Section A-Research paper

HEPATOTROPIC CORRECTION IN THE COMPLEX TREATMENT OF ACUTE INTESTINAL OBSTRUCTION IN PATIENTS WITH DIFFUSE LIVER DISEASES

Urakov Sh.T., Makhmanazarov O.M., Khayitov D.Kh., Kayimov M.T.

Bukhara State Medical Institute named after Abu Ali ibn Sino.

Annotation. The role of hepatoprotective correction in the treatment of patients with acute intestinal obstruction in patients with diffuse liver diseases is considered and studied. 106 patients with acute intestinal obstruction on the background of diffuse liver diseases were examined. The pathogenetic aspects of the development of enteral insufficiency syndrome in this category of patients have been studied in detail. Modern hepatoprotective drugs were included in the complex preoperative and postoperative treatment. The positive effect of this algorithm on the prevention and reduction of the progression and development of liver failure and enteral insufficiency syndrome is substantiated.

Keywords: acute intestinal obstruction, liver failure, enteral insufficiency syndrome, hepatoprotective drugs

The relevance of studies related to acute intestinal obstruction (OCD) in patients with diffuse liver diseases (DIS) is due to complex pathophysiological changes in organs, with this comorbidity of acute surgical pathology and DIS and, accordingly, not always ending with favorable outcomes even if the operation is performed in a timely manner[1]. Despite all the advancements in medical science and practice today, positive results in improving the treatment process can only be achieved through an in-depth understanding and analysis of all the key aspects of the pathophysiological processes that accompany acute intestinal obstruction in patients with diffuse liver diseases and any other pathology [6]. Rapidly progressive endogenous intoxication in patients with acute intestinal obstruction induces activation of the liver's detoxification mechanisms. [7,8]. In this regard, it is necessary to improve the compensatory functional capabilities of the liver, which are the main and fundamental factor for achieving postoperative effectiveness and full rehabilitation of patients in urgent surgery for acute intestinal obstruction. [4, 9]. However, compensated liver function is not only a mandatory

condition for maintaining homeostasis, but also a key factor in situations that require extra costs from the body during the intra- and postoperative periods.

In this regard, a detailed study of the role of hepatoprotective therapy in the treatment of acute intestinal obstruction in patients with diffuse liver diseases becomes timely. The need for this study is also justified by the fact that it is Kupffer liver cells that play a fundamental role in the detoxification of endotoxins [2, 5].

Progressive endotoxemia, in turn, is a mandatory pathophysiological consequence of acute intestinal obstruction and an important link in the pathogenesis of multiple organ failure, which poses the greatest threat to the lives of patients, especially those with diffuse liver diseases [3, 4].

The aim of the study. To evaluate the effect of hepatoprotective therapy carried out in the postoperative period on the results of surgical treatment of acute intestinal obstruction in patients with diffuse liver diseases.

Materials and methods. We conducted a study of 106 patients with acute intestinal obstruction in patients with DIS accompanied by enteral insufficiency syndrome (EIS) who were treated in the 1st surgical department of the Bukhara regional branch, the Republican Scientific Center for Emergency Medical Care in Bukhara in the period from 2020 to 2023.

Among the patients included in the study, there were 51 men and 55 women. 42 patients (39.6%) were under the age of 60 years, 61 patients (57.5%) aged 61-75 years, 3patients (2.8%) were over 75 years old. The main causes that caused acute intestinal obstruction were; obturation by colon tumor, adhesive disease, inversion, invagination, obturation by bezoar of the small intestine and obstruction in the hernial sac. We used a scale for assessing the severity of enteral insufficiency syndrome (EIS) proposed by Professor N.V. Zavada and co-authors. According to this scale: 32 (30.2%) patients had the I degree of EIS, 50 (47.3%) had the II degree, and 24 (22.6%) patients had the III degree.

Morpho-functional assessment of the liver condition was performed using biochemical studies, such as the de Ritis coefficient for the ratio of aspartic and alanine transaminases (AST/ALT), and the MELD scale (Mayo end-stage liver disease), which reliably reflects the severity of hepatic dysfunction.

In our study, a solution for infusions "Riverton" LLC "Dream Pharma LLC, Uzbekistan" was used as a hepatoprotective drug. Its active components are:

succinic acid (5,280 g); N-methylglucamine (meglumin) (8,725 g); riboxin (inosine) (2.0 g); methionine (0.75 g); nicotinamide (0.25 g). Riverton is a balanced infusion solution with a hepatoprotective effect, which accelerates the transition of anaerobic processes to aerobic ones, improves the energy supply of hepatocytes, increases the synthesis of macroergs, increases the resistance of hepatocyte membranes to lipid peroxidation, restores the activity of antioxidant defense enzymes. Riverton reduces cytolysis, which is manifested in a decrease in indicator enzymes: aspartate aminotransferase, alanine aminotransferase. It also helps to reduce bilirubin and its fractions, improves the excretion of direct bilirubin into bile. Reduces the activity of excretory enzymes of hepatocytes - alkaline phosphatase and gamma-glutamyltranspeptidase, promotes the oxidation of cholesterol into bile acids. When administered intravenously, the components quickly distribute in the tissues of the body. Riverton was administered intravenously as a 400 ml drip at a rate of 40 drops per minute. The main group consisted of 52 patients who received complex treatment that included hepatoprotective therapy with a balanced infusion solution of "Riverton". The control group consisted of 54 patients who received traditional standard therapy and did not receive hepato-protection as part of their complex treatment.

Results and their discussion

In the analysis of biochemical indicators in patients with enteric insufficiency syndrome, a normal ratio of ALT and AST was found in 33 (82.5%) patients with stage I EIS, in 10 (17.9%) patients with stage II EIS, and in 2 (6.3%) patients with stage III EIS (Table 1).

Table 1

Groups of patients depending on the level of cytolytic liver damage, taking into account the severity of enteral insufficiency syndrome.

De Ritis Index, points	Degree of ENG., abs., (%)			
	I deg. (n=32)	II deg. (n=50)	III deg. (n=24)	Total (n= 106)
< 0,9	3 (9,4)	30 (60,0)	18 (75,0)	51 (48,1)
0,9-1,7	25(78,1)	8 (16,0)	2 (8,3)	35 (33,0)

> 1,7	4 (12,5)	12(24,0)	4 (16,7)	20(18,9)

Unidirectional increase of alanine transaminase in relation to AST/ALT, developing as a result of some damage to the liver tissue, among the studied patients, was detected in 3 (9.4%) patients with degree I EIS, in 30 (60%) - with degree II EIS and in 18 (75%) - with degree III EIS.

In the same way, in patients with severe damage to the hepatic parenchyma, in addition to changes in other biochemical parameters, a simultaneous increase in AST and ALT was determined. These changes were detected in a smaller number of patients, without sensitive dynamics depending on the severity of enteral insufficiency syndrome. Thus, an excess of the de Ritis index of 1.7 points was registered in 4 (12.5) patients with grade I EIS, in 12 (24%) - with degree II EIS and in 4 (16.7%) - with degree III EIS. As a result of the correlation analysis, the dependence of the change in the severity of cytolytic hepatocyte syndrome on the severity of intestinal damage was not established (Spearman's rank correlation, $p > 0.05$. The severity of liver failure less than 10 points on the MELD scale was detected in 35 (33%) patients: of which 27 (84.4%) people with the I degree of EIS. Moderate violation of detoxification systems of the liver parenchyma was detected in 8 (16%) patients with degree II EIS and was not detected in patients with degree III EIS (Table 2).

Table 2

Distribution of patients depending on the indications of the MELD scale and the severity of EIN

MELD scale, points	Degree of EIS., abs., (%)			
	I deg.(n=32)	II deg.(n=50)	III deg.(n=24)	Total (n=106)
< 10	27 (84,4)	8(16)	0	35 (33)
10-19	5(15,6)	36 (72)	16 (66,7)	57 (53,8)
> 20	0	6(12)	8 (33,3)	14 (13,2)

The MELD scale assessment in the range of 10-19 points was established in 57 (53.8%) patients, of whom 5 (15.6%) had grade I EIS, 36 (72%) had grade II EIS, and 16 (66.7%) had grade III EIS. Exceeding the 20-point mark was observed in 14 (13.2%) patients, of whom 6 (12%) had grade II EIS and 8 (33.3%) had grade III EIS. The conducted statistical analysis revealed a direct correlation between the severity of liver failure in patients with acute intestinal obstruction and the severity of EIS (Spearman's rank correlation, $r < 0.05$).

A significant difference in the number of patients with resolved EIS between the study groups was found only on the 7th day of treatment. Prior to that, in the first days of the postoperative period, the number of patients with grade I EIS did not exceed one-third of the group - 16 (30.8%) patients in the main group receiving hepatotropic therapy and 17 (31.5%) in the group without hepatotropic therapy (Table 3). On the first day after the operation, the number of patients with grade III EIS in the main group was 12 (23.1%), and in the control group, it was 11 (20.4%). The number of patients with grade II EIS was 24 (46.2%) in the main group and 26 (48.1%) in the control group. Therefore, a statistically confirmed equality of the groups was established regarding the severity of EIS (t-test, $p = -0.267$, $p>0.05$) (Table 3).

Table 3

Distribution of patients in the study groups, taking into account the severity of EIS

СЭН	Day of treatment, abs., (%)							
	1-е		3-и		5-е		7-е	
	Main gr. (n=52)	Finite gr. (n=54)	Main gr. (n=52)	Finite gr. (n=54)	Main gr. (n=52)	Finite gr. (n=54)	Main gr. (n=52)	Finite gr. (n=54)
I deg.	16 (30,8)	17 (31,5)	20 (38,5)	17 (31,5)	23 (44,2)	22 (40,7)	41 (78,8)	28 (51,9)
IIdeg.	24 (46,2)	26 (48,1)	28 (53,8)	29 (53,7)	25 (48,1)	25 (46,3)	11 (21,2)	21 (38,9)
III deg.	12 (23,1)	11 (20,4)	4 (7,7)	8 (14,8)	4 (7,7)	7 (12,9)	0	5 (9,3)
tdeg, p	-0,267, p>0,05		-0,161, p>0,05		-0,143, p>0,05		-0,098, p<0,05	

The same changes were observed on the 3rd and 5th days after the surgical intervention in both groups. The number of patients with mild enteric insufficiency increased uniformly in both groups, while the number of patients with severe enteric insufficiency decreased. For example, on the 3rd day of the study, there were 20 (38.5%) patients with grade I EIS in the study group and 17 (31.5%) patients in the control group. By the 5th day, the number of grade I EIS patients in the study group had increased to 23 (44.2%) while in the control group it increased to 22 (40.7%). In addition, the decrease in the frequency of patients with grade III EIS on the 3rd day showed a significant trend, with only 4 (7.7%) cases in the study group and 8 (14.8%) cases in the control group. However, on the 5th day, this trend slowed down, as there were 4 (7.7%) patients with grade III EIS in the study group and 7 (12.9%) in the control group. Nevertheless, statistical analysis confirmed the similarity of changes in the severity of EIS in both groups on these days (Table 3).

On the seventh day of observation, there were 41 (78.8%) patients with grade I EIS in the study group, compared to only 28 (51.9%) in the control group. In addition, there were only 11 (21.2%) patients with grade II EIS in the study group, which was half as many as in the control group, where there were 21 (38.9%) such patients. Moreover, no patients with grade III EIS were detected in the study group, while there were 5 (9.3%) in the control group.

Thus, it can be concluded that on the seventh day of comprehensive therapy, a statistically significant difference in the severity of enteric insufficiency syndrome was observed between the compared groups (t deg., p=-0,098, p<0,05).

Changes in the severity of liver dysfunction had a slightly different trend (table 4). On the first postoperative day, a moderate form of liver dysfunction was observed in half of the patients in both groups: 26 (50%) in the main group and 25 (46.3%) in the control group.

A favorable prognosis for the course of liver dysfunction was observed in 20 (38.5%) patients in the main group and 25 (46.3%) in the control group. An unfavorable prognosis, corresponding to more than 20 points on the MELD scale, was observed in 6 (11.5%) patients in the main group and 4 (7.4%) in the control group (t deg., p = -0.154, p> 0.05).

Importantly, by the third day, half of the patients in both groups had a favorable prognosis for the outcome of liver dysfunction, with 28 (53.8%) in the main group and 26 (51%) in the control group. The number of patients with a relatively unfavorable prognosis on the third day of the study remained practically the same (table 4). In the main group, there were 21 (42%) patients, and in the control group - 23 (45.2%) patients. At the same time, despite the difference in

treatment of patients with an unfavorable prognosis for the course of liver dysfunction on the third day, there were only 3 patients in both groups (5.8% and 5.9%, respectively) (t deg., p = -0.124, p> 0.05).

Table 4

Distribution of patients according to the severity of hepatorenal syndrome

MELD scale	Day of treatment, abs., (%)							
	1st		3rd		5th		7th	
	Main gr. (n=52)	Finite gr. (n=54)	Main gr. (n=52)	Finite gr. (n=51)	Main gr. (n=52)	Finite gr. (n=49)	Main gr. (n=52)	Finite gr. (n=47)
< 10	20 (38,5)	25 (46,3)	28 (53,8)	26 (51)	40 (76,9)	24 (48,9)	50 (96,1)	29 (61,7)
10-19	26 (50)	25 (46,3)	21 (40,3)	23 (45,1)	11 (21,2)	23 (46,9)	2 (3,9)	17 (36,2)
> 20	6 (11,5)	4 (7,4)	3 (5,8)	2 (3,9)	0	2 (4,1)	0	1 (2,1)
t-deg.,	-0,154, p>0,05		-0,124, p>0,05		-3,751, p<0,05		-5,882, p<0,05	

However, on the 5th day of the postoperative period, among patients who were prescribed a hepatoprotective agent, 40 (76.9%) had a favorable prognosis according to the MELD score. Among patients without correction of liver dysfunction, there were 24 (48.9%) individuals. At the same time, patients with MELD scores in the range of 10-19 points in the main group were the remaining 11 (21.2%) individuals, while in the control group there were twice as many, and they accounted for 23 (46.9%) patients (Table 4).

There were no patients with an unfavorable prognosis for liver dysfunction in the main group, while there was one patient (-1, 2.1%) in the control group. Accordingly, the dynamics of liver dysfunction control identified by us in the main group had a significantly faster trend compared to patients who were not prescribed a hepatoprotective agent (t-deg., P =-3,751, p<0,05).

After a week of complex treatment, we found that in the main group of patients with a favorable course of liver dysfunction, there were 50 (96.1%) patients, and with a relatively unfavorable prognosis - 2 (3.9%), there were no patients with an unfavorable prognosis (Table 4). In the control group, there were 29 (61.7%) patients with a favorable prognosis according to the MELD score, and 17 (36.2%) patients with a relatively unfavorable prognosis.

However, by the 7th day of treatment, a patient with an unfavorable prognosis for liver failure (2.1%) was identified in the group of patients who did not use a hepatoprotective agent. In addition, by this day of observation, there was a statistically significant difference between the studied groups in the treatment outcomes (t-deg., P -5,882, p<0,05).

Conclusion

1. In cases of acute intestinal obstruction in patients with diffuse liver disease accompanied by the syndrome of enteric insufficiency, there is a correlation between an increase in the de Ritis index in 51.9% of cases and an unfavorable prognosis according to the MELD score in 58.5% of cases, which requires mandatory hepatotropic correction of liver dysfunction in such patients.
2. With an equal number of patients with varying degrees of enteric insufficiency syndrome identified on the first day after surgery, by the third day in the group of patients receiving a balanced infusion solution with hepatoprotective action, "Riverton", there is a more pronounced tendency towards a decrease in the frequency of patients with grade III enteric insufficiency syndrome compared to the group of patients without hepatoprotective therapy.
3. The trend of reducing the severity of liver dysfunction is much more successful in the group of patients receiving "Riverton" than in the group of patients without hepatoprotective therapy, and by the 5th day it is practically equal to zero.
4. In the group of patients receiving hepatotropic therapy with "Riverton", the intersection of the curves of mild and moderate severity of liver dysfunction occurs on the 3rd day, earlier than in patients with the syndrome of enteral insufficiency without hepatotropic therapy, where it is observed only by the 5th day.
5. Hepatoprotective therapy significantly improves the outcomes of treating acute intestinal obstruction in patients with diffuse liver diseases and should be recommended for inclusion in algorithms and protocols for the comprehensive treatment of such patients.

References

1. Dibirov MD, et al. Prevention and treatment of hepatorenal syndrome in acute intestinal obstruction. Surgery named after N.I. Pirogov Journal, 2010; Khirurgiia (Mosk) 2010; 8: 33-37.
2. Changes in the hemostasis system in patients with acute surgical pathology / S.Yu. Muravyov et al. // Russian Medical and Biological Bulletin named after academician I.P. Pavlov. - 2014. - No. 4. - P. 124-128.

3. Karimov SH.I. Ways of preventing intestinal failure syndrome in acute intestinal obstruction. Shoshilinch tibbiyot axborotnomasi, 2016, X (3) 29-34.
4. Korymasov E.A., Ivanov S.A., Kenarskaya M.V. Algorithm for the diagnosis and treatment of enteric insufficiency syndrome in peritonitis // I.I. Grekov Journal of Surgery. - 2021. - Vol. 180, No. 2. - P. 28-36.
5. Maltseva L.A., Mishchenko E.A., Kutovoy A.B., et al. Enteral tolerance in critically ill patients (literature review) // Emergency Medicine. - 2020. - Vol. 16, No. 1. - P. 36-44.
6. Milyukov V.E. et al. Morphofunctional changes of the hemocirculatory bed of the liver in various types of acute small bowel obstruction // Regional hemodynamics and microcirculation. 2018; 17(3): 92–101.
7. Tkhorievsky A.V., Prisyazhnyuk A.O., Slobodyanyuk R.M. Helping the practicing physician: enteral route for correcting intestinal insufficiency syndrome in patients after surgery // Emergency Medicine. - 2019. - No. 2 (97). - P. 130-137.
8. Catena F., De Simone B., Coccolini F., et al. Bowel obstruction: a narrative review for all physicians // World J. Emerg. Surg. - 2019. doi:10.1186/s13017-019-0240-7
9. Milyukov V.E., Sharifova K.M. Multiple organ manifestations of liver failure in acute small bowel obstruction // Surgery (Moscow). - 2019. - No. 9. - P. 73-79. doi:10.17116/hirurgia201909173.