Original Article

The effect of entecavir on Hepatitis B virus-related cirrhosis

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ABSTRACT

Objective: To explore the efficacy of Entecavir on hepatitis B virus-related decompensated cirrhosis.

Methodology: One Hundred two cases of hepatitis B virus-related decompensated cirrhosis patients were randomly divided into treatment group (N=51) and control group (N=51). Both groups received conventional treatment, meanwhile treatment group received Entecavir for anti-virus treatment.

Results: Comparison of liver function between the two groups was statistically significant (P < 0.01) at week 4, 8 and 12 after antiviral therapy, liver fibrosis contrast of two groups was statistically significant (P < 0.01) at week 4, 8 and 12 after antiviral therapy.

Conclusions: Although Entecavir can be effective in treating hepatitis B virus-related decompensated cirrhosis, its resistance and course of treatment need to be further evaluated.

KEY WORDS: Entecavir, Hepatitis B virus, Cirrhosis.

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INTRODUCTION

Hepatitis B virus is the most common cause for cirrhosis in China. Studies have showed that antiviral therapy can significantly improve hepatitis B virus-related decompensated cirrhosis.[1] Since interferon is not a good option for the treatment of decompensated cirrhosis, nucleoside analogues for hepatitis B virus has caught more and more attention. Because Entecavir is effective in treating hepatitis B virus[2], in this study, the authors used Entecavir to treat 51 hepatitis B virus-related decompensated cirrhosis patients to find out its efficacy.

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METHODOLOGY

The study was performed with the approval of ethics committee in Suining Central Hospital. One hundred two patients hospitalized for hepatitis B virus-related decompensated cirrhosis between September 2009 and December 2011 in China were randomly divided into treatment group (N=51) and control group. Treatment group contained 28 males and 23 females, aged 23 to 66(mean ±SD: 35±3.0), in which 30 patients had HbeAg(+) and 27 patients were HBVDNA(+).

Control group contained 31 males and 20 females, aged 25 to 67 (mean ±SD:37±2.5), in which 23 patients had HbeAg(+) and 28 patients were HBVDNA(+). There was no significant difference (P>0.05) in age, gender, state of illness and positive rates of HbeAg between both the groups. All patients received nutrition support,

liver protection, anti-fibrosis and symptomatic treatment. Both groups received intravenously: 10% glucose solution (250ml) plus matrine 150 mg/day, 10% glucose solution (250ml) plus compound diisopropylamine dichloroacetate and 10% glucose solution (250ml) plus hepatocyte growth-promoting factor 100 mg/day, treatment group received plus Entecavir 0.5 mg/day orally.[3] Liver function and liver fibrosis of the two groups were examined before treatment and at the week 4, 8 and 12 after the treatment. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), albumin (ALB), total bilirubin (TBIL) of liver function indexes and III procollagen (PC III), laminin (LN), hyaluronidase (HA) of liver fibrosis indexes between the two groups were compared.

Statistical Analysis: All information and data were examined using SPSS 16.0 statistical software. T-test was used to examine the data between two groups. Variance analysis was used for multiple comparisons. Statistically significant *p* value was defined as a value <0.05.

RESULTS

Liver function indexes: There were no significant differences in liver function (Table-I) between the two groups before treatment. In treatment group, the difference before and after treatment was significant respectively at week 4, 8 and 12 all P <0.01. Meanwhile, no significant difference (P > 0.05) before and after treatment in control group was found until week 12. Significant differences (P <0.01) in liver function of the two groups were found at week 4, 8 and 12 after treatment. Moreover no significant difference (P>0.05) in treatment group after treatment was found.

Liver fibrosis index: There were no significant differences in liver fibrosis (Table-II) between the two groups before treatment. In treatment group, the difference before and after treatment was significant respectively at week 4, 8 and 12, all P <0.01. Meanwhile, no significant difference (P > 0.05) before and after treatment in control group was found until week 12. Significant differences (P <0.01) in liver fibrosis of the two groups were found at week 4, 8 and 12 after treatment. Furthermore, no significant difference (P>0.05) in care group after treatment was found.

DISCUSSION

Hepatitis B virus-related decompensated cirrhosis is always associated with many complication, such ascites, jaundice, hepatic encephalopathy, esophagus varicosis rupture haemorrhage, even primary carcinoma of liver.[4,5] One-year survival rate for decompensated cirrhosis patients was 55% to 70% and five-year survival rate was only 14% to 35%.[6,7] The goal of the treatment for hepatitis B virus-related cirrhosis patients is to suppress the replication of the virus, keep the HBeAg being negative and prevent the deterioration of liver function, therefore anti-hepatitis B virus treatment plays very important role in treating cirrhosis. Nucleoside analogues antiviral long term therapy can effectively prevent the complications of cirrhosis, hepatitis B - related liver cancer, and reduce mortality for chronic hepatitis B patients.[8]

Table-I: Liver function of both groups before and after treatment.

Groups	*Number*	*AST(u/L)*	*ALT(u/L)*	*ALB(g/L)*	*TBIL(umol/L)*
Treatment group	51				
Before treatment		97.5±49.9	165.3±13.4	26.0±8.3	136.1±16.2
4 weeks after treatment		46.1±18.9a	104.6±17.9a	29.0±5.4a	109.8±11.8a
8 weeks after treatment		43.9±16.8a	103.2±0.8a	31.3±4.9a	104.3±2.5a
12 weeks after treatment		42.1±11.9a	99.8±6.7a	32.6±5.8a	100.8±6.1a
Control group	51				
Before treatment		97.3±36.9	165.2±22.7	27.1±6.0	166.9±39.0
4 weeks after treatment		95.2±18.2c	165.1±26.9c	26.5±3.2c	172±23.8c
8 weeks after treatment		91.7±27.2c	154.6±24.2c	27.2±4.6c	163.8±29c
12 weeks after treatment		85.2±18.3bc	140.2±24.8bc	28.2±5.8bc	151±16.8bc

a Compared with treatment group before treatment, P<0.01.
b Compared with control group before treatment, P<0.05.
c Compared with corresponding week in treatment group, P<0.01.

Table-II: Liver fibrosis of both groups before and after treatment.

Group	*Number*	*LN(ng/mL)*	*HA(ng/mL)*	*PC□(ng/mL)*
Treatment group	51			
Before treatment		182.3±24.8	316.5±26.3	124.6±9.3
4 weeks after treatment		100.3±22.5a	225.6±24.5a	104.1±8.6a
8 weeks after treatment		99.4±8.9a	223.4±27.5a	101.3±16.1a
12weeks after treatment		98.3±6.4a	218.1±26.1a	100.7±14.9a
Control group	51			
Before treatment		179.2±24.9	328.6±22.5	133.6±15.8
4 weeks after treatment		170.8±26.3c	325.7±11.8c	131.2±12.1c
8 weeks after treatment		165.1±26.9c	318.2±23.1c	127.8±13.5c
12 weeks after treatment		151.6±16.4bc	297.1±30.5bc	116.2±14.7bc

a Compared with treatment group before treatment, P<0.01.
b Compared with control group before treatment, P<0.01.
c Compared with corresponding week in treatment group, P<0.01.

Since its introduction, the number of candidates listed for orthotopic liver transplantation caused by decompensated HBV-related cirrhosis in the United States has fallen significantly.[9] Entecavir is one of the high-performance and safe nucleoside analogue for chronic hepatitis B.[10,11] 1.2% viral resistance was found among the patients treated with Entecavir for 5 years.[12] Shim JH et al[13] reported that the cumulative survival rate of the HBV-related cirrhosis patients who received hepatic transplantation was 87.1% after 1-year treatment of Entecavir. Compared with usual treatment in this study, routine treatment combined with Entecavir for the treatment of hepatitis B virus-related decompensated cirrhosis patients had a better effect on liver function and liver fibrosis, but no significant improvement was found at week 4, 8 and 12. Further study of the course of Entecavir on antivirus is needed.

Compared with other nucleoside analogues for treating hepatitis B virus, Entecavir had an obvious advantage and represented an interesting first-line treatment option for treating patients with hepatitis B virus[14], but its resistance was found among the people who received long term treatment of Entecavir. The Symphysial treatment of several kinds of antiviral drugs could reduce the resistance to hepatitis B virus.[15] The safety of long term treatment with Entecavir cannot be ignored, such as its carcinogenicity, which need to be studied further.[16]

In this study, we found that the improvements of the liver function of hepatitis B virus-related cirrhosis patients treated by Entecavir was not obvious, but Entecavir may have an effect on preventing the deterioration of the liver function. Since the follow-up period of this study was short, the effects of Entecavir on hepatitis B virus-related decompensated cirrhosis patients during the later period of the course was uncertain, which in turn precluded the study of its resistance, safety and course of treatment. Further study should have a longer follow-up period, which can help us to identify the resistance of Entecavir and its course of treatment, and effect of antiviral combination therapy on hepatitis B virus-related cirrhosis patients should be further evaluated.

In summary, the treatment with Entecavir on hepatitis B virus-related decompensated cirrhosis patients could improve the liver function and delay the liver fibrosis effectively through anti-hepatitis B virus.

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