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Research Progress in the Diagnosis and Treatment of Liver Cirrhosis

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Abstract

Liver cirrhosis is caused by one or more reasons. It is a progressive chronic liver disease characterized by diffuse fibrosis, pseudolobule and regenerative nodule of liver tissue. It can lead to severe complications such as upper gastrointestinal hemorrhage, hepatic encephalopathy, secondary infection, canceration and so on, which seriously affects people's health and life. Treatment and reversion of liver fibrosis has always been the goal of scholars all over the world. This paper summarizes many related literature and research in recent years, and reviews the clinical causes and treatment of liver cirrhosis, so as to open up a new way for the treatment of patients with liver cirrhosis.

Keywords

Cirrhosis, Pathogenesis, Treatment, Review.

1. INTRODUCTION

Liver cirrhosis is a clinically common chronic progressive liver disease, which is caused by one or more causes of long-term or repeated effects of diffuse liver damage. Histopathologically, there are extensive hepatocyte necrosis, residual hepatocyte nodular regeneration, connective tissue hyperplasia and fibrous septal formation, leading to structural destruction of the hepatic lobule and formation of pseudolobules. The liver gradually deforms and hardens and develops into cirrhosis [1]. In the early stage, due to the strong liver compensatory function, there were no obvious symptoms. In the later stage, liver function damage and portal hypertension were the main manifestations, accompanied by multiple system involvement. In the advanced stage, a lot of Complications such as upper gastrointestinal bleeding, hepatic encephalopathy, secondary infection, hypersplenism, ascites, and cancer often occurred, which have seriously affected the health and life of patients and have become a global public health problem. This article reviews the pathogenesis and treatment of liver cirrhosis, summarized as follows:

2. THE CAUSE OF CIRRHOSIS

Liver cirrhosis is often further developed from chronic liver diseases including hepatitis virus, ethanol, drugs and poisons, parasites, metabolism and heredity, cholestasis, immune abnormalities and other diseases caused by various liver diseases with a course of more than half a year. Due to long-term cause stimulation, abnormal metabolism and immune inflammatory reaction, liver parenchymal cells can be damaged and liver fibrosis can be initiated [2].Therefore, the common causes of cirrhosis are similar to those of chronic liver disease, which usually include: HBV and HCV infection; alcoholic liver disease; nonalcoholic

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fatty liver disease; autoimmune liver disease, including primary biliary cirrhosis, autoimmunity Hepatitis and primary sclerosing cholangitis; genetic and metabolic diseases, including hepatolenticular degeneration, hemochromatosis, hepatic amyloidosis, hereditary hyperbilirubinemia, alpha-1 antitrypsin deficiency Disease, hepatic porphyria, etc.; drugs or chemical poisons; parasitic infections, mainly schistosomiasis, clonorchiasis, etc.; caused by circulatory disorders, common with Budd-Chiari syndrome and right heart failure; liver cirrhosis with unclear etiology [3].

Most cirrhosis has only one cause, and it can also have multiple causes at the same time, such as overlapping infections of hepatitis B virus (HBV) and hepatitis C virus (HCV); long-term heavy drinking in patients with hepatitis B or hepatitis C.In addition, based on the main causes, some synergistic factors can promote the development of cirrhosis, such as obesity, insulin resistance, certain drugs.

3. THE PATHOLOGICAL MECHANISM OF CIRRHOSIS

Among the cells involved in the process of liver fibrosis, activated hepatic stellate cells (HSCs) are key cells for the formation of fibrous tissue. Different causes of stimulation can cause chronic liver damage, liver cells undergo apoptosis, necrosis or necrotic apoptosis, leading to inflammation of the liver [4]. Hepatocytes, Kupffer cells, liver sinusoidal endothelial cells, and lymphocytes can stimulate quiescent HSCs located in the disse space by releasing cell contents, cytokines, and reactive oxygen species, and activate them into myofibroblasts. , produces a large amount of extracellular matrix (ECM), forming fibrous septum and capillarization of hepatic sinuses, , resulting in liver fibrosis, accompanied by vascular proliferation in the fibrous septum. [5] After the body is infected with schistosomiasis, hepatic fibrosis occurs after the granuloma is formed at the entrance of the hepatic sinus with the blood epidemic. Hepatic sinus capillary vascularization, myofibroblastic contraction and parasite egg granuloma can cause hepatic sinus stenosis and increased blood flow resistance, which is an important pathological basis for portal hypertension. Sinusoidal microcirculatory disorder delays the recruitment of anti-viral T lymphocytes, thereby delaying the clearance of the virus, and ultimately aggravating the tissue damage caused by the T lymphocytes that are continuously activated by the antigen, which is one of the causes of chronic hepatitis prolonged [6]. . Lymphocytes can activate HSC or promote apoptosis, and play a role in the formation and regression of liver fibrosis [7, 8]. The activation of free radicals in chronic liver injury leads to decreased oxidative stress and anti-peroxidation defense mechanisms in the liver, and is involved in the development of tissue remodeling and liver fibrosis, especially in alcoholic hepatitis and nonalcoholic steatohepatitis. The intrahepatic profibrotic microenvironment has received attention in recent years, and it can attract some subtypes of lymphocytes, especially macrophages, to regulate the formation or digestion of liver fibrosis. In addition, intestinal microbial action, tissue hypoxia, anaerobic pro-inflammatory environment, acquired modification of liver fibrosis progression and tissue stiffness during liver fibrosis development also affect the progression of liver fibrosis [2].

4. TREATMENT OF CIRRHOSIS

4.1. Etiological Treatment

Etiological treatment is the key to the treatment of cirrhosis. As long as there is a controllable cause, etiological treatment should be started as soon as possible. The treatment strategy should aim at multiple inhibitions in the formation and development of liver fibrosis, including treatment of primary disease or removal of pathogenic factors, such as long-term effective inhibition of hepatitis virus replication, alcohol withdrawal, etc., can reduce sustained liver damage, thereby promoting fibrosis Repair of liver tissue. Chronic inflammatory response is the premise of fibrosis formation. Inhibiting inflammation and promoting liver damage repair are

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important measures against liver fibrosis [9]. Inhibiting the formation and deposition of ECM in the liver and promoting its degradation is a key strategy for the treatment of liver fibrosis. Effective inhibition of HBV replication or clearance of HCV can significantly improve the degree of liver fibrosis in patients with hepatitis B or C, and some patients can achieve liver reversal of fibrosis [10]. Other studies have found that removing the cause (especially alcohol intake, HBV or HCV infection) can reduce the risk of decompensation complications in patients with cirrhosis and improve the survival rate of patients. To this end, patients with decompensated cirrhosis need to abstain from alcohol in the first time and control hepatitis B virus and hepatitis C virus infection. Treatment of intestinal-hepatic axis disorders by oral antibiotic administration (rifaximin), improvement of circulatory system dysfunction (long-term supplementation of albumin), reduction of inflammatory status (statins) and reduction of portal hypertension (beta blockers) can reduce the disease progression in patients with decompensated cirrhosis [11].

4.2. Anti Inflammatory and Anti Fibrosis Treatment

Anti-inflammatory and anti fibrosis therapy can be considered for patients who are unable to receive etiological treatment, or whose liver inflammation or fibrosis still exists or progresses after adequate etiological treatment. Commonly used anti-inflammatory and liver protecting drugs include glycyrrhizic acid preparation, silymarin class,

polyene phosphatidylcholine, bicyclo-ethanol, adenosine methionine, glutathione and so on.These drugs can reduce the damage of liver tissue, promote the repair and regeneration of liver cells, alleviate intrahepatic cholestasis, and improve liver function by inhibiting inflammatory reaction, detoxification, immunoregulation, scavenging reactive oxygen species and free radicals, regulating energy metabolism, improving the stability, integrity and fluidity of liver cell membrane [12].As for the treatment of anti-fibrosis, there is no clinically effective anti-fibrotic western medicine, and traditional Chinese medicine has played an important role [13].Many clinical studies [14-16] have found that these drugs can further reduce liver fibrosis in patients with chronic hepatitis B on the basis of antiviral treatment. Some Chinese medicines can enhance the expression of matrix metalloproteinase-13 and inhibit the expression of matrix metalloproteinase-2 and tissue matrix metalloproteinase inhibitor 1/2 in CCL4-induced hepatic fibrosis in rats. It can also play an anti fibrosis role by inhibiting the signal pathway of TGF - β1 [17].

4.3. Treatment of Cirrhosis Complications

Common complications of cirrhosis include: gastrointestinal bleeding, hepatic encephalopathy, ascites, infection, splenomegaly with hypersplenism, portal vein thrombosis (PVT), primary liver cancer, etc. Due to space limitations, we only introduce the treatment of gastrointestinal hemorrhage and hepatic encephalopathy here.

3.3.1 Gastrointestinal bleeding

Gastrointestinal hemorrhage is the most common complication of cirrhosis. The main causes of gastrointestinal bleeding include rupture of esophagogastric varices, portal hypertensive gastropathy and portal hypertensive enteropathy. The bleeding often occurs suddenly, and the amount of bleeding is large, the condition is critical, and the mortality rate is high [18]. The principles of treatment are: stopping bleeding, restoring blood volume, reducing portal pressure, and preventing complications. In the acute phase of bleeding, fasting water should be used and fluid replenishment should be made. Portal pressure can be reduced with terlipressin, somatostatin and its analogs or pituitrin. The use of proton pump inhibitors (also available as H2 blockers) to inhibit acid, increase the pH of the gastric juice, and help stop bleeding. Use antibiotics, third-generation cephalosporins or quinolones for 5-7 days. Infusion of red blood cells if necessary, target value of hemoglobin concentration "70 g / L. For patients with

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coagulopathy, fresh plasma, prothrombin complex and fibrinogen can be added. Significantly reduced platelets can be transfused with platelets. Vitamin K1 (5-10 mg/d) can be used for a short period of time when vitamin K1 is deficient [19]. Three-cavity and two-capsule tubes may be considered when the drug treatment is not effective; or emergency endoscopic ligation, sclerosing agent or tissue adhesive treatment, and the effect and safety of the drug combined with endoscopic treatment is better; feasible interventional therapy (TIPS) ,Surgical treatment. High-risk patients with acute bleeding should receive early (72h) TIPS. Gastric varices bleeding is preferred for balloon occlusion of retrograde venous atherosclerosis [20].In the acute stage of hemorrhage, patients should be fasted and fluid should be replenished reasonably.

3.3.2 Hepatic encephalopathy

Hepatic encephalopathy (HE) is the most serious complication of liver cirrhosis and the most common cause of death. Early recognition and timely treatment are the key to improve the prognosis of hepatic encephalopathy. It is very important to remove the predisposing factors, such as common infection, gastrointestinal bleeding and electrolyte disorder. At the same time, we should pay attention to screen whether there is abnormal portosystemic shunt. The main therapeutic methods are to promote the excretion of ammonia, reduce the production of ammonia, clean the intestines, reduce the absorption of enterotoxin and correct the imbalance of amino acids. Lactulose, lactitol, L-ornithine L - aspartate [21] and alpha crystalline rifaximin and the like [22]. At the same time, we must pay attention to nutritional support treatment. In recent years, 80.3% of patients with cirrhosis have been found to have malnutrition, and excessive restriction of protein diet for a long time can cause muscle loss and HE. Correct assessment of the nutritional status of patients, early nutritional interventions can improve the quality of life of patients, reduce the incidence of complications, and prolong the survival of patients [23]. When hepatic encephalopathy is complicated with hepatic failure, on the basis of medical treatment, some artificial liver models can be used to improve HE, which can remove some inflammatory factors, endotoxin, blood ammonia, bilirubin, etc. to some extent. [24, 25]. The effect of medical treatment is not ideal, and recurrent refractory HE with liver failure is an indication for liver transplantation [26].

5. SUMMARY

To sum up, liver cirrhosis is a multi-factorial disease that seriously affects people's health. Reversing and blocking the progression of cirrhosis has been the goal of clinical scientists, but due to the complexity of the mechanism of liver fibrosis, and There are still many deficiencies and problems in the limitations of cognition. Clinicians and researchers should be good at discovering problems in medical practice and scientific research, and pay full attention to them. This will definitely improve the anti fibrosis effect in the future.

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