Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 6
http://ojs.bbwpublisher.com/index.php/JCNR
Online ISSN: 2208-3693
Print ISSN: 2208-3685

Clinical Efficacy and Incidence of Adverse Reactions of Entecavir Combined with Long-Acting Interferon in Treating Hepatitis B

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Abstract: *Objective:* To explore and analyze the clinical efficacy and incidence of adverse reactions of entecavir combined with long-acting interferon in treating hepatitis B. *Methods:* The study was conducted from January 2020 to December 2022, and the research subjects were 69 hepatitis B patients admitted to our hospital. The patients were divided into a research group (n = 35) and a control group (n = 34). Patients in the control group were treated with entecavir, while patients in the study group were treated with entecavir combined with long-acting interferon. The antiviral efficacy, liver function indicators, clinical effectiveness, and incidence of adverse reactions were compared between the two groups. *Results:* The HBV-DNA negative conversion rate and HBeAg seroconversion rate of the patients in the study group were higher than those of the control group, and the virological breakthrough rate was lower than that of the control group (P < 0.05); the alanine transaminase (ALT), aspartate aminotransferase (AST), and total bilirubin (TBIL) levels of the patients in the study group were all lower after treatment. In the control group, the albumin (ALB) level was higher than that in the control group (P < 0.05). The clinical effective rate of patients in the study group was higher than that in the control group (P < 0.05); there was no significant difference in the incidence of adverse reactions between the two groups (P > 0.05). *Conclusion:* The treatment effect of entecavir combined with long-acting interferon in patients with hepatitis B is significant. It can effectively antiviral and improve the liver function of patients. The incidence of adverse reactions is low and can be promoted and applied.

Keywords: Entecavir; Long-acting interferon; Hepatitis B

Online publication: November 27, 2023

1. Introduction

Hepatitis B is viral hepatitis caused by the hepatitis B virus (HBV). It can be passed from an infected mother to her baby, by blood, or by body fluids. The early symptoms of patients are usually mild, mainly manifesting as fatigue, loss of appetite, anorexia, and liver discomfort. Exacerbation can lead to symptoms such as liver palms, discoloration, splenomegaly, and spider nevi. Liver function abnormalities can be discovered through laboratory examinations [1]. Hepatitis B is a highly contagious cause of cirrhosis or liver cancer, so early treatment is

required. Entecavir is an antiviral drug that inhibits and kills HBV virus by inhibiting HBV polymerase. Long-acting interferon is a broad-spectrum antiviral drug that can block HBV replication [2]. 69 hepatitis B patients were included in this study, and the clinical effect of entecavir combined with peginterferon therapy was explored.

2. Materials and methods

2.1. General information

The study was conducted from January 2020 to December 2022, and the research subjects were 69 hepatitis B patients admitted to our hospital. The patients were divided into a research group (n = 35) and a control group (n = 34). The research group consisted of 19 males and 16 females, aged 32–55 years old, with an average of 43.59 ± 3.62 years old. The course of disease for the patients in this group ranged from 1 to 6 years, with an average of 3.48 ± 0.65 years. On the other hand, the control group consisted of 20 males and 14 females, aged 34–54 years old, with an average of 43.52 ± 3.68 years old. The course of disease of the patients in this group ranged from 1 to 5 years, with an average of 3.52 ± 0.61 years. There were no significant differences between the general information of the two groups of patients ($P > 0.05$).

Inclusion criteria: (1) Diagnosed with hepatitis B according to the "Guidelines for the Prevention and Treatment of Chronic Hepatitis B," and positive for hepatitis B e antigen (HBeAg); (2) no other liver diseases; (3) Understood the research content and agreed to participate in the study.

Exclusion criteria: (1) Presence of liver cirrhosis and liver cancer, (2) recent consumption of hepatitis B treatment drugs, (2) presence of allergies to the drugs used in this study.

2.2. Methodology

Both groups received essential symptomatic treatments such as liver protection, immune regulation, and anti-hepatic fibrosis, and the patients were given a suitable diet plan. Patients in the control group were treated with 0.5 mg dispersible entecavir tablets orally once a day, and the drugs were administered for 6 months.

Patients received long-acting interferon treatment (subcutaneous peginterferon α-2b injection) alongside entecavir tablets. The injection was given once a week, with a single dose of 80 μg, and the treatment lasted for 6 months.

2.3. Evaluation criteria

(1) After six months of treatment, the antiviral efficacy of the two groups of patients was evaluated by detecting HBV-DNA expression through polymerase chain reaction. If HBV-DNA expression was not detected, the patient was considered HBV-DNA negative. The level of HBeAg was detected by electrochemiluminescence, and seroconversion of HBeAg was determined based on the disappearance of HBeAg. A virological breakthrough was considered when the increase of HBV-DNA in the patient exceeded $1\log_{10}$ U/mL, and the virological breakthrough rates of the two groups of patients were calculated. (2) The levels of alanine transaminase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL), and albumin (ALB) were detected by enzyme-linked immunosorbent assay before and after six months of treatment. (3) The clinical efficacy of the treatment received in the two groups of patients was evaluated after six months of treatment. The treatment was considered highly effective if HBV-DNA became undetectable and liver function normalized. The treatment was considered effective if there was a significant improvement in liver function indicators and a reduction of HBV-DNA by two or more orders of magnitude. (3) The incidence of adverse reactions in the two groups was also recorded.

2.4. Statistical analysis

The research data were processed using SPSS 23.0 software. A t-test was applied to the measurement data, which was expressed as mean ± standard deviation; while the χ^2 test was used for count data, which was expressed as percentages (%). Statistical significance was considered when $P < 0.05$.

3. Result

3.1. Antiviral efficacy

As shown in **Table 1**, the research group had a higher HBV-DNA negative rate and HBeAg seroconversion rate compared to the control group. Additionally, the research group showed a lower virological breakthrough rate than the control group ($P < 0.05$).

Table 1. Comparison of antiviral efficacy between the two groups (*n* [%])

Group	HBV-DNA negative conversion rate	HBeAg seroconversion rate	Virological breakthrough rate
Research group ($n = 35$)	26 (74.3)	22 (62.9)	1 (2.9)
Control group ($n = 34$)	17 (50.0)	13 (38.2)	6 (17.6)
χ^2	4.331	4.183	4.138
P	0.037	0.040	0.041

3.2. Liver function indicators

Table 2 illustrates that following treatment, the patients in the study group exhibited lower levels of ALT, AST, and TBIL compared to the control group. Furthermore, the levels of ALB were higher in the study group compared to the control group ($P < 0.05$).

Table 2. Comparison of liver function indicators between the two groups (mean ± standard deviation [U/L])

Group	ALT		AST		TBIL		ALB	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Research group ($n = 35$)	105.92 ± 5.83	36.28 ± 2.91	90.11 ± 3.64	36.28 ± 5.53	19.04 ± 1.28	12.84 ± 0.75	33.69 ± 2.74	39.15 ± 4.41
Control group ($n = 34$)	105.88 ± 5.74	49.75 ± 4.26	90.08 ± 3.59	55.69 ± 7.84	19.11 ± 1.25	16.92 ± 1.18	33.72 ± 2.68	37.09 ± 2.38
t	0.029	15.376	0.034	11.912	0.230	17.193	0.046	2.404
P	0.977	0.000	0.973	0.000	0.819	0.000	0.963	0.019

3.3. Clinical efficacy

As shown in Table 3, the treatment received in the research group is more effective than the one received in the control group ($P < 0.05$).

Table 3. Comparison of clinical effectiveness between the two groups (*n* [%])

Group	Markedly effective	Effective	Ineffective	Total efficacy
Research group ($n = 35$)	25	8	2	33 (94.3)
Control group ($n = 34$)	19	7	8	26 (76.5)
χ^2				4.416
P				0.035

3.4. Incidence of adverse reactions between the two groups

In the research group, there was 1 case of fever and 1 case of joint pain; the rate of adverse reactions was 5.7%. In the control group, there were 2 cases of fever, 1 case of leukopenia, and 1 case of joint pain; the rate of adverse reaction was 11.7%. There was no significant difference between the incidence of adverse reactions between the two groups ($P > 0.05$).

4. Discussion

Hepatitis B is caused by an infection of the HBV. A hepatitis B patient's liver is accompanied by inflammatory necrosis, fibrosis, and other lesions. The main clinical symptoms of hepatitis B are dizziness, fatigue, loss of appetite, anorexia, and liver discomfort. Continued aggravation can lead to cirrhosis or liver cancer [3]. Hepatitis B is an infectious disease with various transmission routes, including mother-to-child transmission, contact with infected body fluids, and exposure to contaminated blood. It poses a significant risk to public health and necessitates prompt treatment and intervention measures [4].

The primary clinical treatments for hepatitis B include antiviral medications, therapies to reduce liver fibrosis, enhancing liver function, and immune regulation. Among these options, antiviral treatment is a crucial approach for managing hepatitis B. Entecavir, a nucleoside-based anti-HBV drug, structurally resembles the natural nucleosides present in the human body. Following administration, it competitively binds to HBV-DNA polymerase, affecting HBV-DNA reverse transcriptase and preventing HBV-DNA from binding to ATP, thereby inhibiting its replication [5,6]. Entecavir has significant antiviral efficacy compared to other types of nucleoside anti-HBV drugs. Entecavir has a rapid onset of action and a low likelihood of drug resistance. It is generally well-tolerated, with minimal severe adverse reactions in the body. This medication is effective in controlling the hepatitis B virus and alleviating hepatitis B-related symptoms [7,8]. Interferon is a broad-spectrum antiviral drug widely used in clinical practice. Interferons do not directly inhibit or kill viruses. Instead, it binds to cell surface receptors, prompting cells to produce antiviral proteins and regulate the immune functions of T and B lymphocytes. This mechanism contributes to effective antiviral outcomes [9]. Compared to other types of interferons, the renal metabolism rate of peginterferon alpha-2b injection is lower, which is only 30%. It binds to interferon receptors, exerting a long-lasting antiviral effect, making it an effective treatment option for HBeAg-positive hepatitis B patients [10]. Combining entecavir with long-acting interferon for hepatitis B treatment utilizes distinct antiviral pathways, substantially enhancing the antiviral effectiveness and improving treatment outcomes.

The results of this study showed that the antiviral efficacy and clinical effectiveness of the treatment received in the research group were better than those of the control group, suggesting that entecavir combined with long-acting interferon therapy can improve the efficacy of the overall treatment. This is because entecavir can effectively inhibit the initiation, reverse transcription, synthesis, and other aspects of HBV-DNA replication, thereby blocking viral replication. The antiviral efficacy of entecavir is related to the patient's immune function, hepatitis activity, cytotoxicity, and antigen-related cell function. Entecavir alone is not effective for some patients [11]. Peginterferon α-2b injection can induce cells to secrete proteins with antiviral functions, thereby inhibiting HBV-DNA. The drug has long-lasting efficacy, and its efficacy is not easily affected. It can compensate for the shortcomings of using entecavir alone significantly improving the treatment effect [12]. The results of this study showed that all indicators of liver function in the study group after treatment were better than those in the control group, suggesting that entecavir combined with long-acting interferon treatment can improve liver function in patients with hepatitis B.

Therefore, it is essential to use effective antiviral drug intervention to improve the patient's liver function.

Both entecavir and long-acting interferon have antiviral effects, but they work through different mechanisms. When used together, they complement each other, resulting in enhanced antiviral effectiveness and improved liver function indicators in patients [13,14]. This study showed that there was no significant difference in the incidence of adverse reactions between the two groups of patients, suggesting that entecavir combined with long-acting interferon treatment is safe. This is because entecavir is mainly metabolized by the kidneys and does not accumulate in the patient's body. The plasma clearance rate of peginterferon α-2b injection is relatively low, but the drug must only be administered once a week. Our patients did not experience severe adverse reactions after low-dose administration, so the combined use of the two does not increase the incidence of adverse effects [15].

5. Conclusion

The analysis above indicates that the combination treatment of entecavir and long-acting interferon is highly effective for patients with hepatitis B. It provides effective antiviral action, enhances liver function, and has a low incidence of adverse reactions, making it a promising approach for broader application. However, it is important to note that this study had a small sample size, lacked cross-sectional research involving multiple centers, and may benefit from further refinement in its process. Additionally, the study's duration was relatively short, and there remains a need for further research into the treatment mechanism for hepatitis B patients using entecavir and long-acting interferon.

Disclosure statement

The author declares no conflict of interest.

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