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PREVALENCE OF CHRONIC LIVER DISEASES AND THROMBOHEMORRHAGIC COMPLICATIONS (LITERATURE REVIEW).

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Abstract:

The literature review provides data on the pathology, etiology of diffuse hepatitis, the role of diffuse liver damage in the development of diffuse liver damage, hemorrhagic complications and the mechanisms of the disease. A qualitative analysis of the number of hemostasiological tests, which are widely used in general practice and are essential in the diagnosis of diseases in patients with chronic diffuse liver diseases, was carried out.

Keywords: Hepatotropic viruses, hepatitis, liver cirrhosis, hemostasis.

Many pathogenetic aspects of pathogenetic disorders in chronic liver diseases remain unexplored [15, 26, 30]. One of the most common causes of chronic hepatitis and liver cirrhosis is infection with hepatitis B and C [17, 27, 28, 29]. At the same time, more than 180 hepatotoxic drugs have been identified, of which 6 groups seriously injure the liver. For example, 50% of drugs are hepatotoxic, especially in women this effect is more pronounced. Medicines cause hepatocellular damage, even liver necrosis, which is clinically manifested mainly by jaundice, fever, and increased liver enzymes [8]. Timely diagnosis of chronic hepatitis and liver cirrhosis and appropriate will reduce the risk of many complications [16, 24, 25].

Chronic diffuse liver diseases are one of the urgent problems of modern medicine and occupy one of the leading places among gastrointestinal diseases. The incidence of chronic hepatitis and liver cirrhosis is increasing worldwide. Over the past decades, the incidence of liver cirrhosis has been consistently high, and patients with chronic diffuse liver diseases in specialized hospitals account for 30% of the total number of patients. The consequences of the disease lead to long-term incapacity for work, disability and increased mortality of each patient [22].

The clinical manifestations of cirrhosis of the liver are different, because they affect almost all systems of the body. The main symptoms of the disease are the presence of pertension in the system of portal vessels and liver-cell failure. The main causes of death in liver cirrhosis are hepatic coma (40-60%) and bleeding from the upper parts of the gastrointestinal system (20-40%). Liver cancer, intercurrent infections and hepatorenal syndrome are almost rare. Timely detection of this pathology allows to significantly increase the life expectancy of such patients and improve the quality of life [9].

According to the 2017 World Health Organization (WHO), viral hepatitis is common, but the western Pacific region has the highest incidence of hepatitis B at 6.2% (115 million). Hepatitis virus infection is 6.1% (60 million) in African countries, 3.3% (21 million) in Eastern Mediterranean countries, 2% (39 million) in Southeast Asia, 1.6% (15 million), in American countries it is 0.7% (7 million). According to the data published by WHO, chronic diffuse liver diseases continue to increase, affecting more than 2 billion people in the world. Those infected with hepatitis C virus are 2.3% of the population (15 million) in the Western Pacific region, 1.5% (14 million) in European countries, 1% (11 million) in African regions, 1% (7 million.) and 0.5% (10 million) in Southeast Asian regions [22].

Over the past few years, chronic hepatitis B has been reported in Russia at 14-16 cases per 100,000 population, and chronic hepatitis C at 11 cases per 100,000 population. In Russia, cirrhosis of the liver is the 6th leading cause of annual death from ischemic heart disease, trauma and accidents, as well as cancer, i.e. 47,200 (2%) deaths. Most of the patients die in the fifth or sixth decade of life, that is, in the working age[21].

The incidence rate of viral hepatitis in the Republic of Uzbekistan is rapidly decreasing. In 2014, compared to 1990, the incidence of viral hepatitis decreased by 7.1 times, that is, from 882.0 cases to 123.5 cases per 100,000 population. In 2014, compared to 2009, the incidence of viral hepatitis decreased by 18.6%. At the same time, non-jaundic forms are 10-15 times more common, and the number of relapses is very rare after viral hepatitis[23].

Issues of pathogenesis, diagnosis and correction of the hemostasis system are increasingly attracting the attention of specialists in various fields of medicine. The liver plays an important role in maintaining hemostasis, which is very important for doctors dealing with liver pathology in their practice. Blood coagulation factors, anticoagulant proteins, components of the fibrinolysis system, and thrombocytopoiesis stimulators are synthesized by hepatocytes, so diffuse changes in its parenchyma lead to complex disorders of blood coagulation. The liver plays a key role in the process of blood clotting, because liver pathology leads to a functional deficiency of hepatocytes, which synthesize all factors of

hemostasis. Damage to hepatocytes leads to the development of chronic hepatitis or liver cirrhosis, which determines the severity and duration of the disease. It is known that only 10-15% of hepatocytes can provide a normal level of blood clotting factors for the functioning of the coagulation system. To evaluate the coagulation and anticoagulation systems, it is necessary to study all aspects of hemostasis. The processes occurring in the body are in constant dynamic balance, and liver diseases lead to a violation of balance and homeostasis. Changes in hemostasis in end-stage liver disease have a significant impact on the risk of bleeding complications [11].

Hypocoagulation, hypercoagulation, and hyperfibrinolysis are often observed in patients with liver failure. In addition, the reticuloendothelial system reduces the activated forms of hemostatic factors. Liver dysfunction in acute and chronic diseases leads to changes in the blood coagulation system and is manifested by bleeding or thrombosis. Bleeding is the most common complication of liver cirrhosis due to synthesis of coagulation factors, activation of fibrinolysis, thrombocytopenia and thrombocytopathy. Appearance of hemorrhagic features such as skin hemorrhage, bleeding from the nose, gums, intestines, uterus and other places indicates the imbalance of the coagulation system in chronic hepatitis and liver cirrhosis. Bleeding from the gastrointestinal tract significantly worsens the prognosis and course of the disease [5].

The main causes of hemorrhagic symptoms are: a decrease in platelets, an international standardized ratio (INR), a decrease in prothrombin time (PV) and activated partial thromboplastin time (AQTV), a violation of the number and function of platelets, a decrease in the level of coagulation factors (II, V, VII, IX , X, XI), decreased fibrinogen content, vitamin K deficiency, decreased thrombin and fibrinolysis inhibitors [2].

However, in patients with cirrhosis of the liver, as platelets change, coagulation disorders can cause bleeding or clotting disorders. Standard coagulation tests, including PV and AQTV, are designed to monitor therapy because they do not detect levels of anticoagulant proteins, but is designed to measure the early stages of thrombin generation and initial clot formation. Bleeding from esophageal and gastric varices is the most dangerous and frequent complication of portal hypertension. At the first bleeding from dilated vessels of the esophagus, mortality is observed in 50-70% [10], and at the stage of decompensation this indicator reaches 76-80% [5].

Bleeding is repeated in 28-70% of cases during the year and in 80-90% of cases in two years, so all such patients need mandatory preventive treatment. Determining the risk of bleeding does not depend on the age and gender of patients, but on the degree of liver decompensation. Recurrence of gastroesophageal bleeding due to portal hypertension (PG) in patients with cirrhosis of the liver is one of the complex problems of modern medicine. Recurrent bleeding leads to conservative treatment in every third patient, and blood loss causes anemia and increases decompensation of liver function. If portal hypertension is not treated, the average life expectancy of patients with liver cirrhosis does not exceed 19 months [1].

A 5-year retrospective analysis by scientists from Sweden's Karolinska University showed that preventive and conservative treatment of acute bleeding in patients complicated by bleeding from varicose veins using various methods increased their survival from 31% to 49%. It is known that the microcirculation system and connective tissue are the first to respond when affected by various pathological factors. In this case, the endothelium, which is the main component of the microcirculation system, regulates vascular permeability, controls hemostasis, performs transport and barrier functions, modulates inflammatory processes, and ensures the metabolism of the extracellular matrix [6].

According to a number of authors, the presence of gene mutations in the endothelium worsens the prognosis of chronic hepatitis C, increases renin-angiotensin system dysfunction and inflammation. These scientists assumed the contribution of allelic polymorphism of blood clotting genes, genes responsible for platelet receptors, but the available literature is very conflicting. Manifestations of chronic hepatitis C infection can lead to the development of cryoglobulinemia, however, the role of hemostasis and platelet receptor allele genes in the formation of cryoglobulinvasculitis associated with chronic viral hepatitis has not been sufficiently studied [10].

Cirrhosis of the liver is often accompanied by hypersplenism, which is the main cause of secondary thrombocytopenia and hemorrhagic syndrome. However, in patients with liver cirrhosis, the decrease in the level of fibrinolysis inhibitors leads to increased fibrinolysis and may be another factor in bleeding [19].

Assessment of fibrinolysis in patients with chronic viral liver pathologies is expressed by the level of tissue plasminogen activator and plasminogen inhibitor. Although some studies show an increase in fibrinolysis, other scientists show that the level of fibrinolytic inhibitors and the decrease in the level of fibrinolytic factors are in balance, and there are no significant changes in the fibrinolysis system in patients with liver cirrhosis. Since the level of blood coagulation disorders and the increase in fibrinolytic activity correspond to the severity of liver cirrhosis, the treatment of bleeding in patients with liver cirrhosis should not only regulate blood coagulation changes, but also reduce fibrinolytic activity [4].

Although blood coagulation tests may change in the direction of hypocoagulation in patients with cirrhosis of the liver, it is incorrect to assume that these patients do not coagulate at all. On the other hand, there are many opinions about the frequent tendency of patients with liver pathology to hypercoagulation and thrombosis. At the same time, despite increased fibrinolysis, currently there is a lot of information in the literature about normal or increased blood coagulation in patients with liver cirrhosis. In patients with cirrhosis of the liver, thrombocytopenia and high levels of PV, AQTV, and MNOs in the blood may cause blood clotting [14].

The occurrence of bleeding or thrombosis in patients with liver cirrhosis depends on the degree of balance between the coagulant and anticoagulant systems. The cause of thrombosis is an increase in factor VIII and von Willebrand, a

decrease in protein C, protein C, antithrombin III, and plasminogen. In patients with liver cirrhosis, venous thrombosis is treated using routine anticoagulant heparin and vitamin K therapy, but this can cause high-grade bleeding[18].

Some authors' studies show that the hemostatic system is in balance in patients with cirrhosis of the liver, because the decrease in procoagulant proteins is accompanied by a decrease in the level of anticoagulant proteins. Despite the many disturbances of various components of hemostasis, the hemostatic balance is maintained for a long time even when the liver is severely damaged. Anticoagulant therapy is considered safe for the treatment of portal vein thrombosis in patients with cirrhosis. Currently, an optimal algorithm for the prevention and treatment of thrombosis in patients with liver cirrhosis has not been developed. In patients with liver cirrhosis and acute renal failure, a single dose of antithrombin may be an alternative to continuous prophylactic doses of heparin during long-term renal replacement therapy [5].

At the same time, the use of anticoagulant therapy remains an urgent problem in patients with portal vein thrombosis. In patients with cirrhosis of the liver, anticoagulant therapy is carried out together with the prevention of the consequences of portal hypertension and varicose veins [13]. Anticoagulant administration in patients with liver cirrhosis is associated with increased risk of bleeding, mainly due to portal hypertension [3]. Therefore, when prescribing anticoagulants, it is necessary to take into account the risk of possible complications of anticoagulant therapy in this patient [2].

Patients with end-stage liver disease are thought to be at increased risk of bleeding during any invasive procedure (any surgery, including transplantation or minimally invasive procedures). Invasive procedures, bleeding or thrombosis lead to poor results. Studying indicators of blood coagulation factors (prothrombin index, fibrinogen concentration, etc.), factors such as a significant decrease in platelets and erythrocytes are the cause of the prevalence of thrombosis or bleeding. In the final stage of liver disease, patients often study the pathology of parameters used to analyze coagulation hemostasis. However, if there are no obvious signsof bleeding, treatment with coagulants is not required. In cases of excessive fluid retention and increased portal venous pressure, transfusion of blood components should be avoided, and coagulation factor concentrates should be used to restore blood coagulation [20].

Indications and contraindications of surgery include assessment of the functional state of the liver, determination of prognostic factors such as the state of the hemostasis system before surgery. The study of these factors is an integral part of preparation for surgical treatment of portal hypertension. However, the issue of determining the degree of hepatocellular dysfunction, the characteristics of hemostasis system disorders in liver cirrhosis has not yet been resolved and appears as an actual problem of hepatological surgery [12].

Despite the measures to combat viral hepatitis and cirrhosis of the liver, it is necessary to improve measures aimed at early detection, diagnosis, differential diagnosis, treatment of patients with chronic hepatitis and liver cirrhosis and their complications. Thus, the excessive complexity of the optimal methods of treatment and prevention of hemorrhagic syndrome in patients with liver cirrhosis, the study of the results of surgical interventions shows that this problem is very relevant [7].

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