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A differentiated approach to the treatment of patients with acute cholangitis

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Abstract
The study was based on the treatment results of 217 patients with mechanical jaundice of benign genesis complicated by purulent cholangitis. In 53 patients with cholemic endotoxicosis after preliminary minimally invasive decompression of the bile ducts various methods of treatment were used. In 17 patients (group I), traditional treatment including infusion and antibiotic therapy was used; in 18 patients (group II) plasmapheresis was used in combination with indirect electrochemical oxygenation (IECO) of plasma with sodium hypochlorite; and in 18 (group III) with additional ozonation of plasma (PA with IECO + Ozone) and subsequent reinfusion of detoxified plasma. Comparative evaluation of the laboratory parameters dynamics in the process of treatment in groups 2 and 3 did not reveal any significant differences. Hyperleukocytosis before operative treatment is noted in both groups. However, after surgical treatment in group 1 patients, the leukocytosis parameters are normalized only at the time of discharge, which indicates more pronounced purulent intoxication. At the same time, in patients of groups 2 and 3 there was a more rapid decrease and normalization of leukocytosis on the 5th postoperative day. The developed differential surgical tactic with the implementation of minimally invasive decompression and the use of plasmapheresis allows to stop the phenomenon of endotoxicosis, cholestasis and liver dysfunction and thereby improve the results of treatment.

Keywords: purulent cholangitis, endogenous intoxication, plasmapheresis, indirect electrochemical detoxification of plasma

1. Introduction
Purulent cholangitis is one of the most frequent and severe complications of benign and malignant diseases of the biliary tract. Acute purulent cholangitis and biliary sepsis are different manifestations of the infectious and inflammatory process that occurs locally and systemically [1, 4]. Cholangitis and biliary sepsis are manifested as a complex of organic and functional, general and local pathological changes in the body as a result of the development of the infectious process in the bile ducts and occur when their passability is disturbed and observed in 17-83% of patients with choledocholithiasis, stenosis of the Fater papilla, Mirizzi syndrome [2, 6, 10]. Cholangitis is detected in more than 80% [1, 5] of patients with posttraumatic strictures of bile ducts, and cicatricial stenosis of the biliodigestive anastomoses.
The inflammatory process in the bile ducts is characterized not only by the local purulent-destructive process, but also by systemic disorders that quickly lead to severe endogenous intoxication and severe organ dysfunction. This condition is most often considered as a cholangitis, the severity of morphological and clinical manifestations of which is very diverse [3, 7, 11].
It is believed that without surgical intervention, acute purulent cholangitis leads to death in 100% of cases. Postoperative mortality according to different authors, varies considerably and amounts to 13-60% [3, 6, 8]. In the surgical treatment of cholangitis, significant advances have been made related to the introduction of modern minimally invasive interventions, but there are a number of unresolved problems. One of them is cholemic endotoxicosis, accompanied by an increase in the level of metabolites in the blood plasma (bilirubin, urea, creatinine, residual nitrogen, transaminases, oligopeptides with an average molecular weight, etc.) [2, 10]. Postoperative mortality varies widely, ranging from 8 to 27% [3, 8].
Based on the fact that the main cause of mortality is endotoxemia, the question naturally arises about the detoxification therapy. Plasmapheresis is the most studied method of adjuvant therapy. With convincing evidence of the effectiveness of plasmapheresis in purulent cholangitis, further research is needed to increase its effectiveness by reducing the volume of plasma replacement and the possibility of reinfusion to patients with purified plasma.

2. Purpose of the study
Improvement of the surgical treatment results of patients with acute cholangitis by differentiated application of minimally invasive methods of preliminary decompression of bile ducts and improved method of detoxification - plasmapheresis.

3. Materials and methods
The study was conducted on the basis of the Samarkand State Medical Institute clinic. The research is based on treatment results of 217 patients with hyperbilirubinemia, acute cholangitis, biliary sepsis and severe biliary sepsis. The majority of patients were women - 136, men were 81. The average age of the patients was 65,3 ± 8,7 years.
Diagnosis of acute cholangitis and biliary sepsis is based on the history, clinical picture (the Sharko triad, Reynolds pentada) and laboratory examination which allows to calculate the degree of organ failure according to SOFA score (Sepsis

organ failure assessment) and the severity of the systemic inflammatory reaction according to the SIRS criteria (Systemic inflammatory response syndrome). Clinical manifestations of acute cholangitis were chills, a sudden rise in body temperature to 38-40° C with a rapid decrease. In 63% of patients chills were accompanied by jaundice in the first days of the disease. The most frequent clinical symptoms were pain, jaundice, fever. The classical triad of Charcot and the Reynolds pentad were relatively infrequent (in 37% and 9% of cases).

Thus, there were no absolute reliable clinical signs that make it possible to distinguish acute cholangitis from acute cholecystitis. Therefore, in the diagnosis of acute cholangitis, we gave preference to highly informative laboratory and instrumental methods of diagnostics.

Laboratory and instrumental diagnostics in addition to the generally accepted clinical analysis include determining the level of bilirubin and its fractions in blood serum, the activity of serum aminotransferase, alkaline phosphatase, protein content and its fractions, cholesterol, prothrombin, thymol and sublimate samples.

Non-invasive methods of preoperative diagnostics of acute cholangitis, biliary sepsis and pathologies of hepatopancreatoduodenal organs, against which they occurred, in addition to physical examination included ultrasound, computer tomography. Endoscopic studies included choledochoscopy, fibrogastroduodenoscopy, laparoscopy, retrograde pancreatocholangiography. The definitive diagnosis is established during the operation by characteristic changes in the wall of the bile duct and bile with microflora examination.

The most common cause of cholangitis and biliary sepsis is choledocholithiasis (65.9%), acute destructive cholecystitis (6.9%), rupture of echinococcal cysts in holedoch (6.0%), stricture of the terminal section of choledochus (6.0%), stricture of the larger duodenal papilla - 5,5% stricture of biliodigestive anastomosis and Mirizzy syndrome, respectively, 5.1% and 5.0%.

All the patients with acute cholangitis and biliary sepsis underwent surgical treatment. Depending on the type of operation 6 groups of patients were identified, which are presented in Table. 1.

Table 1: Types of surgery

№	Surgeries	amount
1	Endoscopic papillosphincterotomy (EPST)	23
2	Percutaneous-transhepatic cholangiostomy (PTCS)	5
3	Cholecystectomy, choledocholithotomy, external drainage of choledochus	160
4	End-to-side hepatojejunoanastomosis on Roux limb	24
5	Cholecystectomy drainage of the cystic duct by Abbe-Pikovsky	21
6	Choledochotomy, external drainage of choledochus	12
Total		**217**

The tactics of surgical treatment of patients with acute cholangitis complicated by biliary sepsis were strictly differentiated. At the same time, a three-stage method of decompression, plasmapheresis and sanation of the bile ducts were predominantly used.

Decompression of the bile ducts allowed to delay the radical operation and perform it in a more favorable period. Indications for EPST and PTCS were considered choledocholithiasis with inflammatory stricture of the biliary tract or without it which caused the development of acute cholangitis. In view of the initial severe condition at the first stage of treatment the main goal of the undertaken mini-invasive operation was the elimination of purulent cholangitis by decompression and restoration of passage of bile into the duodenum.

According to the results, all the patients were divided into four groups: Group A - patients with mechanical jaundice without signs of inflammatory reaction (SIRS = 0) - 85 patients; Group B - patients with mechanical jaundice and mild inflammatory reaction (SIRS single sign) (acute cholangitis) - 79 patients; Group C - patients with two or more signs of SIRS (biliary sepsis) - 40 patients; Group D - patients with two or more signs of SIRS and organ dysfunction SOFA> 0 (severe biliary sepsis) - 13 patients.

In 164 patients from A and B (85 + 79) groups predominantly (in 160 patient's cholecystectomy, choledocholithotomy and external drainage of choledochus were performed), the one-step operative intervention was done.

53 patients from C and D (40 + 13) groups were treated with plasmapheresis (PA), after preliminary minimally invasive decompression of the bile ducts. After improvement of the patients' condition and normalization of the peripheral blood parameters, operative treatment was performed. Among these patients three subgroups were identified (Table 2).

Table 2: Characteristics of patients with biliary sepsis

Patient groups	Traditional treatment	PA with IECO	PA with IECO and Ozone	Total	%
Biliary sepsis	13	14	13	40	75,5
Severe biliary sepsis	4	4	5	13	24,5
Total	17	18	18	53	100

In 17 patients (group I), along with preliminary decompression of the bile ducts, traditional treatment including infusion and antibiotic therapy was used; in 18 patients (group II) plasmapheresis was used in combination with indirect electrochemical oxygenation (IECO) of plasma with sodium hypochlorite; and in 18 patients (group III) IECO with additional ozonation of plasma (IECO and Ozone) and subsequent reinfusion of detoxified plasma. The criteria for detoxification of exfused plasma which makes possible its reinfusion was determined by Fedorovsky N.M. (2004) (Table 3).

Table 3: Criteria of exfused plasma detoxification

Plasma indices	Criteria for reinfusion
Level of PAMM (by Gabrielian)	<0.24 conv. Units
Hematocrit	<27 U/ml
Bilirubin	<32 mmol/L
Creatinine	<0.2 mmol/L
Urea	<8 mmol/L
The total concentration of albumin	> 35 g/L
The effective concentration of albumin	> 30g/L
The binding capacity of albumin	> 0.86
Reserve binding ability of albumin	> 10 g/L

With the purpose of developing a rehabilitation program for patients with cholangitis and evaluating the appropriateness of using extracorporeal detoxification methods, we set the goal to investigate the effect of plasmapheresis on the main biochemical and specific parameters of intoxication in patients with severe endotoxicosis in cholangitis.

Our proposed method of detoxifying the organism with cholemic endotoxicosis [9] (patent for invention UZ, No. IAP 04630), which involves the extraction of exfused plasma, the addition of sodium hypochlorite solution at a concentration of 1200 mg/L in a volume ratio of 10:1, maintaining the mixture at a temperature of 6-8° C· the precipitate aspiration removal and reinfusion autoplasma, characterized in that after adding the plasma sodium hypochlorite solution resulting mixture is ozonized by bubbling ozone-oxygen gas mixture for 10 minutes, after which the mixture is left for 3-4 hours (without exposure of O_3 plasma exposure time is an average of 8-12 hours. (RU 2033190 C).

4. Results & Discussion

Comparative evaluation of the laboratory parameters dynamics in the process of treatment in groups 2 and 3 did not reveal any significant differences. Hyperleukocytosis before operative treatment is noted in both groups. However, after surgical treatment in group 1 patients, the leukocytosis parameters are normalized only at the time of discharge, which indicates more pronounced purulent intoxication. At the same time, in patients of groups 2 and 3 there was a more rapid decrease and normalization of leukocytosis on the 5th postoperative day.

The initial increase of the leukocyte index of intoxication (LII), acute increase in the day of the operation takes place in all the study groups. In patients of Group 1 a significant decrease in this indicator was observed by 46.9% at the time of discharge. On the contrary, in patients of groups 2 and 3 there was a significant decrease in this indicator on day 6 (64.1%) and complete normalization at the time of discharge, which is associated with a more effective treatment of endotoxicosis.

Significant hyperbilirubinemia was noted in all patients. The highest rates of total and direct bilirubin followed by a slow decrease were found in the group 1. In contrast, patients in groups 2 and 3 showed a decrease in total bilirubin by 79.7% on the first and 85.4% on the third day after the operation, which led to a more rapid normalization of this indicator. A slow decrease in the level of bilirubin in group 1, despite decompression of the biliary tract, reflects the preservation of cholestasis and impaired hepatic cell function. Preliminary decompression and plasmapheresis in patients of groups 2 and 3 ensured rapid arrest (on day 3) of cholestasis, endotoxicosis, and liver dysfunction.

Patients in group 1 had high rates of creatininemia on the first day after surgery, which persisted for a long time, indicating liver failure in patients with severe endotoxicosis and cholestasis, which was aggravated by an operating trauma. In contrast, in patients in groups 2 and 3, creatinine chemistry remained within the normal range throughout the postoperative period, preliminary decompression and plasmapheresis contributed to the prevention of hepatic renal failure. The effectiveness of reducing the basic indices of endogenous intoxication of Groups 2 and 3 is shown in Table 4.

Table 4: Indicators of the effectiveness of the main indices of endogenous intoxication decrease

Indicators	On admission	After decompression	2 days after PA with IECO	2 days after PA with IRCO and Ozone
total protein, g/L	77,3±0,3	76,5±0,2	74,5±0,5	74,6±0,45
urea, mmol/L	16,3±0,8	14,1±0,6	7,2±0,3	7,1±0,3
creatinine, mmol/L	0,2±0,01	0,16±0,01	0,07±0,01	0,07±0,01
total bilirubin, mmol/L	218,2±16,4	197,4±9,8	39,3±2,7	38,1±2,5
alanine aminotransferase	0,96±0,04	0.85±0,03	0,09±0,05	0,09±0,04
aspartate minotransferase	1,5±0,05	1,3±0,06	0,2±0,08	0,19±0,09
molecules of medium mass, cond. units	0,85±0,09	0,73±0,08	0,40±0,05	0,39±0,04
total concentration of albumin, g/L	38,7±1,4	37,9±1,1	36,3±2,0	36,4±2,1
effective albumin concentration, g/L	18,3±0,5	19,7±0,6	35,2±0,5	35,1±0,5
binding ability of albumin, cond. units	0,46±0,03	0,53±0,04	0,9±0,07	0.9±0,08
leukocyte index of intoxication	3,7±0,01	3,2±0,02	2,8±0,02	2,7±0,03

As it can be seen from the Table 4 the combination of PA and IECO with additional plasma and ozone treatment more efficient in many ways, except that an additional effect by the ozone reduced exposure time from 4-16 (average 8-12 h.) to 3-4 hours. The reliability of the data was checked using t-criteria Student P = 0.05 in relation to the initial indicators.

Comparative analysis of laboratory parameters established their normalization in patients of the groups 2 and 3 on the 5th-6th day, which corresponds to the optimal timing of the operation.

The greatest number of complications occurred in patients of the 1st group (17.7%), in patients of the 2nd and 3rd groups - 9.7% and 8.1%, respectively. The most frequent of them - suppuration of the postoperative wound, acute hepatic-renal failure, cholemic bleeding and peritonitis.

There was a higher postoperative mortality in Group 1 (6.4%), which was 2 times higher than in the 2nd and 3rd groups of patients (3.2%). The main cause of death was acute hepatic-renal failure, angiocholitis, and sepsis. In the 2nd and 3rd groups the severest patients with purulent obstructive cholangitis died. Preliminary decompression and sanation of the biliary tract with plasmapheresis in these patients led to a

reduction in lethal outcomes and duration of hospitalization on average by 5-9 days.

In patients with severe endogenous intoxication, in the postoperative period the most severe endotoxicosis and multiple organ failure were preserved in patients of the 1st group. On the contrary, in patients of groups 2 and 3 the best results of surgical treatment were noted due to the developed medical diagnostic algorithm. Thus, the differentiated treatment and diagnostic tactics for acute cholangitis complicated by biliary sepsis using the 3-stage method of decompression, plasmapheresis and sanation of the bile ducts is the most rational for this category of patients which is confirmed by a significant reduction in the number of complications, a decrease in postoperative mortality, recovery.

5. Conclusions

The most informative instrumental and laboratory methods which allow to establish the diagnosis and severity of purulent cholangitis at the early stage are: echography of hepatopancreatoduodenal region in dynamics and ERCP, bilirubin, creatinine levels, leukocytosis, indices of intoxication.

The most severe degree of endogenous intoxication was detected in patients who underwent operative intervention without plasmapheresis sessions, which was accompanied by high lethality (6.4%). Preliminary minimally invasive decompression, a course of detoxification therapy including plasmapheresis can reduce postoperative lethality by 4 times, the number of complications - by 2 times, and accelerate the clinical recovery of patients.

The developed differential surgical tactic with the implementation of minimally invasive decompression and the use of plasmapheresis allows to decrease the phenomenon of endotoxicosis, cholestasis and liver dysfunction and thereby improve the results of treatment.

The proposed method of plasmapheresis is a highly effective method of preoperative preparation of patients with severe degree of cholemic endotoxicosis, which helps stabilize cytolytic activity (lowering of alanine aminotransferase and aspartate aminotransferase) and cholestatic (lowering of bilirubin) process, which improves protein-synthetic liver function, allows to eliminate the main clinical manifestations in severe patients and thereby significantly expand the indications to surgical treatment.

Regeneration of the plasma exfused with plasmapheresis during 3-4 hours with a solution of sodium hypochlorite and additional ozonization provides a reduction in its toxicity and makes it suitable for reinfusion in the patient's organism. The proposed improved plasmapheresis with reinfusion of extracorporally modified autoplasma allows to reduce the need for donor protein preparations, reducing the risk of possible immune reactions, the risk of infection of the patient with hepatitis B and C viruses, human immunodeficiency virus, cytomegalovirus, herpes virus.

6. References

1. Davlatov SS *et al.* Plasmopheresis in the treatment of cholemic endotoxicosis // Академический журнал Западной Сибири. 2013; 9(1):30-31.
2. Kantola T, Koivusalo AM, Hockerstedt K, Isoniemi H. The effect of molecular adsorbent recirculating system treatment on survival, native liver recovery, and need for liver transplantation in acute liver failure patients. Transpl Int., 2008; 21:857-866.
3. Kasimov S, Abdurakhmanov Z, Davlatov S, Aripova J. Haemosorption In Complex Management Of Hepatargia. The International Journal of Artificial Organs. 2013; 36(8):548.
4. Patzer JF. 2nd Thermodynamic considerations in solid adsorption of bound solutes for patient support in liver failure. Artif Organs, 2008, 499-508.
5. Багненко СФ, Шляпников СА, Корольков АЮ. Современные подходы к этиологии, патогенезу и лечению холангита и билиарного сепсиса // Бюллетень сибирской медицины, 2007; 3:27-32.
6. Давлатов СС. Новый метод детоксикации плазмы путем плазмафереза в лечении холемического эндотоксикоза //Бюллетень Северного Государственного медицинского университета. 2013(1):6-7.
7. Даценко БМ, Борисенко ВБ. Механическая желтуха, острый холангит, билиарный сепсис: их патогенетическая взаимосвязь и принципы дифференциальной диагностики //Новости хирургии, 2013; 21:5.
8. Иоффе ИВ, Потеряхин ВП, Плазмаферез в комплексном лечении механических желтух, обусловленных холедохолитиазом // Украинский журнал экстремальной медицины имени Г.О. Можаева, 2009; 10(1):122-125.
9. Курбаниязов ЗБ, Давлатов СС. Способ детоксикации организма при холемическом эндотоксикозе //UZ Официальный бюллетень. 2011(5):10-11.
10. Корольков АЮ. Острый холангит и билиарный сепсис патогенез, диагностика, профилактика и лечение: дис. – автореф. дис. на соискание учёной степени доктора мед. наук: спец. 14.00. 27 Хирургия/АЮ Корольков, 2009.
11. Шаповальянц СГ. и др. Эндоскопические методы в лечении рубцовых послеоперационных стриктур желчевыводящих протоков. // Анналы хирургической гепатологии, 2007; 2:70-77.