ORIGINAL RESEARCH

Evaluation of the Curative Effect of Treating HBV-related Liver Fibrosis/Cirrhosis Based on the Method of Removing Turbidity and Regulating the Liver

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ABSTRACT

Objective • This study investigated the effectiveness of a technique for eliminating cloudiness and managing liver function in treating liver fibrosis/cirrhosis associated with the Hepatitis B virus (HBV).

Methods • From January 2022 to January 2023, the researchers' hospital treated 200 patients with HBV-related liver fibrosis/cirrhosis. These patients constituted two groups for the study: the control group, consisting of 100 cases who received routine treatment, and a study group, consisting of 56 cases who received treatment with a combination of turbidity removal and liver regulation, in addition to the standard treatment given to the control group. The researchers then compared factors such as liver function, level of liver fibrosis, liver stiffness measurement (LSM), and renal function between the two groups. Additionally, the researchers assessed the effectiveness of those treatments and any adverse reactions that may have occurred.

Results • The study group demonstrated significantly higher clinical effectiveness than the control group after undergoing treatment, with statistical significance ($P < .05$). Post-treatment, both groups experienced lower GGT, ALT, and AST levels than their pre-treatment levels. Additionally, the study group had higher AIB levels than their pre-treatment levels. There was a statistically significant difference between the study and control groups regarding these biomarkers ($P < .05$), as the study group exhibited lower GGT, ALT, AST, TBIL levels and higher AIB levels. Furthermore, both groups displayed decreased HA, IV-C, PC III, and LN levels post-treatment compared to their pre-treatment values. The study group had significantly lower HA, IV-C, PC III, and LN concentrations than the control group ($P < .05$). Regarding LSM measurements after treatment for both groups, while there was a decrease in LSM values from their respective pre-treatment readings for each group, no significant difference was observed between them ($P < .05$). Moreover, the incidence of adverse reactions experienced by individuals in the study group following treatment was significantly lower than that of individuals in the control group ($P < .05$)

Conclusion • Treatment based on removing turbidity and regulating the liver can effectively relieve the clinical symptoms of patients with HBV-related liver fibrosis/cirrhosis, promote the liver function to return to normal, relieve the degree of liver fibrosis, and reduce the LSM value. The curative effect is significant and worthy of clinical application. (*Altern Ther Health Med.* 2023;29(8):710-716).

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BACKGROUND

Chronic hepatitis B is an infectious disease caused by hepatitis B virus infection. There are 350 million chronic hepatitis B virus patients worldwide annually and 90 million chronic hepatitis B virus-infected people in China, of which 15% - 40% will develop cirrhosis and end-stage liver disease. The annual incidence of liver function compensation in compensatory cirrhosis is 3.3% - 4.0%, and the 5-year cumulative incidence is as high as 16% - 20%. If patients have liver function decompensation, the 5-year cumulative survival rate is as low as 14%.[1-2]

Persistent HBV infection can cause different liver damage, eventually leading to hepatitis, liver fibrosis, cirrhosis, and hepatocellular carcinoma. Fibrosis is related to the progression of liver disease and is a crucial factor in the prognosis of liver disease and the risk of hepatocellular carcinoma.[1] In advanced fibrosis, the reversal of fibrosis occurs too slowly, which may cause life-threatening complications.[1] Liver fibrosis is the precursor of liver cirrhosis, the final pathological result of

various chronic liver diseases, and is a diffuse liver process characterized by fibrosis and abnormal nodular structure. Liver cirrhosis is a common cause of death globally.[3]

Activation of hepatic stellate cells is a critical event in fibrosis. The exfoliation and capillarization of hepatic sinus endothelial cells are the main factors causing liver dysfunction in cirrhosis.[4] Currently, drugs such as tenofovir and entecavir constitute frequent clinical treatment of HBV-related liver fibrosis/cirrhosis, but no drugs can eradicate HBV. Thus, patients need to take medicines for life.[5] Most Western drugs only target a single gene or protein; if patients take those drugs long-term, they will suffer various adverse reactions. Therefore, seeking effective and safe drugs to treat liver fibrosis and cirrhosis6 is urgent.

The essential perspective of traditional Chinese medicine is the treatment based on syndrome differentiation and the holistic view. Traditional Chinese medicine has thousands of years of clinical experience, has a good curative effect in the treatment of complex diseases, has the characteristics of multi-component, multi-channel, multi-target, and low toxicity, and has a wide range of sources. Traditional Chinese medicine also has unique advantages and massive potential in treating HBV-related liver fibrosis/cirrhosis[7]. Based on these historical precedents, this study will explore the treatment of HBV-related liver fibrosis/cirrhosis by removing turbidity and regulating the liver.

DATA AND METHODS

Clinical Data

This study took place in the researchers' hospital from January 2022 to January 2023. Two-hundred patients with liver fibrosis/cirrhosis related to HBV comprised the study group and control group, each comprising 100 cases. A random number table served as the means to divide the patients into groups.

The study group consisted of 59 males and 41 females, ranging in age from 31 to 76 years old, with an average age of 51.93 (± 10.98) years. The existing duration of the disease ranged from 1 to 7 years, with an average duration of 3.87 (± 0.67) years. The Child classification of liver function revealed that 21 scored Grade A, 45 as Grade B, and 34 as Grade C.

The control group comprised 61 males and 39 females, ranging from 30 to 74 years old. The average age of the participants was 51.01 (± 11.04) years. The existing disease duration ranged between 1 and 7 years, with an average duration of 3.79 (± 0.76) years. The Child liver function grading consisted of 23 cases classified as Grade A, while Grade B had 46 cases and Grade C had 31. No significant differences emerged when comparing the two groups ($p > 0.05$). The research protocol followed all relevant requirements as outlined in the Helsinki Declaration by the World Medical Association.

Diagnostic Criteria

Diagnostic Criteria of Western Medicine. Based on the *Expert Consensus on the Diagnosis of Hepatic Fibrosis by Instantaneous Elastography (2018 Update)*[8] and the Diagnosis and Treatment of Liver Cirrhosis[9], guidelines have been established for diagnosing HBV-related liver fibrosis/cirrhosis. These guidelines state that all patients must be infected with HBV to meet the diagnostic criteria. For liver fibrosis, patients with normal alanine aminotransferase (ALT) levels and a liver stiffness value (LSM) equal to or greater than 12.0 kPa are diagnosed with cirrhosis. Patients with LSM values between 9.0-12.0 kPa are diagnosed with advanced liver fibrosis, while those with LSM values between 6.0-9.0 kPa are diagnosed with mild liver fibrosis (unless ALT is normal, no clear stage of liver fibrosis can be determined). This information provides essential guidance for accurately diagnosing HBV-related liver disease and determining its severity based on specific clinical criteria outlined by these expert sources.[8,9]

Based on the Expert Consensus on the Diagnosis of Hepatic Fibrosis by Instantaneous Elastography (2018 Update)[8] and the Diagnosis and Treatment of Liver Cirrhosis[9], guidelines have been established for diagnosing HBV-related liver fibrosis/cirrhosis. These guidelines state that all patients must be infected with HBV to meet the diagnostic criteria. For liver fibrosis: patients with normal alanine aminotransferase (ALT) levels and liver stiffness value (LSM) ≥ 12.0 kPa are diagnosed with cirrhosis. Patients with LSM values between 9.0-12.0 kPa are diagnosed with advanced liver fibrosis, while those with LSM between 6.0-9.0 kPa are diagnosed with mild liver fibrosis (unless ALT is normal, no clear stage of liver fibrosis can be determined).

The above data provided crucial information in accurately diagnosing liver disease related to HBV and assessing its severity using specific clinical criteria. The normality of ALT levels among patients served as a means to stage further diagnosis of liver cirrhosis. Using an ultrasound, the researchers considered several criteria: (1) irregular or rough liver surface, (2) disproportionate size of liver lobes, (3) uneven echo enhancement in liver tissue, (4) dilation of the portal vein, and (5) spleen enlargement. These factors play a significant role in identifying and evaluating HBV-related liver disease.

Diagnostic Criteria of Traditional Chinese Medicine. The Principles for Formulating Clinical Research on New Chinese Medicines (Trial Implementation in 2002) established the diagnostic criteria for the syndrome characterized by blood stasis-blocking collaterals.[10] Key symptoms of the syndrome include (1) hypochondriac pain that is consistent and unchanging; (2) large, firm, and full abdomen that feels hard and resistant to pressure; (3) exposed blue muscles on the abdominal wall; and (4) enlargement of the spleen or liver resulting in a subhypochondrial mass. Additional symptoms may include: (1) dull complexion; (2) Presence of red dots or streaks on the chest, abdomen, neck, and head; and (3) distended sublingual veins. The tongue pulse: may exhibit a purple or dark coloration with ecchymosis (bruising) present. The pulse itself would be fine and constricted.

Inclusion and Exclusion Criteria

Individuals who met the above diagnostic criteria possessed normal mental awareness and communication abilities, and provided informed consent were eligible for this study. However, individuals with severe chronic hepatitis or liver cancer, those with significantly abnormal liver function [ALT > 4 × upper normal limit value, or total bilirubin (TBil) > 5 × normal upper limit value, those with dysfunction in the hematopoietic system, individuals allergic to the drug under investigation, those suffering from liver fibrosis/cirrhosis due to other causes, individuals who have previously taken anti-HBV drugs and anti-liver fibrosis medications, as well as pregnant or lactating women were excluded from participation in the study.

METHODS

During the study, the control group received entecavir orally at a dosage of 0.5 mg per time, once daily. Additionally, they received Diamine glycyrrhizinate enteric-coated capsules orally 150 mg/time, 3 times/day, continuously treated for three months. These medications' specific manufacturer and batch numbers were Suzhou Dongrui Pharmaceutical Co. Ltd., batch number 210752624, and Chia Tai Tianqing Group Pharmaceutical Co., Ltd., batch number 210317110, respectively.

Based on the treatment in the control group, the study group received treatment based on the theory of removing turbidity and regulating the liver. The prescription was: 9 g Bupleurum chinense, 9 g Pinellia ternata, 10 g Scutellaria baicalensis, 6 g Coptis chinensis, 15 g Atractylodes macrocephala, 15 g Poria cocos, 15 g Codonopsis pilosula, 12 g Angelica sinensis, 15 g vinegar turtle shell, 10 g Psoralea, 10 g Curcuma officinalis, 15 g Paeonia alba, 15 g Scutellaria barbata, 9 g Magnolia officinalis, and 6 g roasted licorice, boiled in 1000 mL water for two times, decocted to 200 mL, and taken separately in the morning and evening, all for 3 times.

Observation Indicators

The researchers compared the two groups' liver function, liver fibrosis level, LSM, and renal function for curative effects. They also tallied any adverse reactions. Prior to treatment and after three months of treatment, patients with an empty stomach had 5mL of blood collected. The blood was then examined after centrifugation using an automatic biochemical analyzer to determine the levels of γ- Glutamate transpeptidase (GGT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL), and albumin (AIB).

Using the evaluation criteria for therapeutic outcomes, the researchers observed the clinical efficacy of both groups. Of significant efficacy, notable improvements included clinical symptoms such as hypochondriac pain. The liver function returned to normal, and there was no tenderness experienced in the liver and spleen, which also showed reduced swelling. In cases where none of the improvements were evident, the outcome fell under the invalid category. One adds significant efficacy and effective rate categories to calculate the total effectiveness rate.

Table 1. Comparison of Clinical Efficacy Between the Two Groups n (%)

Group	n	Significant efficacy	Effective	Invalid	Efficiency rate
Study group	100	67	31	2	98 (98.00)
Control group	100	45	42	13	89 (87.00)
χ^2 value					6.664
P value					.010

To measure the liver fibrosis level, the researchers compared the blood taken from patients before and after three months of treatment using radioimmunoassay to determine the levels of hyaluronic acid (HA), type IV collagen (IV-C), type III procollagen (PC III), and laminin (LN).[i] Measurements were conducted 10 times consecutively on the left midaxillary line, right midaxillary line, and the anterior axillary line between the seventh and eighth intercostal spaces. LSM was the median value among the measurements.[ii]

A shear wave tissue quantitative ultrasound diagnostic instrument detected LSM values before treatment and three months after treatment. The researcher measured the left and right midaxillary lines and the anterior axillary line between the 7th and 8th ribs 10 times and recorded the median liver stiffness measurement (LSM) value. Renal function measurement compared 5mL of blood collected from patients with an empty stomach before and after three months of treatment and sent for examination after centrifugation. An automatic biochemical analyzer measured the serum creatinine (Cr) and urea nitrogen (BUN) levels. Detailed observations of adverse reactions included dizziness, headache, fatigue, nausea, and other adverse reactions during the medication.

Statistical Methods

The researchers used SPSS 21.0 software for data analysis. The liver function, liver fibrosis level, and renal function measurement data presented as mean ± standard deviation(s) that underwent a *t* test for analysis. Count data was expressed as percentages (%) and analyzed using the chi-square χ^2 test. The observed difference had statistical significance with a $P < .05$.

RESULTS

Comparison of Clinical Efficacy Between The Two Groups

After treatment, the clinical efficacy of the study group was higher than that of the control group, with a statistically significant difference ($P < .05$), as shown in Table 1.

Comparison of Liver Function Between the Two Groups

Before treatment, there was no statistically significant difference in the GGT, ALT, AST, TBIL, and AIB levels. After treatment, the levels of GGT, ALT, AST, and TBIL in the two

i. The kits used for these measurements were purchased from Shenzhen Mindray Bio-Medical Electronics Co., Ltd., with batch number 202240111.

ii. LSM value: Fibrotouch (Wuxi Heskell Medical Technology Co. LTD, product number FT7000-002-012, batch number FT7000-002) was utilized to measure LSM before treatment and after three months of treatment

Table 2. Comparison of Liver Function Between the Two Groups ($\bar{x} \pm s$)

Group (n)	n	GGT (U/L)		ALT (U/L)		AST (U/L)		TBIL (U/L)		AIB (g/L)	
		Before treatment	After 3 months of treatment	Before treatment	After 3 months of treatment	Before treatment	After 3 months of treatment	Before treatment	After 3 months of treatment	Before treatment	After 3 months of treatment
Study group	100	182.38 ± 9.91	150.87 ± 9.07	114.29 ± 9.76	57.98 ± 8.76	71.52 ± 8.65	33.87 ± 9.07	42.21 ± 4.38	15.0 ± 3.13	27.09 ± 3.29	37.37 ± 3.65
Control group	100	181.89 ± 8.89	160.73 ± 10.09	114.98 ± 9.69	64.37 ± 9.03	71.87 ± 9.09	39.76 ± 9.38	42.32 ± 4.43	19.03 ± 3.42	27.83 ± 3.43	32.03 ± 3.87
t		0.368	-7.267	-0.502	-5.079	-0.279	-4.614	-0.177	-8.499	-1.557	10.038
P value		.713	<.001	.616	<.001	.781	<.001	.861	<.001	.121	<.001

Abbreviations: GGT, γ-glutamyl transpeptidase; ALT, Alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin; AIB, albumin.

Table 3. Comparison of Liver Fibrosis Indexes Between the Two Groups ($\bar{x} \pm s$)

Group (n)	n	HA (μg/L)		IV-C (μg/L)		PC III (μg/L)		LN (μg/L)	
		Before treatment	After 3 months of treatment	Before treatment	After 3 months of treatment	Before treatment	After 3 months of treatment	Before treatment	After 3 months of treatment
Study group	100	363.28 ± 20.81	298.76 ± 22.19	187.82 ± 23.72	162.18 ± 24.09	203.29 ± 23.98	132.19 ± 26.91	272.19 ± 27.98	220.71 ± 32.91
Control group	100	362.17 ± 22.18	318.76 ± 24.09	185.76 ± 20.19	173.98 ± 23.27	200.87 ± 22.76	146.29 ± 24.29	270.67 ± 26.93	236.98 ± 30.76
t		0.365	-6.106	0.661	-3.523	0.732	-3.891	0.391	-3.612
P value		.715	<.001	.509	<.001	.465	<.001	.696	<.001

Abbreviations: HA, hyaluronic acid; IV-C, Collage Type IV; PC III, pro-collagen III; LN, laminin.

Table 4. Comparison of LSM Between the Two Groups ($\bar{x} \pm s$)

Group	n	LSM (mg/L)	
		Before treatment	After 3 months of treatment
Study group	100	15.21 ± 1.61	14.09 ±1.34
Control group	100	15.15 ± 1.56	14.91 ±1.42
t		0.331	-12.557
P value		.739	<.001

Abbreviations: LSM, liver stiffness measurement.

Table 5. Comparison of Renal Function Between the Two Groups ($\bar{x} \pm s$)

Group	n	Cr (μmol/L)		BUN (mmol/L)	
		Before treatment	After 3 months of treatment	Before treatment	After 3 months of treatment
Study group	100	78.86 ± 12.87	76.98 ± 10.87	5.83 ± 1.03	5.39 ± 1.09
Control group	100	78.76 ± 11.86	76.87 ± 11.56	5.76 ± 1.12	5.27 ± 1.18
t		0.057	0.069	0.461	0.747
P value		.955	.945	.646	.456

Abbreviations: Cr, Serum creatinine; BUN, urea nitrogen.

Table 6. Comparison of Adverse Reactions Between the Two Groups n (%)

Group	n	dizziness	headache	weakness	vertigo	nausea	Total incidence
Study group	100	1	0	1	0	0	2 (2%)
Control group	100	3	2	4	3	5	17 (17%)
χ^2 value							13.085
P value							<.001

groups were lower than before; the levels of AIB were higher than those before treatment. Compared with the control group, the levels of GGT, ALT, AST, and TBIL in the study group were lower, and the levels of AIB measured higher. The difference was statistically significant ($P < .05$), as shown in Table 2.

Comparison of Liver Fibrosis Indicators Between the Two Groups

Before treatment, there was no statistically significant difference in the levels of HA, IV-C, PC III, and LN between the two groups ($P > .05$). After treatment, the levels of HA, IV-C, PC III, and LN in the two groups were lower than before treatment. Compared with the control group, the levels of HA, IV-C, PC III, and LN in the study group were lower. The difference was statistically significant ($P < .05$), as shown in Table 3.

Comparison of LSM Between the Two Groups

Before treatment, there was no statistically significant difference in the levels of LSM between the two groups ($P > .05$). After treatment, the levels of LSM in the two groups were lower than before treatment. Compared with the control group, the levels of LSM in the study group were lower; the difference was statistically significant ($P < .05$), as shown in Table 4.

Comparison of Renal Function Between the Two Groups

Before treatment, the two groups had no statistically significant difference in Cr and BUN levels ($P > .05$). After treatment, the levels of Cr and BUN in the two groups remained as having no statistically significant difference ($P > .05$), as shown in Table 5.

Comparison of Adverse Reactions Between the Two Groups

After treatment, the total incidence of adverse reactions in the study group was lower than in the control group. The difference was statistically significant ($P < .05$), as shown in Table 6.

DISCUSSION AND SUPPORTING LITERATURE

Cirrhosis of the liver as a result of HBV is a prevalent condition in medical practice. The extensive degeneration and necrosis of liver tissue cells lead to the diffuse proliferation of hepatic fibrous tissue, forming regenerative nodules and lobules. This condition presents various clinical manifestations, such as liver dysfunction and portal hypertension, which can affect multiple organs, including the spleen. These complications can ultimately lead to liver fibrosis and cirrhosis.[11] Chronic viral hepatitis is the most common cause of cirrhosis, with chronic hepatitis B being a primary example. As the disease progresses, chronic hepatitis

B can gradually develop into cirrhosis, with liver fibrosis as a stage in this progression. Since this stage of the disease is reversible,[12] there is substantial clinical significance in implementing active and effective measures to treat HBV-induced liver fibrosis/cirrhosis.

At present, patients who have developed liver fibrosis or cirrhosis as a result of HBV infection typically undergo a combination treatment involving antiviral medications combined with measures to protect the liver. When entecavir enters the body, enzymes can convert it into its active form, tenofovir diphosphate. This active metabolite effectively inhibits DNA elongation and prevents the ongoing replication of hepatitis B virus in patients.[13]

The enteric-coated capsule of diamine glycyrrhizinate is a medication extracted from the traditional Chinese herbal remedy, licorice. Its chemical structure closely resembles the aldosterone steroid ring, enabling it to hinder the deactivation of aldosterone and cortisone. Additionally, the capsule exhibits strong anti-inflammatory properties. It can effectively repair and alleviate inflammatory reactions in liver cells while protecting their membranes. Entecavir promotes the restoration of liver function and suppresses HBV-induced harm to these cells, thereby preventing liver fibrosis.[14]

Studies have recently discounted the effective rate of treating HBV-induced liver fibrosis/cirrhosis with a Western medical antiviral regimen alone. The disease is difficult to control, and long-term use of the drugs can cause various adverse reactions.[6]

TCM categorizes liver fibrosis/cirrhosis caused by HBV based on the clinical symptoms of "swelling," "jaundice," and "hypochondriac pain".[15] According to the TCM, the primary cause of this disease is a deficiency in vital energy, accumulation of pathogenic factors, and blood stasis, which is closely related to the liver, spleen, and kidney.

According to the *Internal Canon of Medicine,*[iii] "The positive qi is stored inside, and evil cannot be interfered with." "When evil is played, its qi will be empty." "The wind and rain are cold and hot, but if qi is not empty, the evil cannot hurt people alone." "The people in empty of qi and full of evil … evil stays in the pulse, and evil accumulates." "The five internal organs are all derived from the marrow of the meridian, to promote blood, blood and qi are disharmony, and all diseases are caused by changes." "Lingshu · Five evils": "If the evils are in the liver, then the two flanks are painful, … the evil blood is inside." The *Treatise on Febrile Diseases and Miscellaneous Diseases*[iv] summarizes the pathological relationship between the liver and spleen as "seeing the disease of the liver, knowing that the liver transmits the spleen, and strengthening the spleen first." There is also a theory that the "liver and kidney are homologous" in traditional Chinese medicine.[7] These classical theories effectively guide diagnosing and treating liver fibrosis/cirrhosis caused by HBV.

This study rests on the theory of removing turbidity and regulating the liver. Bupleurum chinense has a soothing effect on the liver, alleviating feelings of depression, and increasing yang qi. Pinellia ternate reduces swelling, alleviates pain, and relieves nausea and vomiting symptoms. Scutellaria baicalensis helps clear body heat, eliminate dampness, purify fire, and detoxify. Coptis chinensis aids in clearing away heat and dampness from the body, eliminating fire toxins, and relieving constipation. Atractylodes macrocephala promotes diuresis and reduces swelling by firming the skin's surface, reducing perspiration, and drying excess moisture in strengthening the spleen. Poria cocos strengthen the spleen functionally while also having a calming effect on the heart while promoting better water absorption within cells.

Codonopsis pilosula is known for its ability to strengthen the middle and boost energy, improve the function of the spleen and lungs, enhance blood nourishment, and stimulate fluid production. Angelica is commonly used to fortify the blood, promote healthy circulation, regulate menstruation, and alleviate pain. Vinegar soft-shelled turtle has properties that nourish yin energy while also clearing heat from the body. It can help balance latent yang energy, soothe wind-related discomforts, and dissolve knots in the body. Psoralea corylifolia is effective in warming the kidneys and supporting yang energy while absorbing spleen temperature. Curcuma aids in improving blood flow throughout the body by reducing pain symptoms and promoting qi circulation. It also helps uplift mood by alleviating depression symptoms while maintaining heart health through its cooling effect on the blood. The white peony harmonizes health and nourishes the blood. Scutellaria barbata can clear heat, detoxify, eliminate phlegm, and remove blood stasis. Magnolia officinalis eliminates dampness and eliminates phlegm while promoting qi and eliminating accumulation. It also reduces adverse effects and relieves asthma symptoms. The roasted licorice invigorates the spleen, replenishes qi, and calms the body. When these drugs are combined, they benefit the kidneys by strengthening the spleen, dredging the liver, and removing dampness and blood stasis to clear the collaterals effectively.

The results of this study show that after treatment, the clinical efficacy of the study group was higher than that of the control group ($P < .05$), suggesting that the treatment based on the method of removing turbidity and regulating the liver can effectively relieve the clinical symptoms of patients with HBV-related liver fibrosis/cirrhosis. The therapeutic effect is significant.

Luo et al.[16] pointed out that treating liver cirrhosis with traditional Chinese medicine can effectively improve patients' clinical symptoms, and the therapeutic effect is significant. Liu et al.[17] further noted that using traditional Chinese medicine to treat patients with liver fibrosis based on entecavir treatment can effectively inhibit the development of liver fiber and promote the recovery of liver function with an apparent curative effect.

iii. The *Internal Canon of Medicine* (TCM) is widely reputed to be the oldest medical book in existence. It was compiled roughlty 2000 years ago and servesl as the theoretical basis of Traditional Chinese Medicine. Reprints are available in multiple languages.

iv. Zhang Zhongjing authored this important volume in Traditional Chinese Medicine in the early 3rd century. The work was important and influential for its diagnosis and suggested treatments of typhoid and other fevers.

Hu et al.[18] and other researchers pointed out that traditional Chinese medicine decoction can improve the liver function of patients with liver fibrosis. He Jie et al.[19] pointed out that based on conventional liver protection treatment, the application of traditional Chinese medicine decoction in treating liver cirrhosis can improve the clinical efficacy and patients' liver function and liver fibrosis index.

The results of this study showed that following the treatment, there was a decrease in GGT, ALT, AST, and TBIL levels in the study group compared to the control group. The study group's AIB levels were also higher ($P < .05$). These results suggest that employing a technique that removes turbidity and regulates the liver can effectively manage the liver function of patients with HBV-related liver fibrosis/cirrhosis and promote the liver function to return to normal.

Hepatic fibrosis is a pathological change caused by excessive precipitation of diffuse extracellular matrix in the liver, and chronic hepatitis B due to an HBV infection, a prominent cause of liver fibrosis.[20] There is a strong correlation between serum liver fibrosis indicators and the degree of liver fibrosis, consistent with the stages of development.[21] The liver primarily metabolizes HA, and its level is closely related to liver function.

Liver damage leads to a decrease in the number of liver endothelial cells. In the liver, IV-C levels are typically low, but they become highly expressed during the early stage of cirrhosis and hepatitis. The level of IV-C is positively correlated with liver fibrosis, meaning that as fibrosis worsens, IV-C levels increase. PC III is a better indicator of liver fibrosis activity. The higher the level of PC III, the more severe the liver fibrosis. LN primarily exists in the basement membrane of intrahepatic vessels and bile ducts. When there are lesions in the liver, LV synthesis increases and causes an influx of blood into these areas.[21] Therefore, measuring HA, IV-C, PC III, and LN levels can provide an objective prediction and assessment for determining both cell damage and the degree of liver tissue fibrosis.

Peng et al.[22] pointed out that the decoction of traditional Chinese medicine has a good effect on anti-cirrhosis and liver fibrosis. Geng Yaoyao[23] also noted that TCM decoction can effectively reduce the severity of hepatitis B patients with liver fibrosis and has good clinical efficacy. This study showed that after treatment, the levels of HA, IV-C, PC III, and LN in the two groups were lower than before. Compared with the control group, the levels of HA, IV-C, PC III, and LN in the study group were lower ($P < .05$), suggesting that the treatment based on the method of removing turbidity and regulating the liver can effectively reduce the HA, IV-C, PC III, and LN of patients with HBV-related liver fibrosis/cirrhosis, alleviate the degree of liver fibrosis and promote the rehabilitation of patients. This result may be because saikosaponin, the main component of Bupleurum chinense, can play the role of anti-liver injury and liver fibrosis by up-regulating the expression of a pro-apoptotic protein in HSC, down-regulating the expression of anti-apoptotic protein, and inducing HSC apoptosis[24]; The effective component of paeony is total glycosides of paeony, which can reduce the serum ALT and AST levels of CCI4-induced liver injury in rats, and reduce the level of LN and HA in liver tissue.[25]

Transient elastography uses ultrasound to gauge liver stiffness and obtain liver stiffness measurement (LSM), quantified in kilopascal (KPa). This technique is simple to operate, highly reproducible, and dependable for assessing the severity of liver fibrosis and cirrhosis.[26] The LSM value increases with higher liver tissue stiffness, allowing ultrasonic vibration waves to propagate faster within the liver.[26] The findings of this study demonstrate that treatment based on turbidity removal and regulation of the liver can effectively reduce LSM levels in patients with HBV-related liver fibrosis/cirrhosis compared to those who received standard care ($P = .05$).

The results of this study are consistent with those of Zhang et al.[27] and Cai et al.[28] This result may reflect that Pinellia ternata's properties combat inflammation and bacteria and have other pharmacological effects.[29] Similarly, Scutellaria baicalensis exhibits antiviral, antibacterial, antioxidant, free radical elimination, anti-inflammatory properties, neuron protection, and other pharmacological effects.[30] Additionally, Coptis chinensis showcases anti-inflammatory and antibacterial properties and affects the central, circulatory, and digestive systems.[31] Moreover, Atractylodes macrocephala has various pharmacological effects, including anti-inflammatory capabilities and gastrointestinal benefits such as anti-tumor activity.[32] Poria cocos has immune-regulating abilities and diuretic qualities. It also protects the liver and displays antioxidation properties. Furthermore, research has shown its potential to be anti-viral and reduce liver cirrhosis nodules.[33] In addition, Codonopsis pilosula and its active ingredients improve gastric ulcers and enhance gastrointestinal motility. They also exhibit anti-inflammatory potential, antioxidant capacity, and regulate glycolipid metabolism. Finally, they support immune regulation and display anti-tumor activities.[34]

Angelica sinensis possesses properties to enhance blood circulation, promote blood flow, combat arteriosclerosis, inhibit bacteria growth, resist hypoxia, and regulate the body's immune function.[35] Psoralea has antibacterial properties and is known for its anti-tumor, antioxidant, anti-inflammatory, and antidepressant effects.[36] Scutellaria barbata exhibit characteristics such as being anticancerous and having immunomodulatory properties. It also acts as an antigenic agent while showing bacteriostatic effects. Additionally, it possesses anti-inflammatory qualities alongside antipyretic functions. Moreover, it is capable of protecting the liver.[37]

Dong et al.[38] pointed out that treating HBV-related liver fibrosis patients with traditional Chinese medicine will not affect the renal function of patients and has fewer adverse reactions and higher safety. The findings of this study demonstrated that following treatment, the levels of Cr and BUN in both sets of participants yielded no statistical difference when compared to their pre-treatment levels ($P > .05$). Moreover, the total occurrence rate of unfavorable reactions in the study group was lower than in the control

group ($P < .05$). These results suggest that treating HBV-related liver fibrosis/cirrhosis by employing a method focused on removing turbidity and regulating the liver function does not negatively affect the renal function of patients. It also exhibited fewer adverse reactions and greater safety characteristics.

CONCLUSION

The treatment based on removing turbidity and regulating the liver can improve the clinical symptoms of patients with HBV-related liver fibrosis/cirrhosis and has a significant effect. It can promote liver function to return to normal, alleviate the degree of liver fibrosis, reduce the level of LSM, and will not affect renal function. This method has fewer adverse reactions and greater safety, which is worthy of clinical promotion. However, there are limitations to this study. This study has a small sample size and a short period of follow-up. Researchers should plan for increased sample size in future research and extend the length of follow-up to provide a basis for clinical prevention and treatment of HBV-related liver fibrosis/cirrhosis.

AUTHOR DISCLOSURE STATEMENT

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REFERENCES

1. Belopolskaya M, Avrutin V, Kalinina O, Dmitriev A, Gusev D. Chronic hepatitis B in pregnant women: current trends and approaches. *World J Gastroenterol*. 2021;27(23):3279-3289. doi:10.3748/wjg.v27.i23.3279
2. Fang H. Analysis of pharmacist pharmaceutical service methods and value of entecavir in the treatment of chronic hepatitis B. *China Practical Medicine*. 2022;17(21):169-171.
3. Zhang J, Lin S, Jiang D, et al. Chronic hepatitis B and non-alcoholic fatty liver disease: conspirators or competitors? *Liver Int*. 2020;40(3):496-508. doi:10.1111/liv.14369
4. Zhao D, Yu S, Guo P, et al. Identification of potential plasma markers for hepatitis B virus-related chronic hepatitis and liver fibrosis/cirrhosis. *J Med Virol*. 2022;94(8):3900-3910. doi:10.1002/jmv.27761
5. Wang J, Ding W, Liu J, et al. Association of coexistent hepatitis B surface antigen and antibody with severe liver fibrosis and cirrhosis in treatment-naive patients with chronic hepatitis B. *JAMA Netw Open*. 2022;5(6):e2216485. doi:10.1001/jamanetworkopen.2022.16485
6. Shi J, Wang R, Sun K. Meta-analysis of the effect of chaishao liujunzi decoction combined with Western medicine on chronic hepatitis B. *Journal of Practical Chinese Medicine*. 2023;41-44(6):147-149. doi:10.13729/j.issn.1671-7813.Z20221038
7. Li T, Jiang M. Research progress in the treatment of chronic hepatitis B with traditional Chinese medicine. *China Modern Distance Education of Traditional Chinese Medicine*. 2021;19(21):206-208.
8. China Hepatitis Prevention and Control Foundation. Expert consensus on the diagnosis of liver fibrosis using transient elastography (2018 update). *Zhonghua Gan Zang Bing Za Zhi*. 2019;27(3):182-191.
9. Xia Q, He F. *Diagnosis and Treatment of Liver Cirrhosis*. People›s Health Publishing House; 2002.
10. Zheng X. *Guiding Principles for Clinical Research of New Traditional Chinese Medicine (Trial)*. China Pharmaceutical Science and Technology Press; 2002.
11. Yang D, Hu H, Li R, Tang CL, Ma KS, Guo DY. The diagnostic value of contrast-enhanced ultrasound LI-RADS for hepatocellular carcinoma in patients with cirrhosis and chronic hepatitis B. *Abdom Radiol (NY)*. 2022;47(2):630-639. doi:10.1007/s00261-021-03345-9
12. Sonneveld MJ, Hansen BE, Brouwer WP, et al; SONIC-B Study Group. Hepatitis B surface antigen levels can be used to rule out cirrhosis in hepatitis B e antigen-positive chronic hepatitis B: results rrom the SONIC-B study. *J Infect Dis*. 2022;225(11):1967-1973. doi:10.1093/infdis/jiaa192
13. Jeong S, Cho Y, Park SM, Kim W. Differential effectiveness of tenofovir and entecavir for prophylaxis of hepatocellular carcinoma in chronic hepatitis B patients depending on coexisting cirrhosis and prior exposure to antiviral therapy: a systematic review and meta-analysis. *J Clin Gastroenterol*. 2021;55(9):e77-e86. doi:10.1097/MCG.0000000000001548
14. Jin W, Bo W, Fang C. Clinical study of Diwu Yanggan capsule combined with diammonium glycyrrhizinate enteric-coated capsule in the treatment of chronic hepatitis B liver fibrosis. *Journal of Guangxi University of Traditional Chinese Medicine*. 2022;25(06):1-5.
15. Wu S, Zhao X, Zhang J, et al. Effects of entecavir combined with compound biejiruangan tablet on serum liver fibrosis and hepatitis B virus related indexes in patients with hepatitis B cirrhosis in active stage of compensatory stage. *Zhongguo Yaowu Yu Linchuang*. 2022;22(3):269-272.
16. Lu X. Clinical study of Ziyin bBaogan decoction in the treatment of liver cirrhosis. *Guangming Traditional Chinese Medicine*. 2020;35(03):355-357.
17. Liu W, Han T. Effects of Xuefu Zhuyu decoction on hepatic fibrosis and inflammatory factors in decompensated liver cirrhosis of hepatitis B. *Shiyong Yaowu Yu Linchuang*. 2021;24(9):821-825.
18. Hu H, Liu W, Tan L. Effect of tenofovir fumarate combined with Fuzheng Huayu therapy on the degree of liver fibrosis and immune status in patients with hepatitis B cirrhosis. *Hebei Med*. 2021;27(4):686-692.
19. He J, Yu S, Dong J, et al. Curative effect of Fuyuan Huoxue decoction on liver cirrhosis and its effect on liver fibrosis. *New Chinese Medicine*. 2021;53(18):29-32.
20. Ginès P, Castera L, Lammert F, et al; LiverScreen Consortium Investigators. Population screening for liver fibrosis: toward early diagnosis and intervention for chronic liver diseases. *Hepatology*. 2022;75(1):219-228. doi:10.1002/hep.32163
21. Koffas A, Kumar M, Gill US, Jindal A, Kennedy PTF, Sarin SK. Chronic hepatitis B: the demise of the 'inactive carrier' phase. *Hepatol Int*. 2021;15(2):290-300. doi:10.1007/s12072-021-10137-2
22. Peng J, He G, Liang P. Clinical effect of Hugan Jiexian decoction on liver cirrhosis. *Inner Mongolia Traditional Chinese Medicine*. 2021;40(07):47-48.
23. Geng Y. *Clinical observation on Wuzhuyu Wengan Decoction in the Treatment of Hepatitis B Liver Fibrosis with Liver Yang Deficiency*. Shandong University of Traditional Chinese Medicine; 2019.
24. Yu L, Jia A, Song Y. Research progress of saikosaponin in anti-inflammatory, antioxidant and lipid-lowering. *Chinese Journal of Arteriosclerosis*. 2020;28(1):87-92.
25. Yang S, Feng A, Sun Y, et al. Research progress in pharmacological action and mechanism of TGP. *China Modern Applied Pharmacy*. 2021;38(13):1627-1633.
26. Xing Y, Tian Z, Jiang Y, et al. A practical nomogram based on systemic inflammatory markers for predicting portal vein thrombosis in patients with liver cirrhosis. *Ann Med*. 2022;54(1):302-309. doi:10.1080/07853890.2022.2028893
27. Liu W, Han T. Effect of Xuefu Zhuyu decoction on liver fibrosis and inflammatory factors in decompensated hepatitis B cirrhosis. *Practical Medicine and Clinical*. 2021;24(9):821-825.
28. Jiang S, Tan S, Wen J. Chaishao Liujun decoction in the treatment of chronic hepatitis B liver fibrosis and its effect on serum Treg/Th17. *Shaanxi Traditional Chinese Medicine*. 2021;42(9):1229-1232.
29. Li Z, Xuan J, Zhao Z, et al. Research progress in chemical constituents and pharmacological activities of Pinellia ternata. *Liaoning Zhongyiyao Daxue Xuebao*. 2021;23(11):154-158.
30. Huang Y, Wu D, Wang S. Research progress in pharmacological action and drug pair of Scutellaria baicalensis. *China Pharmaceutical*. 2022;31(15):129-133.
31. Fu L, Fu Q, Li J, et al. Research progress in chemical constituents and pharmacological effects of Coptis chinensi. *J Tradit Chin Med*. 2021;49(02):87-92.
32. Du H, He W, Hu H, et al. Research progress in pharmacological action of active ingredients of Atractylodes macrocephal. *Jiangsu Traditional Chinese Medicine*. 2022;54(05):76-80.
33. Zuo J, Qi T, Hu X. Research progress in chemical composition and modern pharmacology of Poria coco. *J Tradit Chin Med*. 2023;51(01):110-114.
34. Xie Q, Cheng X, Hu F, et al. Research progress in chemical composition, pharmacological action and quality control of Codonopsis pilosula. *Shanghai Journal of Traditional Chinese Medicine*. 2020;54(08):94-104.
35. Ma Y, Wu W, Hu J, et al. Research progress in the chemical composition and pharmacological action of Angelica sinensis. *J Tradit Chin Med*. 2022;50(01):111-114.
36. Zhang Y, Lv H. Research progress in the chemical composition and pharmacological action of Psoralea corylifolia. *Electronic Journal of Clinical Medical Literature*. 2020;7(30):195.
37. Jin S, Zhang L. Research progress in pharmacological effect and clinical application of Scutellaria barbata. *Liaoning Zhongyiyao Daxue Xuebao*. 2021;23(08):194-198.
38. Dong Y, Xiang Y, Li L. Ruangan huaxian decoction should be used for the treatment of liver fibrosis in chronic hepatitis B and the improvement of liver function. *China Pharmaceutical and Clinical*. 2019;19(21):3766-3768.