on cellular lipids results in the formation of aldehyde lipid hydroperoxide decomposition products, such as malonic dialdehyde, the increase in values denoting a pro-oxidant activity, which was also found to be significant in our study. MDA values 3 times higher compared to the control group were in all subgroups of the study before decompression. The pro-oxidant aggressiveness was also maintained on the first day after decompression with an involution 3-4 days after drainage, being correlated with the decrease in blood leukocytosis values (p<0.01 (t=2.1)). Analysis of the effect of internal biliary decompression on the prooxidant system demonstrated a decrease in lipid oxidation values after drainage, which is significant over time and is correlated with the decrease in bilirubin values and the inflammation syndrome.

The liver, as the body's metabolic center, has an important role in immunological processes and phagocytosis, thus being a source of antioxidants. It is known that serum bilirubin has the ability to inhibit lipid peroxidation, capturing singlet oxygen, thus being considered as a non-enzymatic liver antioxidant (7, 18, 22), a point that argues for an abundant production of all bilirubin fractions in all forms of jaundice. But the excessive increase in direct bilirubin values in an obstructive jaundice, turns it into a factor of aggression with the mobilization of other antioxidant defense mechanisms. According to studies, the decrease in SOD and CAT values correlates with the duration of jaundice and in prolonged cholestasis shows a late rebalancing (9, 18, 22). Our data reported in all study subgroups a no prolonged jaundice with a minimum duration of 1.48±0.06 and a maximum duration of 4.44±0.38 from onset to hospitalization, a moment that
correlates with direct bilirubin values, ranking all patients in the group with an average degree of severity (17, 21). The decrease in before decompression SOD (p<0.001 (t=6.4)) and CAT (p<0.001 (t=6.7)) is consistent with the severity of jaundice and the presence of inflammation. Comparative analysis of SOD results (I - p<0.05 (t=2.21), II - p<0.05 (t=0.0008), III - p<0.05 (t=0.33)) and CAT (I - p<0.05 (t=2.39), II - p<0.05 (t=3.52); III - p<0.01 (t=2.87)) with the values from the control group, time-dependent, reveals the return of the antioxidant system in all subgroups to values relatively similar to the control group 4 days after decompression.

Thus, our study demonstrates that in the case of the patient hospitalized early for complications of gallstones with a non-prolonged jaundice, classified in the medium severity group, the restoration of the capacities of the antioxidant system returns close to normal values 4-5 days after decompression, being a favorable predisposing factor in reducing intra- and postoperative complications, in case of a second stage surgical intervention in these terms. Therefore, the data-about known in the literature about use of MDA, SOD and CAT values as diagnostic tests to evaluate the severity of jaundice (22, 23), we consider that these parameters and their correlations can be additionally recommended as indicator tests in determining the type of treatment, volume of surgical treatment and operative times.

**CONCLUSIONS**

Oxidative stress is an important pathogenetic element in the self-maintenance and exacerbation of the inflammatory response present in the complications of gallstones associated with cholestatic jaundice. Until the initiation of biliary decompression, in these patients, there is a significant intensification of the peroxidic oxidation of lipids, with a character of a chain oxidation process, and an increase in the level of the final product of lipid peroxidation-malonic dialdehyde, a fact that confirms the need for an immediate decompression. Antioxidant activity before decompression is also compromised, correlating with the degree of endotoxemia and severity of jaundice. It is obvious that, immediately after decompression MDA maintains its values, yielding over time under a complex conservative treatment. Bile drainage, however, creates conditions for increasing the antioxidant capacity and restoring the body’s biological balance, which is more pronounced 4-5 days after decompression, serving as a criterion for the possibility of definitive resolution of gallstones in these terms.

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**REFERENCES**

The effect of bile decompression on pro- and antioxidant markers in the complications of gallstones associated with cholestatic jaundice


