

## Original Article

# The clinical observation of Fuganling water decoction for ninety patients with chronic hepatitis B

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**ABSTRACT** 135 patients with hepatitis B were enrolled and randomly divided into Fuganling treated groups (90 cases) and Yiganning treated groups (45 cases). Fuganling treated group: Decocted twice with mild fire according to the prescription. Took twice orally each day and each treatment period was 30 days. There were 3 periods in all. Yiganning control group: Took 19g each time and 3 times each day. Each treatment period was 30 days. There were 3 periods in all. Both groups added liver-aid tablet and vitamin C to protect the liver during the treatment. The cure rate was 25.6% (23 cases), effective rate was 72.2% (65cases), ineffective rate was 2.2% (2cases) in all 90 chronic hepatitis patients. The total effective rate reached to 97.8%. In Yiganning group, the cure rate was 17.8% (8 cases), effective rate was 58.9% (27cases), ineffective rate was 21.1% (10cases) in all 45 hepatitis patients. The total effective rate was 76.7%. Compared with Yiganning group, the total effective rate of Fuganling group increased 21.1%. Fuganling had an significant therapy effect on chronic hepatitis.

**KeyWords:** chronic hepatitis B; Fuganlingtem (ES) cells, reprogramming, pluripotency, epigenetic modification

Traditional Chinese Medicine (TCM) believes that the original etiological factor for HBV infection is “damp-heat”, which belongs to the category of warm pathogens. By analyzing and differentiating the development of an epidemic febrile disease and by studying conditions of the four systems (Wei, Qi, Ying, Xue) of patients with coagulation disorder, Yingfen syndrome and Xuefen syndrome are diagnosed. As one of the febrile disease characteristics, warm pathogen can injure yin easily, meanwhile “cooling the blood and invigorating blood circulation” is the traditional therapeutic method for Xuefen syndrome. Therefore, we chose TCM (Fuganling water decoction) to treat liver cirrhosis accompanying coagulation disorder by nourishing yin, cooling the blood and invigorating blood circulation.

## 1 Materials and Methods

### 1.1 Composing Prescriptions and Sources

The prescription was provided by Professor Liu Zhiyu, Medical

School of Shandong University based on traditional proved recipes and abundant clinical practices. It was made of six traditional Chinese medicine herbs such as yellow sweet clover (16g), Artemisia Capillaris (12g), Scutellaris (9g), Herba abri (9g), loosestrife (9g), Glycyrrhiza Uralensis(3g).

Yiganning was bought from Jintai Pharmacy and produced by Banzhou Pharmacy limited company of Guangxi with the batch number of zz 5010-079023, 17g/pack .

### 1.2 Clinical Data

#### 1.2.1 Cases Selection

135 patients with hepatitis B were enrolled and divided into Fuganling treated groups (90 cases) and Yiganning treated groups (45 cases) randomly according to Chinese National Hepatitis Control Plan and Diagnostic Criterion .

#### 1.2.2 Patients' Characteristics

In Fuganling treated group, patients with mild was 20cases while patients with moderate was 45 cases and severe patients was 25cases. Of all the 90 cases, 65 cases were males and 25 cases were females. Their ages ranged from 9 to 72 years olds with a mean age of 43 years old while the course ranged from 1 to 8 years with the mean of 4.2 years. In Yiganning treated group, patients with mild was 15cases while patients with moderate was 23 cases and severe patients was 7cases. Of all the 45 cases, 32cases were males and 13 cases were females. Their ages ranged from 12 to 68 years olds with a mean age of 42 years old, while the course ranged

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from 0.8 to 7 years with the mean of 3.9 years. All the patients suffered from abnormal liver function and had positive hepatitis B markers and obvious subjective symptoms such as inertia, inappetence, detesting oils and liver pain before treated. There was no significant difference in age, sex and course between two groups ( $P>0.05$ ). In addition, the alcoholic-toxic hepatitis patients, the pregnant women, lactating women, the patients with the serious heart, lung, brain and kidney diseases were rejected.

### 1.2.3 Therapy

Fuganling treated group: Decocted twice with mild fire according to the prescription Took twice orally each day and each treatment period was 30 days. There were 3 periods in all. Yiganning control group: Took 19g each time and 3 times each day. Each treatment period was 30 days. There were 3 periods in all. Both groups added liver-aid tablet and vitamin C to protect the liver during the treatment. Observed indexes include: 1) Symptoms and Signs: Recorded inertia, inappetence, abdominal distention, liver pain, jaundice, hepatosplenomegaly and ascites every 7days; 2) Liver Tests: Tested AST, ALT,  $\gamma$ -GT and SB every two weeks; 3) Other Tests: Tested albumin(A), globulin(G) and total protein(T) every two days; 4) Hepatitis B Markers: Tested HbsAg, HbeAg, anti-HBc, anti-HBs, anti-HBe, anti-HBcIgM and HBV-DNA every four weeks.

### 1.2.5 Curative Judgment

Divided the curative standard into basic cure, effective and ineffective according to Principles for Clinical Study on Hepatitis Therapy of New Chinese Medicine.

(1) Basic cure: The symptoms disappeared, hepatosplenomegaly retracted or unchanged and had no significant tenderness, liver function recovered and HbsAg, HBeAg, anti-HBc became negative after two courses.

(2) Effective: The symptoms markedly-improved, hepatosplenomegaly unchanged and had no significant tenderness, liver function recovered or decreased to half of the peak, hepatitis B markers

unchanged or one of them became negative.

(3) Ineffective: Subjective symptoms and signs had no improved, liver function and hepatitis markers unchanged.

### 1.2.6 Statistical methods

Measurement data were expressed by  $\pm S$ , inter- and intra groups were analyzed by t text; enumeration data intra groups were compared with U test.

## 2 Results

### 2.1 Effect of Fuganling

The cure rate was 25.6% (23 cases), effective rate was 72.2% (65 cases), ineffective rate was 2.2% (2 cases) in all 90 chronic hepatitis patients. The total effective rate reached to 97.8%. In Yiganning group, the cure rate was 17.8% (8 cases), effective rate was 58.9% (27 cases), ineffective rate was 21.1% (10 cases) in all 45 hepatitis patients. The total effective rate was 76.7%. Compared with Yiganning group, the total effective rate of Fuganling group increased 21.1%.

### 2.2 The effect of Fuganling on improvement of symptoms and signs

The patients' appetite improved, the symptoms such as abdominal distention, hypodynamia and liver pain significantly disappeared after two weeks therapy. One month later, the signs such as hepatosplenomegaly, jaundice disappeared. There was significant difference between two groups ( $P<0.05$ ,  $P<0.01$ ) (Table 1).

### 2.3 The influence of Fuganling and Yiganning on serum liver function indexes

The liver function of both groups were all abnormal pre treatment. The AST, ALT and  $\gamma$ -GT decreased 89.3%, 87.4%, 82.9% in

Table 1

The comparison of symptoms and signs between Fuganling group and Yiganning group pre and post treatment

Symptoms and Signs	Yiganning group			Fuganling group		
	Abnormal cases before treated	Normal cases after treated	Effective rate(%)	Abnormal cases before treated	Normal cases after treated	Effective rate(%)
Inappetence	41	23	76.2	69	69	100.0**
Inertia	45	37	82.2	88	81	92.0*
Liver pain	41	26	63.4	82	81	98.8**
Abdominal Distention	38	22	57.9	53	48	90.1**
Jaundice	37	15	40.5	41	26	63.4*
Hepatomegaly	37	20	54.5	78	72	92.3*
Splenomegaly	36	19	52.7	73	56	76.7*

Noted: Fuganling treated group compared to Yiganning treated group \* $P<0.05$ , \*\* $P<0.01$

Table2  
The comparison of liver function pre and post treatment

Liver function index	Yiganning group				Fuganling group			
	N	Before treated	After treated	Decline rate(%)	n	Before treated	After treated	Decline rate(%)
AST	45	396.64	92.45	78.9	90	432.12	65.09	89.3*
		± 132.13	± 14.32			± 169.74	± 11.69	
ALT	45	346.52	82.13	74.2	90	386.16	48.24	87.4**
		± 106.32	± 16.94			± 123.46	± 8.92	
γ -GT	45	132.62	39.39	69.8	90	126.39	24.66	82.9**
		± 31.68	± 8.25			± 28.32	± 4.32	

Noted: Fuganling treated group compared to Yiganning treated group, \*P<0.05, \*\*P<0.01

Table3  
The influence of Fuganling and Yiganning on serum biochemical index

Tested index	Yiganning group				Fuganling group			
	n	Before treated	After treated	Decline rate (%)	n	Before treated	After treated	Decline rate (%)
SB	36	116.36	36.24	71.2	72	124.92	20.88	84.2
( $\mu \text{ mol} \cdot \text{L}^{-1}$ )		± 28.12	± 6.68			± 28.30	± 5.64	
Total protein	45	66.28	68.70	-	90	66.02	70.18	-
( $\text{g} \cdot \text{L}^{-1}$ )		± 3.12	± 2.43			± 5.48	± 1.96*	
Albumin	45	37.23	37.23	-	90	37.98	41.82	-
( $\text{g} \cdot \text{L}^{-1}$ )		± 4.92	± 4.92			± 3.21	± 3.32*	

Noted: Fuganling treated group compared to Yiganning treated group after treated, \*P<0.05

Table4  
The influence of Fuganling and Yiganning on hepatitis markers

Tested index	Yiganning group			Fuganling group		
	Positive before treated (n)	Negative after treated (n)	Negative rate(%)	Positive before treated (n)	Negative after treated (n)	Negative rate (%)
HbsAg	45	7	15.5	90	37	41.1**
HbeAg	45	15	33.3	90	49	54.4**
anti-HBc	45	9	20.0	90	32	35.5**
anti-HbcIgM	36	8	22.2	82	44	53.6**
HBV-DNA	45	20	44.4	90	53	58.8**

Noted: the treated group compared to the control group, \*\*P<0.01

the Fuganling group while 78.9%,74.2%,69.8% in the Yiganning group .There was significant difference between two groups (P<0.05,P<0.01) as well as pre and post treatment.(Table 2).

#### 2.4 The influence of Fuganling and Yiganning on other serum biochemical indexes

The SB,the total protein and the albumin were all abnormal in both groups before treated .The SB decreased 84.2% after Fuganling treated and there was significant difference comparing to the

Yiganning group (P<0.01).The total protein in both groups increased and there was no significant difference(P>0.05) .The albumin in both groups increased and there was significant difference between two groups (P<0.05).There was significant difference pre and post treatment in each group (P<0.01).(Table 3).

#### 2.5 The influence of Fuganling and Yiganning on the hepatitis markers

The HBsAg ,HBeAg and anti-HBc in both groups were positive

before treated ,that was to say, it was great three positive .There were some negative cases after treated in both groups .The negative rate of HbsAg ,HbeAg and anti-HBc were 41.1%, 54.4%, and 35.5%, respectively in Fuganling group while 15.5%, 33.3%, and 20.0% in Yiganning group. There was significant difference between two groups ( $P<0.01$ ). There was significant difference in the negative rate of the anti-HbcIgM and HBV-DNA ( $P<0.01$ ). It showed that the negative rate in Fuganling group was much higher than in the Yiganning group.(Table 4).

### 3 Discussion

We developed the Fuganling preparation taking the yellow sweet clover as the monarch drug while the *Artemisia Capillaris* and *Scutellaris* as the minister drug based on traditional Chinese medicine theory and modern scientific technology to therapy the hepatitis. We also did a series of researches on its pharmacodynamics such as preventing liver injury, anti-HBV and regulating immune function and acute and chronic toxicity pharmacological experiment. The result showed that the Fuganling played an important role in protecting liver, reducing enzyme and receding jaundice.

This prescription had significant effect on hundreds of acute and chronic viral hepatitis patients during the long clinical observation. It was committed as the priority subject and the ninth five-year key project by the Chinese medicine administration of Shandong Province, Shandong province science and technology commission, national Chinese medicine administration, national medical office and national science and technology commission successively. This study selected 90 chronic viral hepatitis patients based on national standard and was committed by the Shandong provincial department of health. The result suggested that the Fganling played an important role in protecting liver, reducing enzyme and receding jaundice. It can recover the liver function and make the hepatitis markers turn negative .The clinical observation was corresponding

with the normal clinical following up and pharmacological animal and pharmacodynamics experiment .

The animal experimentation showed that this prescription can prevent carbon tetrachloride liver injury, protect liver cell, reduce the malondialdehyde (MDA) level and have the anti-lipid peroxidation effects, thus can keep the liver cell from the inflammatory reaction and the immunologic injury. The duck hepatitis B virus (DHBV) pharmacodynamics experiment under the directions of the Professor Chen Hongshan in the Institute of Medical Biotechnology of the Union Medical University, Chinese Academy of Science showed that Fuganling can significantly inhibit the DHBV-DNA and end the viral replication. The model also suggested that both DHBV and HBV belonged to hepatotropic virus and had the same character of the viral replication. DHBV-DNA polymerase (DHBV-DNAp) was the key enzyme in DHBV-DNA replication. It played an important role during replication and transcription. It prevented the virus by inhibiting DHBV-DNAp and HBV replication. The anti-hepatitis effect of Fuganling mainly related to inhibiting the DHBV-DNAp activity. There was no toxicity during its long process. None of the patients had the headache, nausea, omitting and diarrhea. Only a few of them appeared intestinal increased, soft stool but never appeared the diarrhea and abnormal pain. Fuganling had an significant therapy effect on chronic hepatitis.

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