OCCURRENCE AND COURSE OF HYPERSPLENISM IN PATIENTS WITH CIRRHOSIS OF THE LIVER

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Resume. Diffuse liver disease (DLD) is a lesion of an organ, the morphological substrate of which is necrosis of hepatocytes, fibrosis and further transformation into cirrhosis. Cirrhosis of the liver is characterized by a violation of its lobular structure as a result of progressive fibrosis and the formation of regeneration nodes. In economically developed countries, cirrhosis of the liver is among the six main causes of death of patients aged 35 to 60 years, accounting for 14-30 cases per 100 thousand population. In the USA, mortality from cirrhosis of the liver is 9.1 cases per 100 thousand population. In Russia, due to the increase in the number of patients with viral and metabolic liver lesions, the number of patients with cirrhosis has increased significantly and reaches 14 cases per 100 thousand population. Cirrhotic transformation of liver tissue will irreversibly lead to the development of complications contributing to early disability, disability and death of patients with cirrhosis. In Russia, 47.2 thousand people die from complications of this disease, which is 2% of patients per year.

Keywords: Diffuse liver diseases, liver cirrhosis, liver cirrhosis, hepatocyte, regeneration, decompensation.

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ВСТРЕЧАЕМОСТЬ И ТЕЧЕНИЕ ГИПЕРСПЛЕНИЗМА У БОЛЬНЫХ С ЦИРРОЗОМ ПЕЧЕНИ

Резюме. Диффузные заболевания печени (ДЗП) -это поражение органа, морфологическим субстратом которого является некроз гепатоцитов, фиброз и дальнейшая трансформация в цирроз. Цирроз печени характеризуется нарушением ее долькового строения в результате прогрессирующего фиброза и образования узлов регенерации. В экономически развитых странах цирроз печени входит в число шести основных причин смерти пациентов от 35 до 60 лет, составляя 14-30 случаев на 100 тыс. населения. В США смертность от цирроза печени составляет 9,1 случаев на 100 тыс. населения. В России в связи с ростом количества больных с вирусными и метаболическими поражениями печени количество больных циррозом существенно увеличилось и достигает 14 случаев на 100 тыс. населения. Цирротическая трансформация печеночной ткани необратимо введет к развитию осложнений, способствующих ранней инвалидизации, нетрудоспособности и смерти больных циррозом. В России от осложнений данного заболевания умирает 47,2 тыс., что составляет 2% больных в год.

Ключевые слова: Диффузные заболевания печени, цирроз печени, Цирроз печени, гепатоцит, регенерации, декомпенсации.

Relevance. The problem of treating patients with cirrhosis of the liver remains urgent and unresolved. Cirrhosis of the liver (CP) is an inflammatory process of hepatic tissue characterized by the death of hepatocytes and the proliferation of connective tissue, the formation of fibrosis and regeneration nodes, which progresses, despite the cessation of etiological factors, the number of patients with

cirrhosis of the liver is constantly increasing. The incidence is currently 20-40 cases per 100 thousand population and is continuously growing. According to WHO, in 2007, chronic liver diseases were the cause of 1.382 million deaths worldwide, including 772 thousand cases of cirrhosis of the liver. In the compensation stage, patients with cirrhosis of the liver have a five–year survival rate of 50-62%, in the decompensation stage - 11-40%, organ transplantation is a radical method of treating patients with cirrhosis of the liver. The five-year survival rate after liver transplantation is 80-85%. However, the complexity of the operation, lifelong immunosuppressive therapy, severe complications of the postoperative period, the high cost of the method, strict selection of patients and recipients, lack of donor organs do not allow this method of treatment to be widely used. It should be noted that surgical interventions in patients with cirrhosis of the liver aimed at reducing portal hypertension (TIPS, bypass and devascularization operations, ligation of varicose veins of the esophagus, etc.), organ transplantation are accompanied by a high risk of complications and mortality. Operational mortality in cirrhosis of the liver of class A according to Child-Pugh is 10%, in group B - 31%, in group C - 76%. It is known that the liver has the ability for reparative regeneration, which is not equal in any organ. The mechanisms of the relationship between regenerative processes and resorption of scar tissue in the liver have not yet been fully studied. This continues to attract the attention of researchers to the search for the most effective and low-traumatic methods of stimulating physiologically balanced regeneration of the organ, which will contribute to leveling the adverse manifestations of cirrhotic liver damage and related portal hypertension phenomena. Experiments accumulated on animals by numerous researchers prove the effectiveness of local exposure to drugs, blood components, and thermal effects on stimulating the regeneration of a cirrhotically altered liver. In patients with cirrhosis of the liver, diathermocoagulation of the liver surface, the introduction of fetal cells and an alloplant into the liver tissue, stem cells into the portal system are used. Restoration of the liver structure and clinical and laboratory parameters, after carrying out these methods, the authors note in 3-5 years in patients with

compensated cirrhosis of the liver of class A and B according to Child-Pugh. For patients in the decompensation stage (class C according to Child-Pugh), with disorders in the homeostasis system (hypocoagulation, thrombocytopenia) that prevent surgical interventions, the authors conduct basic therapy.

Most of these invasive methods of stimulating regeneration are quite traumatic for a cirrhotically altered liver, and their stimulating effect is short-term. It is believed that the stimulators of regeneration are substances formed at the time of death of liver cells at the site of one of the types of surgical or thermal effects

The advantages of minimally invasive operations under ultrasound control are obvious. These methods are cost-effective, widely available, and do not require the use of endotracheal anesthesia, since the intervention is performed under local anesthesia or intravenous anesthesia. Ultrasound examination during surgery allows you to study in detail the structure, vascular pattern of the liver, the system of portal veins, to determine the safe path to the affected area of the organ. The failure of conservative therapy, the difficulties of surgical treatment due to hypocoagulation and severe thrombocytopenia, the lack of radical methods of treating patients with cirrhosis of the liver, especially in the decompensation stage (class C to Child-Pugh), were the reason for the use of minimally invasive methods under the control of ultrasound for the introduction of drugs into the liver tissue. Biologically active substances containing a set of growth factors, in particular a highly concentrated fibrinogen solution - cryoprecipitate and alloplant, turned out to be promising stimulators of cirrhotic liver regeneration. In the experiment and in the clinic, it was proved that the application of cryoprecipitate to a traumatically damaged liver can reduce the activity of the inflammatory process in the organ, stimulate the regeneration of hepatocytes without the proliferation of connective tissue.

Objective: to improve the results of treatment of patients with cirrhosis of the liver using minimally invasive surgical interventions under the control of ultrasound.

Materials and methods of research. The composition of the cryoprecipitate includes fibrinogen 68.8±5.4 g /l, fibrin-stabilizing factor FXIII 34.2±2.7 units /ml, fibronectin 16.5±1.4 g/ l, plasminogen 0.78±0.2 g / l, and an immunostimulating

complex (C3, C4 complement component, immunoregulatory cytokine IL 2, proinflammatory cytokines IL 6, IL1, IL 8, IL 4, spont. interferon, α1 – protease inhibitor, circulating immune complexes, α2 macro and β2 microglobulins) [115,117]. The resulting cryoprecipitate was tested in accordance with the current regulations: by the total amount of protein, fibrinogen, purity of the drug, sterility, apyrogenicity, nontoxicity. The cryoprecipitate was harvested and stored in accordance with the regulations, the concentration of coagulating protein was determined in the stored preparation for up to 21 days. For use, the cryoprecipitate was thawed in a standard way, taking into account the volume of the drug, for 3-5 minutes and typed into a syringe. It was injected percutaneously with a 25 Gauge needle under ultrasound control into all segments of the liver for 1-2 ml. In order to prevent bleeding from the puncture canal after the introduction of cryoprecipitate when removing the needle from the liver, we injected thrombin 600-800 IU dissolved in 5 ml of 10% calcium chloride solution into it.

The results of the study. The results of clinical and laboratory studies were studied before and after minimally invasive injection of cryoprecipitate into liver tissue in 72 patients with cirrhosis of class A, B and C by Child-Pugh. 13 (18%) had cirrhosis of class A, 19 (26%) - class B, 40 (56%) - class C according to Child-Pugh. Prior to admission to our hospital, 55 (out of 72) patients suffered from cirrhosis of the liver for a long time (more than 7-10 years), they repeatedly underwent inpatient treatment and were under the supervision of hepatologists, gastroenterologists and infectious diseases specialists. In 22 (out of 72) patients with cirrhosis of the liver there was a single, in 8 - repeated bleeding from varicose veins of the esophagus and stomach, in 8 - hepatic coma. Prior to admission to our clinic, 42 (out of 72) patients were in other hospitals in a decompensated state due to bleeding from varicose veins of the esophagus and stomach, hepatic-renal insufficiency, encephalopathy, anemia, thrombocytopenia on the background of hypersplenism. Conservative therapy, including hepatoprotectors, hemostatics, drugs that reduce portal hypertension, antiviral treatment (for viral etiology of cirrhosis) was ineffective, and these patients were transferred to our hospital to stimulate liver regeneration. the introduction of

cryoprecipitate into the liver revealed positive changes in clinical and laboratory data in a significant ($p<0.05$) number of patients with cirrhosis, compared with the results before treatment. Asthenic syndrome was absent in 58 (81%) patients, jaundice - in 47 (65%), edematous ascitic syndrome - in 41 (58%), encephalopathy - in 14 (19%), dyspepsia - in 17 (23%). Hemorrhagic syndrome became less pronounced in an insignificant (2 out of 72) number of patients. Improvement of clinical manifestations of the disease was accompanied by compensation or absence of violations of laboratory parameters. Indicators of hepatic cell insufficiency decreased to normal in 41 (56%) patients due to an increase in albumin and protein. Cytolysis decreased in 18 (25%) patients due to a decrease in AsAt. Cholestatic syndrome was absent in a significant ($p<0.05$) number of patients: due to a decrease in bilirubin - in 49 (68%), GGTP - in 30 (42%), SCHF in 19 (27%). Anemia was compensated in 23 (32%), hypersplenism decreased in 27 (37%) patients, due to an increase in the number of platelets and normalization of leukocytes.

6 months after the introduction of cryoprecipitate into the cirrhotically altered liver, the majority of patients maintained positive dynamics of clinical and laboratory parameters. In a significant ($p<0.05$) number of patients, compared with the results before and 3 months after the introduction of cryoprecipitate, cytolysis decreased due to a decrease in AsAT in 34 (48%) and AlAT in 22 (31%) patients. However, their average values were 2 times higher than normal, which corresponds to the preservation of regeneration of the hepatic parenchyma. Cholestasis decreased due to a decrease in GTPP in 51 (71%) patients (Table 7). 29 (40%) patients had no hepatic encephalopathy, 65 (54%) had small hepatic signs compared to the results before treatment.

12 months after the introduction of cryoprecipitate into the cirrhotically altered liver, the majority of patients maintained positive dynamics of clinical and laboratory parameters compared with the results before treatment and 3 and 6 months after stimulation of parenchymal regeneration. Clinical manifestations of the disease (asthenic syndrome, jaundice, edematous ascitic syndrome, dyspepsia, encephalopathy, small hepatic signs), which were present before treatment in most

patients, 3, 6 and 12 months after the introduction of cryoprecipitate into the cirrhotic liver, were absent in a significant ($p<0.05$) number of patients.

Examining the clinical and laboratory parameters of 72 patients with cirrhosis before and after after the introduction of cryoprecipitate into the liver, there was a significant improvement after 3 months and the preservation of these parameters for the next 9 months: in 13 (18%) - class A, in 19 (26%) - class B, in 24 (33%) - class C to Child-Pugh. In 9 (13%) patients of Child-Pugh class C, in the decompensation stage, these indicators did not significantly improve. The remaining 7 (9%) patients in the decompensation stage (grade C to Child-Pugh 15-16 points) we observed a negative trend: 4 patients had hepatic cell insufficiency, which was compensated by conservative measures. In 3 out of 7 patients, the parameters of portal blood flow increased, this required the appointment of conservative therapy, which reduced these changes in 2 patients. One (out of 3) patient had bleeding from varicose veins of the esophagus, which was stopped by conservative measures. Complications and deaths during and after the introduction of cryoprecipitate into the liver, despite the thrombocytopenia present in 33% (out of 72) patients, we did not observe.

Conclusions.

1. Cryoprecipitate stimulates the orderly regeneration of a cirrhotically altered liver, contributing to the formation of parenchymal areas with the correct beam arrangement of hepatocytes and the formation of sinusoids, improving the functional activity of the organ and reducing portal hypertension, which has been proven in experiment and clinic.

2. Morphological changes occurring under the influence of cryoprecipitate injected by minimally invasive surgical method into the liver tissue are the basis for improving clinical, laboratory, immunological data, including a decrease in the functional class of cirrhosis (according to Child-Pugh).

3. The developed minimally invasive surgical method of introducing cryoprecipitate together with thrombin into the liver under ultrasound control is a safe method of treating patients with cirrhosis at the stage of compensation and decompensation with hypocoagulation and thrombocytopenia

4. Improvement of blood circulation in hepatic tissue under the influence of cryoprecipitate reduces portal hypertension and the risk of bleeding from varicose veins of the esophagus and stomach in patients with cirrhosis.

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