Influence of compound glycyrrhizin on liver functions, liver fibrosis indexes and inflammatory factors of patients with chronic hepatitis B

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ABSTRACT

Objective: To investigate influence of Compound Glycyrrhizin on liver functions, liver fibrosis indexes and inflammatory factors of patients with chronic hepatitis B. Methods: A total of 96 cases of patients with chronic hepatitis B treated in our hospital from Jan2015 to Jun2016 were selected as subjects, and randomly divided to be 48 cases of observation group and 48 cases of control group. Patients in both of the two groups were received routine liver protecting drug treatment. For observation group, Compound Glycyrrhizin injection was given on the basis of routine treatment. Variations of liver function indexes, liver fibrosis indexes and inflammatory factors between the two groups before and after treatment were compared and observed. Results: No obvious difference showed on AST, ALT, ALB, TBIL levels between two groups of patients before treatment; After treatment, AST, ALT, TBIL in two groups of patients were significantly decreased, ALB were significantly increased. Significant difference showed comparing with prior treatment; After treatment, AST, ALT and TBIL in observation group were (29.53±9.44) U/L, (32.36±10.93) U/L and (10.12±3.22) μmol/L, which were significantly lower than in control group. ALB levels in observation group were (43.57±12.42) g/L, which were significantly higher than ALB levels in control group. Before treatment, no statistical difference showed on HA, LN, IV-C and PCIII levels between two groups of patients. After treatment, HA, LN, IV-C and PCIII in two groups of patients were significantly decreased, which showed significant difference comparing with prior treatment; After treatment, HA, LN, IV-C and PCIII levels in observation group were (97.33±31.75) μg/L, (77.52±23.72) μg/L, (82.92±24.55) μg/L, (15.33±5.11) μg/L, which were significantly lower than in control group. Before treatment, no significant difference showed on IL-2, IL-6 and TNF-α levels between two groups of patients; After treatment, IL-2 levels in observation group were (131.48±30.63) U/mL, which were higher than IL-2 levels in control group. IL-6 and TNF-α levels in observation group were (45.23±16.45) μg/L, (41.75±17.53) ng/L, which were lower than IL-6 and TNF-α levels in control group, differences showed significance. Conclusion: Compound Glycyrrhizin could effectively release liver fibrosis and inflammatory reactions for patients with chronic hepatitis B, and could further improve liver functions.

1. Introduction

Chronic hepatitis B is a common intractable infectious disease on clinic. Situation of its morbidity in our country is quite grim[1-3]. Continuous replication of hepatitis B virus DNA (HBV DNA) could progressively damage liver[4,5], and induce process of liver fibrosis. Too long time of fibrosis and excessive deposition of fibrous tissue could lead to appearance of liver cirrhosis, and further exacerbate the disease[6-9]. In addition, damage mechanism of chronic hepatitis B is closely related with immune inflammatory reactions[10]. In recent years, Compound Glycyrrhizin in hepatitis B therapies has been widely utilized[11]. Our research used Compound Glycyrrhizin to treat patients with chronic hepatitis B, and observe the influence of it on liver functions, liver fibrosis indexes and inflammatory...
factors. Presently reports as follows.

2. Materials and methods

2.1 General materials

A total of 96 cases of patients with chronic hepatitis B treated in our hospital from Jan 2015 to Jun 2016 were selected as subjects. Included requirements showed as follows:

Included standards: (1) Patients were met with diagnosis standards in Chronic Hepatitis B Guideline (2015 revised edition)[12]; (2) Ages were not less than 18 years old; (3) Patients had not been received anti-fibrosis and antiviral treatments, such as immunomodulators and hormones recently.

Excluded standards: (1) Superinfection of hepatitis A, C, E combination; (2) Severe lesion of hyperbilirubinemia, liver cirrhosis and liver cancer combination; (3) Patients with dysfunctions of respiratory system, circulatory system and blood system, etc.; (4) Pregnant women, lying-in women and lactating women. The selected 96 cases of patients were randomly divided to be 48 cases of observation group and 48 cases of control group. In observation group, there were 26 male cases and 22 female cases, the minimum age was 21 years old, the maximum age was 63 years old; Disease courses were ranged from 1-11 years, the average course was (5.12±1.03) years. In control group, there were 28 male cases and 20 female cases, the minimum age was 19 years old, the maximum age was 61 years old; Disease courses were ranged from 1-12 years, the average course was (5.25±1.35) years. Compared with clinical materials between two groups of patients, such as genders, ages and disease courses, the differences showed no statistical significance (P>0.05). The balanced comparability existed.

2.2 Methods

Routine therapies of liver protective medicine were provided to two groups of patients, included potassium magnesium aspartate, vitamins, inosine, hepatocyte growth-promoting factor and so forth. Meanwhile, balance of water and electrolyte were sustained, and complications were positively prevented. For observation group, Compound Glycyrrhizin injection (manufacturer: Xi’an Li Jun Pharmaceutical Co., Ltd.) was given on the basis of routine therapies. Each time 60-80 mL of injection was extracted, and injected into 5% 250 mL Glucose solution for administration via intravenous drip, 1 x/d, continuously used for 8 weeks.

2.3 Observation indexes

Venous blood was separately collected from two groups of patients with empty stomach before and after treatment, stored and waited for detection in -70 °C refrigerator after serum isolated.

(1) Liver function indexes: automatic biochemical analyzer (Model: Siemens 2400, Germany) and related reagents were utilized to detect serum Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), albumin (ALB) and total bilirubin (TBIL) levels in two groups of patients.

(2) Liver fibrosis indexes: chemical light method was used to detect serum hyaluronic acid (HA), laminin (LN), IV-collagen (IV-C) and III-pre-collagen (PCIII) in two groups of patients. The kits were bought from Shenzhen new industry biomedical engineering Limited by Share Ltd.

(3) Inflammatory factors: enzyme immunooassay of solid phase chemiluminescence was utilized to detect interleukin-2 (IL-2) levels. Method of ELISA with double-antibody sandwich was used to detect interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α) levels, the kits were provided by Shenzhen Jingmei Ltd.

2.4 Statistical analysis

SPSS 19.0 was utilized to count and analyze all the detected data. Measurement data were indicated as Mean ± SD. T test of independent sample was used to compare between two groups, paired-samples t test was used to compare within each group. P<0.05 showed that statistical difference was existed compared of two indexes.

3. Results

3.1 Comparison of liver function indexes in two groups

No significant difference showed on AST, ALT, ALB and TBIL levels in two groups of patients before treatment (P>0.05); For observation group, ALT, AST and TBIL were significantly decreased after treatment comparing with the group before treatment, ALB were significantly increased, differences showed significance (P<0.05); For control group, ALT, AST and TBIL were significantly decreased after treatment comparing with the group before treatment, ALB were significantly increased, differences showed significance (P<0.05); After treatment, ALT, AST and TBIL levels in observation group were (29.53±9.44) U/L, (32.36±10.93) U/L and (10.12±3.22) μmol/L, which were significantly lower than ALT, AST and TBIL levels in control group. ALB levels in observation group were (43.57±12.42) g/L, which were significantly higher than ALB levels in control group (P<0.05). See table 1.
Comparison of liver function indexes in two groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>ALT (U/L)</th>
<th>AST (U/L)</th>
<th>ALB (g/L)</th>
<th>TBIL (μmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>48</td>
<td>Before treatment</td>
<td>222.35±44.33</td>
<td>177.33±25.17</td>
<td>36.68±12.24</td>
<td>28.57±9.52</td>
</tr>
<tr>
<td>Control</td>
<td>48</td>
<td>Before treatment</td>
<td>29.53±9.44</td>
<td>32.36±10.93</td>
<td>43.57±12.42</td>
<td>10.12±3.22</td>
</tr>
<tr>
<td>Observation</td>
<td>48</td>
<td>After treatment</td>
<td>220.53±41.50</td>
<td>178.66±27.52</td>
<td>37.10±12.83</td>
<td>29.37±9.29</td>
</tr>
<tr>
<td>Control</td>
<td>48</td>
<td>After treatment</td>
<td>35.34±12.26</td>
<td>38.57±12.63</td>
<td>40.22±10.44</td>
<td>15.47±5.17</td>
</tr>
</tbody>
</table>

Note: Compared with the same group before treatment, IL-2 were significantly increased, IL-6, TNF-α before treatment, differences showed significance (P<0.05); For observation group, HA, LN, IV-C, PCIII were significantly decreased after treatment comparing with the group before treatment (P<0.05); Compared with control group at the same phase, differences showed statistical significance (P<0.05).

Table 2.
Comparison of liver fibrosis indexes in two groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>HA (μg/L)</th>
<th>LN (μg/L)</th>
<th>IV-C (μg/L)</th>
<th>PCIII (μg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>48</td>
<td>Before treatment</td>
<td>186.42±63.42</td>
<td>154.76±50.22</td>
<td>187.57±61.55</td>
<td>82.55±23.63</td>
</tr>
<tr>
<td>Control</td>
<td>48</td>
<td>Before treatment</td>
<td>97.33±31.75</td>
<td>77.52±23.72</td>
<td>82.92±24.55</td>
<td>15.33±5.11</td>
</tr>
<tr>
<td>Observation</td>
<td>48</td>
<td>After treatment</td>
<td>191.52±63.73</td>
<td>157.72±51.55</td>
<td>186.42±63.42</td>
<td>80.54±25.46</td>
</tr>
<tr>
<td>Control</td>
<td>48</td>
<td>After treatment</td>
<td>130.46±42.48</td>
<td>115.82±35.83</td>
<td>97.33±31.75</td>
<td>20.55±3.55</td>
</tr>
</tbody>
</table>

Note: Compared with the same group before treatment, IL-2 were significantly increased, IL-6, TNF-α before treatment, differences showed significance (P<0.05); For observation group, HA, LN, IV-C, PCIII were significantly decreased after treatment comparing with the group before treatment (P<0.05); After treatment, HA, LN, IV-C, PCIII levels in observation group were (97.33±31.75) μg/L, (77.52±23.72) μg/L, (82.92±24.55) μg/L, (15.33±5.11) μg/L, which were significantly lower than in control group (P<0.05). See table 2.

Table 3.
Comparison of inflammatory factors in two groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>IL-2(U/mL)</th>
<th>IL-6(μg/L)</th>
<th>TNF-α (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>48</td>
<td>Before treatment</td>
<td>56.15±10.24</td>
<td>103.42±16.45</td>
<td>91.43±30.55</td>
</tr>
<tr>
<td>Control</td>
<td>48</td>
<td>Before treatment</td>
<td>131.48±30.63</td>
<td>45.23±16.45</td>
<td>41.75±17.53</td>
</tr>
<tr>
<td>Observation</td>
<td>48</td>
<td>After treatment</td>
<td>53.27±12.41</td>
<td>105.76±29.53</td>
<td>89.53±28.42</td>
</tr>
<tr>
<td>Control</td>
<td>48</td>
<td>After treatment</td>
<td>81.47±22.71</td>
<td>72.41±26.42</td>
<td>63.50±18.27</td>
</tr>
</tbody>
</table>

Note: Compared with the same group before treatment, IL-2 were significantly increased, IL-6, TNF-α levels in observation group were (45.23±16.45) μg/L, (41.75±17.53) ng/L, which were lower than in control group, differences showed statistical significance (P<0.05).

3.2 Comparison of liver fibrosis indexes in two groups

No significant difference showed on HA, LN, IV-C, PCIII levels in two groups of patients before treatment (P>0.05); For observation group, HA, LN, IV-C, PCIII were significantly decreased after treatment comparing with the group before treatment, differences showed significance (P<0.05); For control group, HA, LN, IV-C, PCIII were significantly decreased after treatment comparing with the group before treatment (P<0.05); After treatment, HA, LN, IV-C, PCIII levels in observation group were (97.33±31.75) μg/L, (77.52±23.72) μg/L, (82.92±24.55) μg/L, (15.33±5.11) μg/L, which were significantly lower than in control group (P<0.05). See table 2.

3.3 Comparison of inflammatory factors in two groups

No statistical difference showed on IL-2, IL-6, TNF-α levels in two groups of patients before treatment (P>0.05); For observation group, IL-2 were significantly increased, IL-6, TNF-α were significantly decreased after treatment comparing with the group before treatment, differences showed significance (P<0.05); For control group, IL-2 were significantly increased, IL-6, TNF-α were significantly decreased after treatment comparing with the group before treatment, differences showed significance (P<0.05); After treatment, IL-2 levels in observation group were (131.48±30.63) U/mL, which were higher than in control group (P<0.05). IL-6, TNF-α levels in observation group were (45.23±16.45) μg/L, (41.75±17.53) ng/L, which were lower than in control group, differences showed statistical significance (P<0.05).

4. Discussion

Chronic hepatitis B is a common intractable infectious disease on clinic, which is quite popular all over the world. Our country is a high-prevalence area of hepatitis B. So far, there are more than 20000 thousand of patients in our country, and amount of hepatitis B virus carriers is more than 120 million. The disease has become an important public health issue which threatens the human’s life and health[13,14]. Prevention and treatment of chronic hepatitis B have attracted much attention[15,16]. Current research found that suppress or eliminate hepatitis virus, release liver fibrosis, lighten inflammatory reactions to enhance liver functions and prevent liver malignant transformation is a major principle for chronic hepatitis B therapy[17]. Therefore, to observe variations of liver function, liver fibrosis indexes and inflammatory factors is of vital clinical significance to judge medicine effects.

Liver function could most intuitively indicate liver cells condition. Normal liver function indexes include ALT, AST, ALB, TBIL, etc. ALT and AST are significantly increased when acute viral hepatitis happens, which show damage of liver cells[18]; ALB is produced by...
liver. If liver cells function becomes abnormal, ALB levels would be decreased[19,20]. Increase of TBIL indicates dysfunction of liver cells on combination or administration of free bilirubin[18]. Results of our research showed that compared with prior treatment, ALT, AST, TBIL in two groups of patients were significantly decreased after treatment, ALB were significantly increased; While in observation group after treatment, ALT, AST, TBIL levels were (29.53±9.44) U/L, (32.36±10.93) U/L, (10.12±3.22) μmol/L, which were significantly lower than in control group, ALB levels in observation group are (43.57±12.42) g/L, which were significantly higher than in control group. The differences showed statistical significance (P<0.05). The above results indicated that liver function indexes in both of two groups of patients were significantly improved. While Compound Glycyrrhizin utilization showed more obvious improve effects comparing with routine treatments. The results were in accordance with research results from Li YP, et. al.

Liver fibrosis means liver cells damage, necrosis and apoptosis induced by effects of multiple liver damage factors. Hepatitis B is one of the most common pathogenies. Too long time fibrosis could lead to mass synthesis of collagens and protein polysaccharides, and excessive deposition of liver fibrosis extracellular matrix. The disease could further progress to be liver cirrhosis, even the liver cancer[22]. Since HA, LN, IV-C PCIII levels were consistent with degree of liver fibrosis variation, they were considered as commonly used indexes for liver fibrosis evaluation on clinic[23,24]. Results of our research indicated that compared with prior treatment, HA, LN, IV-C PCIII in two groups of patients were significantly decreased after treatment. While after treatment in observation group, HA, LN, IV-C PCIII levels were (97.33±31.75) μg/L, (77.52±23.72) μg/L, (82.92±24.55) μg/L, (15.33±5.11) μg/L, which were significantly lower than in control group. Differences showed statistical significance (P<0.05), which illustrated that effects of releasing liver fibrosis in observation group were more significant. Major active ingredients in Compound Glycyrrhizin include glycyrrhizic acid, cysteine, glycine and so forth. They could stabilize cell membrane, protect undamaged liver cells, and diminish apoptosis of liver cells. The anti-fibrosis function of Compound Glycyrrhizin was speculated as being achieved by suppressing the transformation from hepatic stellate cells to hepatic fibroblasts, suppressing synthesis of liver fibrosis extracellular matrix, and accelerating matrix dissociation[25].

IL-2 is secreted by Th1. It could promote B cells to generate antibodies. IL-6 is secreted by Th2. It is involved with body fluids immune reactions. Researches verified that after hepatitis virus invaded the body, IL-2 amount could be decreased, IL-6 amount could be increased. Th1/Th2 ratios could be imbalanced, and Th1 activity could be suppressed, which could lead to diminish of immune function[26]. Furthermore, liver damage of patients with hepatitis B was positively correlated with inflammatory factor TNF-α. Results of our research indicated that after treatment, IL-2 in both of two groups of patients were significantly increased. IL-6, TNF-α were significantly decreased comparing with prior treatment. While after treatment in observation group, IL-2 levels were (131.48±30.63) U/mL, which were higher than IL-2 levels in control group. IL-6, TNF-α levels in observation group were (45.23±16.45) μg/L, (41.75±17.53) ng/L, which were lower than levels in control group. The differences showed statistical significance (P<0.05), which illustrated that effects of immune function improvement and inflammatory reactions releasing in observation group were more significant. Anti-inflammatory mechanism of Compound Glycyrrhizin might be liver glucocorticoid metabolic control, to directly combine with hormone receptors and suppress activities of interstitial cells, thus to suppress secretion of inflammatory factors IL-6 and TNF-α, and to accelerate expression of IL-2 for anti-inflammatory effects[21].

Above all, Compound Glycyrrhizin is contributed to releasing liver fibrosis and inflammatory reactions in patients with chronic hepatitis B, and then improving liver functions. It is recommended as a clinical expansive medication.

References


