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Progress in Traditional Chinese and Western Medicine Research on Factors Related to Cirrhosis with Abdominal Ascites

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Abstract

Abdominal ascites is one of the common and serious complications in patients with decompensated liver cirrhosis. The most basic cause of abdominal ascites is liver cell degeneration, necrosis, and regeneration, which promotes fibrous tissue proliferation and scar contraction, leading to hardening of the liver texture and formation of cirrhosis, causing portal hypertension and liver function damage, resulting in the formation of abdominal ascites. Abdominal ascites is also an important sign of decompensated liver cirrhosis. The prevention and treatment of abdominal ascites has always been a common difficulty and a hot research topic in clinical work. Therefore, this article comprehensively discusses the related factors of abdominal ascites from the perspective of traditional Chinese and Western medicine.

Keywords

Liver cirrhosis

Abdominal ascites

Influencing factors

Progress in traditional Chinese and Western medicine research

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1. Introduction

Abdominal ascites, as one of the most common and severe complications of liver cirrhosis, occurs in approximately 60% of patients with decompensated liver cirrhosis [1]. Once abdominal ascites develops, the 1-year mortality rate is about 15%, and the 5-year mortality rate ranges from 44% to 85% [2]. Reducing the incidence not only depends on proper treatment but also requires maintaining the activity of hepatocytes. Especially, minimizing liver damage before symptoms appear is crucial to effectively decrease complications and ensure timely treatment. Effective control of abdominal ascites production is key to improving the quality of life for patients with liver cirrhosis. Currently, the treatment of abdominal ascites remains a top priority,

and identifying factors that influence abdominal ascites is a critical aspect of therapy. In recent years, there have been numerous reports on factors related to abdominal ascites. This article summarizes relevant content from both traditional Chinese and Western medicine that can guide clinicians in their practice.

2. High-risk population

2.1. Classification of high-risk populations for abdominal ascites in traditional Chinese medicine

From the perspective of etiology, it can be divided into the following six categories.

2.1.1. Qi stagnation and dampness obstruction type

This population often experiences emotional discomfort, leading to liver qi stagnation, which affects the spleen's transportation function and results in abdominal ascites due to water and dampness retention [3]. Patients typically present with abdominal distension that is not hard to press, fullness or pain under the ribs, frequently accompanied by symptoms such as belching and poor appetite. Combination therapy with Western medicine and modified Li Ling Tang and Chai Hu Shu Gan San has a high treatment efficacy, significantly improving patients' abdominal circumference, 24-hour urine volume, and liver function indicators [4]. Applying traditional Chinese medicine to the navel can promote qi circulation, eliminate dampness, and activate blood circulation. When combined with conventional diuretics, it can enhance urine excretion, improve abdominal distension symptoms, and effectively treat abdominal ascites caused by liver cirrhosis [5].

2.1.2. Dampness-cold obstructing spleen type

This is mostly caused by long-term residence in damp environments or excessive consumption of cold and raw foods, leading to the invasion of dampness-cold pathogens and impeding the spleen's yang energy [6]. Their symptoms of abdominal ascites include abdominal distension, feeling like a water-filled sac when pressed, accompanied by lower extremity edema, abdominal fullness and distension, relief with warmth, and mental fatigue. Professor Li Fazhi treats abdominal ascites with modified Ji Ming San (Cock's Crow Powder) to promote urination and eliminate dampness, further verifying that promoting urination is key to treating this symptom [7]. The combined therapy of modified Ling Gui Fu Ping Tang (Poria Cocos, Cinnamon Twig, and Duckweed Decoction) and warm acupuncture can improve the clinical symptoms of patients with refractory abdominal ascites due to hepatitis B cirrhosis (Dampness-Cold Obstructing Spleen Type), restore liver function, rapidly increase urine output, reduce patient weight and abdominal circumference, and promote the resolution of abdominal ascites in patients with refractory abdominal ascites due to hepatitis B cirrhosis through short-course repeated measurements. The safe use of herbal medicines and standardized acupuncture techniques in the treatment process, along with stable efficacy and high safety, provides a reference for selecting optimized clinical treatment options for refractory abdominal ascites [6].

2.1.3. Dampness-heat accumulation type

This type may be caused by exogenous dampness-heat pathogens, or excessive alcohol consumption and overeating of rich and greasy foods, leading to the generation of dampness and heat and their accumulation in the middle jiao. The main symptoms include abdominal distension and hardness, urgent abdominal fullness, restlessness, and bitter taste in the mouth, thirst without desire to drink, and dark and scanty urine [8]. Adopting a modified formula of clearing heat and dispelling dampness to treat liver cirrhosis with abdominal ascites due to dampness-heat accumulation can effectively relieve clinical symptoms, reduce ascites, improve physical condition and liver function, enhance the effectiveness of disease treatment, and is safe [9]. Prolonged accumulation of dampness-heat can lead to heat entering the nutritive and blood levels, causing blockage of blood vessels and collaterals. This can result in liver cirrhosis with abdominal ascites complicated by blood stasis. Patients can achieve better treatment results with Li Dan Xiao Gu Tang combined with acupoint application, which is beneficial for improving abdominal ascites symptoms, liver function, and coagulation function [10].

2.1.4. Blood stasis in liver and spleen type

This is usually caused by liver qi stagnation, poor blood circulation, and blood stasis blocking the liver

and spleen meridians [11]. Patients with this condition exhibit exposed blue veins on their abdomen, hard lumps under the ribs, abdominal distension, and a dull, dark complexion. The treatment of patients with liver cirrhosis, abdominal ascites, and portal hypertension of the blood stasis in liver and spleen type with traditional Chinese medicine Shenlong powder applied to the navel combined with diuretics can reduce abdominal ascites, improve coagulation function, and portal and splenic vein hemodynamic indicators, with significant effects [11].

2.1.5. Spleen and kidney yang deficiency type

This condition is caused by factors such as long-term illness, physical weakness, or excessive sexual activity, leading to yang deficiency in the spleen and kidneys. Abdominal ascites in this type manifests as abdominal distension, discomfort, morning widening, and evening urgency, fatigue, chilliness, cold limbs, and edema [12]. The efficacy of umbilical irradiation therapy with a liver disease therapy instrument for the treatment of hepatitis B liver cirrhosis with abdominal ascites (spleen and kidney yang deficiency type) is significant [13]. Compared to spironolactone alone, the combination of Jianpi Lishui decoction and spironolactone has a significant effect on the treatment of patients with liver cirrhosis and abdominal ascites of the spleen and kidney yang deficiency type, which can alleviate symptoms and signs, and improve liver function and coagulation function [14].

2.1.6. Liver and kidney yin deficiency type

This is often caused by the depletion of yin essence in the liver and kidneys due to prolonged warm diseases or emotional internal injuries. Patients with this condition exhibit abdominal distension, possibly with exposed blue veins, a dull complexion, purple lips, dry mouth, and restlessness [15]. The modified Yi Guan Jian decoction combined with conventional western medicine has a significant effect on the treatment of liver cirrhosis with abdominal ascites, which can alleviate clinical symptoms, improve quality of life, and liver function [16]. The clinical efficacy of the liver-nourishing and kidney-tonifying diuretic formula for the treatment of liver cirrhosis with abdominal ascites and liver-kidney yin deficiency syndrome is very good. No adverse reactions occurred during or after treatment, indicating that this formula has a definite clinical effect on treating this syndrome, can significantly improve patients' clinical symptoms and signs, and has a diuretic effect with good safety [15].

2.2. Classification of high-risk groups for abdominal ascites in Western medicine

2.2.1. Elderly people over 60 years old

With the improvement of medical technology, the life expectancy of patients with liver cirrhosis has been extended, and the number of patients with decompensated liver cirrhosis who can survive to over 60 years old has gradually increased. As the aging of the world's population intensifies, the proportion of patients diagnosed with liver cirrhosis after entering old age is also increasing year by year [17]. Due to the multiple comorbidities common in the elderly population and organ function differences in physiological and pathological aspects compared to young and middle-aged individuals, the liver's ability to synthesize albumin is significantly reduced, further decreasing the albumin content in the plasma [18]. This allows water from blood vessels to leak into the abdominal cavity, forming abdominal ascites. However, elderly patients often have comorbidities such as hypertension, diabetes, and cardio-cerebrovascular diseases. If abdominal ascites occurs, the prognosis is poor, and severe complications such as hepatorenal syndrome and hepatic encephalopathy are likely to develop.

2.2.2. Children

The age distribution of abdominal ascites in children is as follows: Infants (28 days to 1 year) are most commonly affected by liver cirrhosis caused by biliary atresia; toddlers (1 to 3 years) and preschoolers (3 to 6 years) are more often affected by malignant tumors, with lymphoma and leukemia being the main causes. Infectious diseases that cause abdominal ascites in children are mainly tuberculosis infections [19]. The factors contributing to abdominal ascites vary among different age groups, and examination and treatment should be tailored to the characteristics of each disease to control its progression.

2.2.3. Patients with decompensated liver cirrhosis

Abdominal ascites is one of the most common and severe complications of patients with decompensated liver cirrhosis. It indicates that the liver cirrhosis has

progressed to a more severe stage, and the degree of liver function damage has exceeded the normal body's compensatory range. About 20% of patients with decompensated liver cirrhosis have abdominal ascites as their first clinical manifestation, and more than 75% of patients have abdominal ascites.

2.2.4. Patients with poorly controlled viral hepatitis (such as hepatitis B and hepatitis C)

Long-term viral damage to the liver can easily progress to cirrhosis, which in turn can lead to abdominal ascites. Hepatitis B virus (HBV) infection is one of the main causes of cirrhosis [20]. Cirrhosis is the end-stage of liver disease, and abdominal ascites is its most common complication, severely affecting patients' quality of life and prognosis [21]. Abdominal ascites accompanied by severe jaundice is a prominent manifestation of decompensated cirrhosis, and its occurrence and development are closely related to hepatitis virus infection, liver microcirculation disorders, and severe damage to liver cells [22].

2.2.5. People who consume large amounts of alcohol for a long time

Alcohol directly damages liver cells, leading to inflammation and liver cell death, resulting in liver fibrosis and increasing the risk of abdominal ascites as a complication of cirrhosis [23]. Initially, alcoholic cirrhosis was more common in Western countries, but with the recent prevalence of alcohol culture in China, coupled with the inherent deficiency of alcohol detoxification function in Chinese genes, alcoholic liver disease has been increasing year by year, and the proportion of cirrhosis has increased from 10.8% in 1999 to 24.0% in 2003. With the country's vigorous prevention and treatment of viral hepatitis, the proportion of alcoholic cirrhosis may be even higher, and it may even become the main cause of cirrhosis in China in the future. The quality of life of patients with alcoholic cirrhosis and abdominal ascites is greatly reduced, and the disease has a poor prognosis and high fatality rate, shortening the survival time of patients and causing significant harm and concern worldwide [24].

2.2.6. Patients with autoimmune liver disease

Autoimmune liver disease is an inflammatory liver disease characterized histologically by dense mononuclear cell infiltration within the portal veins and serologically by the presence of non-organ and liver-specific autoantibodies as well as elevated levels of immunoglobulin G (IgG), but without a known etiology [25]. For example, primary biliary cholangitis can cause bile stasis and liver damage, leading to abdominal ascites. Diseases such as autoimmune hepatitis and primary biliary cholangitis can cause the immune system to attack liver tissue, impairing liver function and making it prone to abdominal ascites. In recent years, there have been an increasing more case reports of autoimmune liver diseases (AILD) in China [26]. The essence of autoimmune hepatitis is hepatocyte and cholangiole damage mediated by the body's autoimmune response [27].

2.2.7. Patients with right heart failure

The liver is a vascular-rich organ that accounts for 25% of total cardiac output, making it very sensitive to hemodynamic changes in chronic heart failure. In diseases of right heart failure, such as congestive heart failure, constrictive pericarditis, and severe tricuspid regurgitation, congestive liver disease occurs around the veins due to intake and collagen formation, leading to cardiac liver or "cardiac cirrhosis." Both arteriovenous congestion and long-term liver fibrosis can result in increased portal hypertension and sinusoidal dilation, leading to the formation of protein-rich exudate and abdominal ascites [28]. People with liver congestion, such as those with chronic heart dysfunction, may experience poor blood flow from the liver due to poor heart function, leading to long-term liver congestion, which can easily cause liver cirrhosis and subsequent abdominal ascites. Long-term recurrent chronic heart dysfunction, constrictive pericarditis, and hepatic venous obstruction can cause liver congestion, an imbalance between hepatocyte damage and regeneration, and ultimately lead to liver cirrhosis. Liver cirrhosis caused by heart disease is called cardiogenic cirrhosis [29].

3. Related factors of concurrent abdominal ascites

The following are the related factors of the formation of liver cirrhosis complicated with abdominal ascites.

3.1. Portal hypertension

Liver cirrhosis leads to increased portal vein pressure and impeded blood flow, resulting in fluid leaking into the abdominal cavity and forming abdominal ascites [30]. Clinically, the degree of portal hypertension can be evaluated by measuring indicators such as portal vein diameter, splenic vein diameter, and portal vein blood flow velocity [31].

3.2. Hypoalbuminemia

Impaired liver function leads to insufficient synthesis of albumin, and reduced albumin levels cause a decrease in plasma colloid osmotic pressure, making it easier for fluid to leak into tissue spaces [32]. During liver cirrhosis, the synthetic function of hepatocytes decreases, leading to a reduction in plasma albumin. Hypoproteinemia lowers plasma colloid osmotic pressure, allowing fluid to leak from blood vessels into tissue spaces and the abdominal cavity, forming abdominal ascites. The lower the serum albumin level, the higher the incidence of abdominal ascites, and the severity of abdominal ascites is also closely related to albumin levels.

3.3. Activation of the renin-angiotensin-aldosterone system (RAAS)

The renin-angiotensin-aldosterone system (RAAS) has a wide range of biological effects, including regulating long-term blood pressure and extracellular fluid volume (fluid balance) in the body. It acts on multiple organs in the body, and its effector molecules, PRA, AngII, and ALD, are important active factors. Liver cirrhosis may be accompanied by decreased kidney function, known as hepatorenal syndrome, which further exacerbates fluid accumulation. Patients with liver cirrhosis have a reduced effective circulating blood volume, which stimulates the activation of RAAS. Activation of RAAS leads to renal vasoconstriction, water and sodium retention, and aggravates the formation of abdominal ascites. The use of drugs such as angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) to inhibit RAAS activation may have a certain effect on reducing abdominal ascites [33]. When abdominal ascites forms, it is accompanied by local and systemic activation of RAAS, increased secretion of AngII and ALD, which leads to sodium and water retention, further promoting the occurrence and development of abdominal ascites [34].

3.4. Increased lymph fluid

Liver diseases are often accompanied by systemic inflammatory responses, which increase capillary permeability and promote the formation of abdominal ascites. In liver cirrhosis, the production of intrahepatic lymph fluid increases, exceeding the drainage capacity of the thoracic duct. The lymph fluid leaks from the surface of the liver capsule and the portal lymphatics into the abdominal cavity, forming abdominal ascites. Currently, there is no specific detection method to evaluate the degree of increased lymph fluid production, but it can be indirectly inferred by observing the nature and composition of the abdominal ascites. Its occurrence is closely related to portal hypertension and liver function damage caused by excessive water and sodium retention after the progression of liver cirrhosis. This complication generally appears in the decompensated phase of liver cirrhosis, and if not treated promptly and actively, it may further lead to immune dysfunction and induce abdominal cavity infection [35].

3.5. Infection

Patients with liver cirrhosis have a weakened immune system and are prone to infections such as spontaneous bacterial peritonitis. Infection can exacerbate liver damage, leading to increased abdominal ascites [36]. Active prevention and treatment of infections are crucial for reducing the occurrence and progression of abdominal ascites. Systemic inflammation and immune system activation play a vital role in the development of abdominal ascites in liver cirrhosis. Firstly, portal hypertension increases intestinal mucosal permeability, facilitating the transfer of pathogen-associated molecular patterns from the intestinal lumen to the temporary circulation via the mesenteric lymphatics, resulting in systemic infection and endotoxemia [37]. Abdominal infection is a common complication of advanced liver disease. Bacterial translocation is considered a key step in the pathogenesis of intestinal bacterial infections, primarily spontaneous bacterial peritonitis (SBP) in patients with liver cirrhosis. The inpatient mortality rate ranges from 20% to 40% and can reach up to 78% [38]. Regarding liver function, both groups of patients showed

significant improvement in liver function levels after treatment, with the observation group demonstrating better improvement than the control group ($P < 0.05$). Conclusion: In the treatment of patients with liver cirrhosis and abdominal ascites, combining rifaximin therapy with conventional treatment can effectively control inflammation levels, improve the intestinal flora environment, and enhance liver function. The treatment effect is significant, providing a reference for establishing standard treatment protocols for liver cirrhosis with abdominal ascites [39]. Human adipose-derived mesenchymal stem cell exosomes demonstrate significant anti-fibrotic effects both in vitro and in vivo, regulating liver fibrosis through the PI3K-AKT-mTOR signaling pathway. Association with metabolomics reveals that human adipose-derived mesenchymal stem cell exosomes primarily regulate choline metabolism, which may affect the PI3K-AKT-mTOR pathway [40].

3.6. Gut-liver axis

Due to the key role of the gut-liver axis in the formation of abdominal ascites, its pathophysiological mechanism involves intestinal flora imbalance triggering inflammatory responses, impaired liver function affecting fluid balance, and coagulation dysfunction [41]. In clinical treatment of abdominal ascites, apart from targeting the liver disease itself, methods such as regulating intestinal flora and improving intestinal mucosal barrier function are often employed. For instance, probiotics are used to adjust the balance of intestinal flora, and drugs like octreotide are applied to reduce visceral blood flow and lower portal vein pressure, thereby alleviating intestinal congestion and damage to the intestinal mucosal barrier. This aims to reduce the generation of peritoneal fluid and promote its absorption [42]. The gut-liver axis plays a central role in the occurrence, development, and treatment of abdominal ascites through various interactions involving intestinal flora, liver function, and coagulation function. A deep understanding of the gut-liver axis mechanism is crucial for the prevention and treatment of abdominal ascites [43].

3.7. Imbalance of intestinal flora

3.7.1. Impaired intestinal mucosal barrier

Normal intestinal flora contributes to maintaining the integrity of the intestinal mucosal barrier. When flora imbalance occurs, the intestinal mucosal barrier function may weaken, allowing harmful substances such as bacteria and toxins within the intestine to more easily penetrate the intestinal wall and enter the peritoneal cavity, triggering peritoneal inflammation and leading to the production or exacerbation of abdominal ascites.

3.7.2. Bacterial translocation

An imbalance of intestinal flora can promote the translocation of intestinal bacteria to extraintestinal tissues such as mesenteric lymph nodes, liver, and peritoneal cavity. Bacteria reproduce and release toxins within the peritoneal cavity, stimulating the peritoneum and causing peritoneal inflammatory responses. This increases the permeability of peritoneal capillary blood vessels, allowing fluid to leak into the peritoneal cavity and form abdominal ascites [44].

3.7.3. Immune dysfunction

The intestinal microbiota plays a crucial role in regulating the body's immune function. Dysbiosis can lead to abnormal immune function, where the immune system cannot effectively clear antigenic substances in the abdominal cavity. Persistent immune responses can cause inflammation in the abdominal cavity, which in turn affects the balance of fluids in the abdomen and promotes the formation of abdominal ascites [45].

3.7.4. Liver function damage

Dysbiosis of the intestinal microbiota may affect the liver's metabolic and detoxification functions. For example, the production of excessive endotoxins that enter the liver via the portal vein can damage liver cells, leading to decreased liver function. This reduces the liver's ability to synthesize plasma proteins such as albumin, causing a decrease in plasma colloid osmotic pressure and allowing fluid to leak from blood vessels into the abdominal cavity, forming abdominal ascites.

These are some common mechanisms by which intestinal microbiota dysbiosis can affect abdominal ascites, although actual situations may vary due to individual differences, underlying diseases, and other factors.

3.8. Other factors

3.8.1. Long-term medication

Certain antibiotics and anti-epileptic drugs can be toxic to the liver, and long-term use can cause liver damage, which in severe cases can induce ascites [46].

3.8.2. Inherited metabolic diseases

Conditions such as hepatolenticular degeneration and hemochromatosis can lead to abnormal liver metabolism, damage, and cirrhosis, predisposing to abdominal ascites. Some studies suggest that genetic factors may play a role in the development of comorbid abdominal ascites, although the specific mechanisms remain unclear [47].

3.8.3. Immune system factors

Autoimmune reactions that attack liver cells can cause chronic inflammation, liver fibrosis, and abdominal ascites. Other complications of liver cirrhosis, such as spontaneous bacterial peritonitis, endotoxemia, hepatorenal syndrome, and gastrointestinal dysfunction, are also closely related to the development of abdominal ascites [48].

3.8.4. Endocrine factors

Increased secretion of antidiuretic hormone and abnormal hormone levels, such as atrial natriuretic peptide, may also be related to the formation of abdominal ascites.

3.9. Difficulties in the individualized treatment of liver cirrhosis complicated with abdominal ascites in traditional Chinese medicine

3.9.1. Complex etiology and difficult syndrome differentiation

The etiology of liver cirrhosis is diverse, including viral infection, alcohol damage, autoimmunity, etc. Liver cirrhosis caused by different etiologies may have similarities and different characteristics in the manifestations of traditional Chinese medicine syndromes. Accurate syndrome differentiation requires comprehensive consideration of multiple factors, which places high demands on the clinical experience and syndrome differentiation ability of traditional Chinese medicine doctors.

3.9.2. Changing condition and difficult medication

The condition of liver cirrhosis is often dynamically changing. As the disease progresses, the patient's symptoms, signs, and traditional Chinese medicine syndromes continue to evolve. From early liver depression and spleen deficiency to later stages, there may be multiple complex syndromes such as liver and kidney yin deficiency, blood stasis obstructing collaterals. How to adjust individualized treatment plans and medications in a timely manner based on changes in the condition is a difficulty.

3.9.3. Individual differences and difficult formula adjustment

Different patients have differences in physical constitution, age, living habits, and psychological state, and have different tolerances and reactions to medications. Some patients may be sensitive to certain Chinese medicinal components and prone to adverse reactions, while others may require higher doses to achieve therapeutic effects. This increases the difficulty of individualized medication.

3.9.4. Complex efficacy evaluation

The efficacy evaluation of individualized treatment of liver cirrhosis in traditional Chinese medicine does not have clear laboratory indicators and imaging standards like Western medicine. Traditional Chinese medicine mainly relies on comprehensive judgments based on symptoms, signs, tongue manifestations, pulse conditions, etc., and lacks objective and quantitative indicators. This makes the efficacy evaluation relatively complex and affects the accurate adjustment of the treatment plan.

3.9.5 Poor compliance with long-term treatment

The treatment of liver cirrhosis is typically a long-term process. Individualized traditional Chinese medicine treatment requires patients to take Chinese herbal medicines for an extended period, combined with adjustments to diet and lifestyle. However, some patients may find it difficult to adhere to long-term standardized treatment due to factors such as the unpleasant taste of Chinese herbal medicines, inconvenience in administration, or inadequate understanding of the disease. This can affect the treatment outcome.

4. Outlook

Abdominal ascites is the result of multiple interacting factors. Portal hypertension, hypoproteinemia, activation of the renin-angiotensin-aldosterone system (RAAS), increased lymph production, infection, and other factors interact, leading to the formation and development of abdominal ascites. Clinicians should consider these factors comprehensively and develop individualized treatment plans to improve patient outcomes and quality of life. Meanwhile, further research on the related factors of abdominal ascites in traditional Chinese and Western medicine may help develop new treatment methods and drugs, bringing more hope to patients with liver cirrhosis.

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