

# Clinical Study on Treatment of Chronic Severe Intrahepatic Cholestatic Hepatitis with Liu Xi Decoction

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**Abstract:** Objective: Chronic severe intrahepatic cholestasis hepatitis is a clinical refractory disease. We have achieved good results in the treatment of chronic severe intrahepatic cholestasis hepatitis with Liu Chen Tang. This study aims to explore the clinical efficacy of Liu Chen Tang in the treatment of chronic severe intrahepatic cholestasis hepatitis. Methods: Thirty-five patients with chronic severe intrahepatic cholestatic hepatitis were randomly divided into Chinese medicine treatment group (n=23) and control group (n=12). The changes of symptoms, signs such as yellow eyes and body, fatigue, nausea, low food intake, and yellow urine and liver function including serum total bilirubin (TBIL), direct bilirubin (DBIL), alanine aminotransferase (ALT),  $\gamma$ -glutamyl peptide transferase (GGT), before and after treatment were observed. Results: The improvement of the above indicators in the treatment group was significantly better than that of the control group ( $P < 0.01$  or  $P < 0.05$ ). The effective rate of the treatment group was 95.6%, and the effective rate of the control group was 58.3%. Conclusion: Through the application of Liu Xi Decoction in the treatment of chronic severe intrahepatic cholestatic hepatitis, it was observed that the treatment group was significantly better than the control group. Liu Xi Decoction is an effective prescription for the treatment of chronic severe intrahepatic cholestatic hepatitis and is worthy of further popularization and application.

**Keywords:** Liu Xi Decoction, Chronic Severe Cholestatic Hepatitis, Clinical Research

## 1. Introduction

Chronic hepatitis B is a common clinical disease. In the process of chronic hepatitis B development, many patients have changed into chronic severe intrahepatic cholestatic hepatitis. Although the incidence rate is not very high, it is difficult to treat. Chronic severe intrahepatic biliary hepatitis is clinically characterized by severe yellowing, fatigue, nausea, low food intake, and yellow urine. The mechanism of this disease is mainly due to bile secretion, excretory dysfunction and capillary bile duct lesions of hepatocytes, resulting in a decrease in bile flow. Western medicine adopts the methods of protecting liver, choleric and removing jaundice, with poor curative effect, long course of treatment and high cost. In recent years, we have applied Zhu

Liangchun and his disciple-Qiu Zhiji's Liu Xi Decoction [1] to achieve good results in the treatment of chronic severe intrahepatic cholestatic hepatitis [2]. The summary report is as follows:

## 2. Materials and Methods

### 2.1. General Information

35 cases were outpatients or hospitalized patients in our hospital. They were randomly divided into Chinese medicine treatment group (n=23) and control group (n=12). In the Chinese medicine treatment group, there were 18 males and 5 females; the age ranged from 17 to 80 years, with an average of 48 years; the course of disease was 6 months to 10 years, with an average of 2.6 years; in the control group, 9 males and

3 females, with a course of 8 months - 9 years, an average of 2.4 years; aged 20-75 years, an average of 46 years. There were no significant differences in gender, age, and duration of disease between the two groups.

## 2.2. Diagnostic and Exclusion Criteria

Diagnosis complies with the diagnostic criteria for cholestatic hepatitis in the diagnostic criteria for chronic hepatitis cirrhosis in the 2000 Viral Hepatitis Prevention Program or the 2015 Guidelines for the Prevention and Treatment of Chronic Hepatitis B [3, 4], and all cases Have a history of chronic hepatitis B, liver function test serum Total bilirubin (TBIL) significantly increased (serum total bilirubin > 171 $\mu$ mol/L), mainly direct bilirubin (DBIL, ALT), prothrombin activity > 60% or application of vitamin K intramuscular injection After one week can be increased to more than 60%, serum bile acid, gamma glutamyl transpeptidase (GGT), alkaline phosphatase levels can be significantly increased, jaundice for more than 3 weeks, and Color ultrasound, CT and other imaging examinations exclude extrahepatic biliary obstructive jaundice and liver cancer with symptoms such as yellow eyes, yellow body, fatigue, nausea, poor appetite, and yellow urine [5].

## 2.3. Therapeutic Methods

The Chinese medicine treatment group was given Liu Xi Decoction, which was composed by diverse wormwood herb (liujinu) 15g, herba siegesbeckiae (xixiancao) 30g, bupleurum (chihu) 12g, radix paeoniae alba (chishao) 30g, bighead atractylodes rhizome (baizhu) 10g, poria cocos (fuling) 10g, rhizoma cyperi (xiangfu) 10g, radix curcumae (yujin) 10g, herba lycopi (zelan) 20g, alisma (zexie) 10g, capillary Artemisia (yinchen) 30g, fructus hordei germinates (maiya) 30g, etc [6, 7]. Those with obvious blood stasis add Salvia miltiorrhiza (danshen) and Rubia rubra (qiancao), etc. those with qi deficiency add Astragalus membranaceus (huangqi) 20g and Codonopsis pilosula (dangshen) 15g; heat obviously add Scutellaria baicalensis (huangqin) 10g, Gardenia jasminoides (zhizi) 10g and Rhubarb (dahuang) 6g, etc.; those with yin deficiency reduce Poria cocos (fuling), Alisma (zexie), add radix rehmanniae (shengdi) 10g, Ligustrum lucidum (nuzhengzi) 15g, Eclipta Grass (hanliancao) 20g, etc, inappetence, add Hawthorn (shanzha) 10g and Raphanus seed (laifuzi) 15g, etc [8]. Chinese herbal granules (from Guangzhou Yifang pharmaceutical company), one dose per

day, divided into two servings. The control group was given an intravenous infusion of 10% GS 250ml with Ganlixin 150mg once a day, 100mg of hepatocyte growth factor was added to 10% GS 250ml intravenously once a day, 30ml of Yinzhihuang injection was added to 10% GS 250ml intravenous drip, once a day [9]. Both groups were treated for 1 month, and 2 to 3 courses of treatment were continued depending on the condition.

## 2.4. Observed Indicators

Changes in symptoms and signs such as yellow eyes, yellow body, fatigue, nausea, low food intake, and yellow urine; liver function once every two weeks, including serum total bilirubin (TBIL), direct bilirubin (DBIL), alanine aminotransferase (ALT),  $\gamma$ -glutamyl peptide transferase (GGT), and the like [10].

## 2.5. Efficacy Criteria

The efficacy evaluation criteria of the "Viral Hepatitis Prevention and Control Program" were used to evaluate the effect of treatment. Significant effect: Symptoms and signs disappeared, serum bilirubin and transaminase decreased to normal or near normal; effective: Symptoms and signs improved significantly, serum bilirubin, transaminase decreased more than 50% before treatment, but not close to normal; invalid: symptoms and signs did not change significantly, serum bilirubin, transaminase did not decrease significantly, or did not meet the above criteria, or further worsened. Total effective rate = (obvious effective number of cases + number of effective cases)/total number of cases  $\times$  100% [1].

## 2.6. Statistical Methods

SPSS 21.0 statistical analysis software was used. Measurement data were expressed by ( $\bar{x} \pm s$ ), analyzed by t test; count data were analyzed by  $\chi^2$  test,  $P < 0.05$  was considered statistically significant.

# 3. Results

## 3.1. Changes in Symptoms and Signs

The main symptoms and signs of the Chinese medicine treatment group and the control group before and after treatment, the Chinese medicine treatment group improved symptoms significantly better than the control group. The results are shown in Table 1.

Table 1. Comparison of the number of improved symptoms and physical symptoms in the two groups (number of cases).

group	weak		poor appetite		jaundice		Urine yellow	
	Pre-treatment	After treatment						
treatment	20	18*	22	22**	23	22*	23	22*
control	9	4	10	6	12	8	12	7

\* $p < 0.05$ , \*\* $p < 0.01$  compared with the control group.

### 3.2. Changes of Liver Function

Changes in TBIL, DBIL, ALT and GGT before and after treatment in the Chinese medicine treatment group and the control group. The results are shown in Table 2.

Table 2. Changes of TBIL, DBIL, ALT and GGT before and after treatment in both groups ( $\bar{x} \pm s$ ).

group	ALT (IU/L)		GGT (IU/L)		TBIL ( $\mu\text{mol/L}$ )		DBIL ( $\mu\text{mol/L}$ )	
	Pre-treatment	After treatment	Pre-treatment	After treatment	Pre-treatment	After treatment	Pre-treatment	After treatment
treatment	551.3 $\pm$ 259.8	36.5 $\pm$ 8.7**	339.2 $\pm$ 171.6	39.9 $\pm$ 23.0**	266.9 $\pm$ 122.7	30.8 $\pm$ 50.1**	135.3 $\pm$ 72.1	16.2 $\pm$ 25.9**
control	542.4 $\pm$ 218.1	133.4 $\pm$ 90.9	346.2 $\pm$ 143.6	123.8 $\pm$ 88.1	254.3 $\pm$ 127.8	118.5 $\pm$ 82.7	140.1 $\pm$ 65.5	59.7 $\pm$ 28.9

\* $p < 0.05$ , \*\* $p < 0.01$  compared with the control group.

### 3.3. Comparison of Curative Effect Between Two Groups

Comparison of the efficacy between the Chinese medicine treatment group and the control group, The results are shown in Table 3.

Table 3. Comparison of the efficacy of the two groups (number of cases).

group	n	obvious effect	Effective	Inefficacy	Total effective rate
treatment	23	17	5	1	95.6%**
control	12	4	3	5	58.3%

\* $p < 0.05$ , \*\* $p < 0.01$  compared with the control group.

In the Chinese medicine treatment group, 17 patients were markedly effective, 5 were effective, 1 were ineffective, and the total effective rate was 95.6%. In the control group, 4 patients were markedly effective, 3 were effective, 5 were ineffective, and the total effective rate was 58.3%. After statistical treatment, the difference between the treatment group and the control group was highly significant ( $p < 0.01$ ).

## 4. Discussion

Chronic severe Intrahepatic cholestatic hepatitis is clinically characterized by severe yellowing, fatigue, nausea, low food intake, and yellow urine. Liver function tests showed a significant increase in total bilirubin and direct bilirubin (serum total bilirubin  $> 171 \mu\text{mol/L}$ ), and jaundice lasted for a long time. The mechanism of this disease is mainly due to bile secretion, excretory dysfunction and capillary bile duct lesions of hepatocytes, resulting in a decrease in bile flow. There are generally hepatocyte degeneration, necrosis and infiltration of inflammatory cells in the portal area and lobule. The combination of bilirubin and excretion disorders are associated with aggravation of liver disease. Long-term hyperbilirubinemia, especially indirect hyperbilirubinemia, which is mainly caused by indirect bilirubin, can be deposited in hepatocytes, leading to liquefaction or coagulative necrosis of hepatocytes. Hyperbilirubinemia can not only aggravate liver cell damage, but also inhibit the release and activity of various factors related to bilirubin metabolism. Therefore, serum total bilirubin is progressively elevated, and prothrombin activity (PA) is gradually decreased, and become non-hepatic parenchymal necrotizing chronic severe hepatitis [11, 12]. Therefore, long-term hyperbilirubinemia will seriously affect the prognosis of patients, and the use of active treatment to accelerate the regression of jaundice is the key to

improving the prognosis of patients [13].

Chronic hepatitis B is a common clinical disease. In the process of chronic hepatitis B development, many patients have changed into chronic severe intrahepatic cholestatic hepatitis. Although the incidence rate is not very high, it is difficult to treat. Western medicine adopts the methods of protecting liver, choleric and reducing yellow, with poor curative effect, long course of treatment and high cost. In recent years, we have applied Zhu Liangchun and his disciple Qiu Zhiji's Liu Xi Decoction to achieve good results in the treatment of chronic severe jaundice [14]. Mr. Zhu Liangchun pointed out that due to the puzzlement of liver depression and spleen dampness for a long time, the liver and gallbladder failed to drain normally, and the jaundice could not be cured for a long time, and the liver and gallbladder stasis was often blocked. It was sthenia syndrome. It is advisable to use Liuxi Decoction to soothe the liver and relieve depression, clear away heat and dampness, promote blood circulation and remove blood stasis. Diverse wormwood herb (liujin) and herba siegesbeckiae (xixiancao), calming liver and removing blood stasis, detoxifying and activating blood circulation, eliminating disease and dispersing knots, eliminating jaundice and reducing enzymes, have the function of dominating hepatic jaundice [15]. These two herbs are the main ones in the prescription and have the compatibility characteristics of the prescription; herba lycopi (zelan), alisma (zexie) and capillary Artemisia (yinchen), clearing liver, eliminating gallbladder, eliminating yellow, dredging Triple Energizer; Poria cocos (fuling) and bighead atractylodes rhizome (baizhu) to invigorate spleen and dispel dampness; long-term jaundice will be blood stasis, so bupleurum (chaihu), radix paeoniae alba (chishao), rhizoma cyperi (xiangfu) and radix curcumae (yu jin) soothing liver depression, nourishing blood and promoting blood circulation, fructus hordei germinates (maiya)

for stomach-strengthening and digestion. According to the clinical symptoms, it should be added or subtracted appropriately. Due to proper compatibility and pathogenesis, the prescription can achieve good clinical effect and is worthy of further popularization and application [7].

## 5. Conclusion

Through the application of Liu Xi Decoction in the treatment of chronic severe intrahepatic cholestatic hepatitis, it was observed that the treatment group was significantly better than the control group. Liu Xi Decoction is an effective prescription for the treatment of chronic severe intrahepatic cholestatic hepatitis and is worthy of further popularization and application.

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## References

- [1] Qiu Zhiji, Zhu Jianhua, Ma Yuqing. Zhu Liangchun's characteristics of miscellaneous diseases and integrity [M]. Beijing: Traditional Chinese Medicine Publishing House, 2004, 211-212
- [2] Jiang Xuelian, Zhang Guodong, Sun Yunting, Wei Ming, Yang Jichao, Liu Zhixue. Clinical study of Liu Xi Decoction in the treatment of chronic severe intrahepatic cholestatic hepatitis [J]. Chinese medical emergencies, 2008 (09): 1217-1218.
- [3] Chinese Medical Association Infectious Diseases and Parasitic Diseases Branch, Liver Diseases Branch. Diagnostic criteria for viral hepatitis [J]. Chinese Journal of Integrated Traditional and Western Medicine, 2001, 11 (1): 56-60
- [4] Wang Guiqiang, Wang Fusheng, Cheng Jun, Ren Hong, Zhuang Hui, Sun Jian, Li Lanjuan, Li Jie, Meng Qinghua, Zhao Jingmin, Duan Zhongping, Hou Jinlin, Jia Jidong, Tang Hong, Sheng Jifang, Peng Yu, Lu Fengmin, Xie Qing, Wei Come. Guidelines for the Prevention and Treatment of Chronic Hepatitis B (2015 Edition) [J]. Journal of Practical Hepatology, 2016, 19 (03): 389-400.
- [5] Huang Dawei, Ye Chunsheng, Wang Xiaodong. Observation on the efficacy of reusing blood circulation and removing blood stasis combined with western medicine in the treatment of refractory jaundice [J]. Hubei Journal of Traditional Chinese Medicine, 2017, 39 (07): 25-26.
- [6] Jiang Yiming, Jiang Xuelian, Liu Xinjun et al. Study on the optimization of liver fibrosis in patients with chronic hepatitis B treated by traditional Chinese medicine [J]. World Journal of Integrated Traditional Chinese and Western Medicine, 2015, 10 (01): 75-77.
- [7] Jiang Yiming, Jiang Xuelian, Wang Huikai et al. Clinical study of Liu Xiaoyao Wuqi Decoction in the treatment of chronic hepatitis B liver fibrosis [J]. Modern Journal of Integrated Traditional Chinese and Western Medicine, 2016, 25 (24): 2655-2657.
- [8] Jia Jianying, Lu Yuliang, Wang Huikai, Jiang Xuelian. Professor Jiang Xuelian's treatment of hepatitis B virus [J]. Shanxi Chinese Medicine, 2018, 39 (09): 1301-1303.
- [9] Zhou Houqin, Zhang Wei, Lu Xiaohua, Yang Yuxue, Wang Yingying, Zhao Yanling. Research progress in the treatment of cholestatic hepatitis with traditional Chinese medicine [J]. Evaluation and analysis of drug use in hospitals in China, 2018, 18 (12): 1588-1590+1594.
- [10] Wan Wanxiang, Wang Daguang, Shi Jia, Chen Hongkuan, Deng Linlin. Effect of Integrative Chinese and Western Medicine on Cholestatic Hepatitis [J]. Shanxi Journal of Traditional Chinese Medicine, 2017, 33 (07): 20+25.
- [11] Ji Yang, Guo Mingxing. Treatment of 38 cases of chronic type B cholestatic hepatitis with Ligan Huihuang Mixture [J]. Journal of Integrated Traditional and Western Medicine on Liver Diseases, 2018, 28 (03): 180-181.
- [12] Wang Chengbai. Diagnosis and treatment of chronic severe hepatitis with integrated traditional Chinese and Western medicine [M]. Hebei Zhengding: Handout of the Second National Advanced Chinese and Western Medicine Treatment of Hepatic Diseases, 2003, 35-51
- [13] Yan Ying, Song Maozhou, Liang Chaorong. Clinical observation of adenosylmethionine combined with ursodeoxycholic acid in the treatment of chronic severe cholestatic hepatitis B [J]. Journal of Shanxi College of Traditional Chinese Medicine, 2013, 14 (03): 68-69.
- [14] Jiang Xuelian, Liu Xinjun. On the Treatment of Huangqi Disease in "The Golden Chamber" [J]. Chinese Journal of Emergency Medicine, 2014, 23 (02): 298-299.
- [15] Liu Xinjun, Jing Xuelian. Clinical research progress of traditional Chinese medicine in the treatment of chronic hepatitis B liver fibrosis [J]. Journal of Binzhou Medical College, 2013, 36 (06): 437-439.

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