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Clinical Value of Hepatitis B Virus RNA Detection in Patients with Chronic Hepatitis B Infection

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Abstract: *Objective:* To study the clinical value of hepatitis B virus pregenomic RNA (HBV-pgRNA) detection in the treatment of hepatitis B. *Methods:* 60 patients with hepatitis B were included in the study. Serum HBV-pgRNA and HBV DNA levels in different phases of infection and during treatment were detected, and serum hepatitis B surface antigen (HbsAg) titer was detected by chemiluminescent immunoassay. DNA was extracted from liver biopsy tissue, and covalently closed circular DNA was detected to predict the therapeutic value in patients. *Results:* At the initial stage of treatment, the level of HBV-pgRNA in phase I, II, III, and IV showed a gradual decrease. Comparing the levels of HBV-pgRNA before and after treatment, we found that the level of HBV-pgRNA was significantly lower after treatment ($P < 0.05$). Among the indicators for predicting HBsAg seroconversion, the accuracy of HBV-pgRNA level was 85.0% (51/60). *Conclusion:* The clinical value of HBV-pgRNA detection in the treatment of hepatitis B is high.

Keywords: Hepatitis B virus pregenomic RNA; HBV-pgRNA ; Detection; Hepatitis B; Treatment; Clinical value

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1. Introduction

Hepatitis B is an infectious disease caused by hepatitis B virus (HBV). It is a global health problem, especially in Asia. Hepatitis B is a chronic viral infection that can lead to serious consequences, such as cirrhosis and liver cancer. At present, the treatment for hepatitis B is antiviral therapy, but there are great differences in the treatment effect; some patients may even experience treatment failure or relapse [1-4]. HBV-pgRNA is the pregenomic RNA of HBV, which plays an important role in HBV replication. In recent years, several studies have shown that the detection of HBV-pgRNA can be used to evaluate the effect of antiviral therapy [5,6]. Therefore, we explore the clinical value of HBV-pgRNA detection in the treatment of hepatitis B. The natural history of chronic HBV infection can be divided into four phases: (1) immune tolerance; (2) immune clearance; (3) low replicative or inactive carrier, and (Ⅳ) reactivation [7]. In this study, 60 patients were selected.

2. Materials and methods

2.1. Baseline data

From June 2021 to May 2022, 60 patients with chronic hepatitis B were selected from the Department of Infectious Diseases and Department of Gastroenterology of Shaanxi Provincial People's Hospital. Their

diagnosis was in line with the Guidelines for the Prevention and Treatment of Chronic Hepatitis B (2019) [7]. The ratio of male to female was 30:30, and their age ranged from 23 to 61 (25.2 ± 2.5). There were 3, 29, 9, and 19 cases in phase I, II, III, and IV, respectively. The research protocol was approved by the Ethics Committee of Shaanxi Provincial People's Hospital, and all patients signed the informed consent.

2.2. Methods

Upon admission to the hospital, blood was collected from patients with chronic hepatitis B virus infection on an empty stomach in the morning, and alanine transaminase (ALT) and aspartate transaminase (AST) were determined by rate method.

Using 200 μL of serum, quantitative polymerase chain reaction was performed, and relevant kits were used to extract RNA and obtain complementary DNA (cDNA) through reverse transcription. Serum HBV RNA was determined, and quantitative detection of HBV DNA was performed.

Chemiluminescence immunoassay was used to measure serum hepatitis B surface antigen (HbsAg) titer. The detection limit was 0.05 IU/mL, and the initial value was higher than the detection limit of 250 IU/mL. The sample was diluted at 1:500 for detection.

After cutting the 30 mm formalin-fixed paraffin-embedded liver biopsy tissue into 6 mm, DNA was extracted, double-stranded (ds)DNA and single-stranded (ss)DNA were replicated using relevant reagents, and HBV covalently close circular DNA (cccDNA) was further quantified.

2.3. Statistical analysis

SPSS 25.0 was used for data processing. Measurement data were expressed as mean ± standard deviation, and *t*-test was performed; count data were expressed as percentage (%), and chi-square test was performed. $P < 0.05$ indicates statistically significant results.

3. Results

At the initial stage of treatment, the level of HBV-pgRNA in phase I, II, III, and IV showed a gradual decrease (7.32 ± 1.17 $\log_{10}$ copies/mL, 6.64 ± 0.44 $\log_{10}$ copies/mL, 4.66 ± 1.05 $\log_{10}$ copies/mL, and 5.25 ± 0.37 $\log_{10}$ copies/mL).

Comparing the levels of HBV-pgRNA before and after treatment, the HBV-pgRNA level was singificantly lower after 12 months of treatment (6.22 ± 1.15 $\log_{10}$ copies/mL versus 3.66 ± 0.42 $\log_{10}$ copies/mL; $P < 0.05$, $t = 16.1968$).

In this study, among the indicators for predicting HBsAg seroconversion, the accuracy of HBV-pgRNA was 85.00% (51/60).

4. Discussion

HBV-pgRNA is an important component in the replication of HBV and plays a key role in HBV infection. Recent studies have shown that HBV-pgRNA detection has certain clinical value in evaluating the treatment response and efficacy in hepatitis B patients [8,9]. In the present study, we explore the clinical value of HBV-pgRNA detection in the treatment of hepatitis B and analyze its advantages and limitations in clinical application.

4.1. Clinical application of HBV-pgRNA detection in the treatment of hepatitis B

The application of HBV-pgRNA detection in the treatment of hepatitis B is mainly reflected in three aspects. First, HBV-pgRNA detection can be used to evaluate the efficacy of antiviral therapy. Some studies have shown that a decrease in HBV-pgRNA level reflects the treatment response and efficacy of antiviral therapy in hepatitis B patients [10,11]. For example, the greater the reduction in HBV-pgRNA levels, the better the

treatment response and efficacy. Therefore, HBV-pgRNA detection can be used to guide the treatment plan and thus improve the treatment effect. Second, HBV-pgRNA detection can be used to predict drug resistance. Several studies have shown that changes in HBV-pgRNA levels can predict drug resistance in HBV. For example, HBV-pgRNA levels that do not decline or rebound might suggest that the virus has developed drug resistance. Therefore, HBV-pgRNA detection can be used to guide the selection and adjustment of drugs to prevent the emergence of drug resistance in HBV [12]. Third, HBV-pgRNA detection can be used to assess HBV replication activity. Some studies have shown that the level of HBV-pgRNA can reflect the replication activity of HBV [13-15]. Therefore, HBV-pgRNA detection can be used to assess HBV replication activity before and after treatment to guide treatment options and monitor treatment effects.

4.2. Advantages and limitations of HBV-pgRNA detection

The advantages of HBV-pgRNA detection are as follows: (1) HBV-pgRNA detection can directly reflect HBV replication activity; it is more sensitive and accurate than traditional serological indicators; (2) HBV-pgRNA detection can be used to evaluate the efficacy of antiviral therapy and drug resistance in HBV to guide treatment plans and drug adjustments [16]; (3) HBV-pgRNA detection can be used to monitor HBV replication activity and predict the progress of the disease.

However, HBV-pgRNA detection has several limitations, such as (1) the relatively complicated detection method, which is costly and requires high-tech laboratories and equipment support; (2) a lack of standardized detection methods and standard reference values, which may render differences in results between different laboratories; and (3) the numerous factors that affect the level of HBV-pgRNA, including the patient's immune status, virus serotype and genotype, *etc*., thereby requiring a comprehensive analysis. The study concluded that the level of HBV-pgRNA in phase I, II, III, and IV showed a gradual decrease at the initial stage of treatment. Comparing the levels of HBV-pgRNA before and after treatment, we found that level of HBV-pgRNA was significantly lower after treatment ($P < 0.05$). Among the indicators for predicting HBsAg seroconversion, the accuracy of HBV-pgRNA level was 85.00% (51/60).

Overall, HBV-pgRNA detection has clinical value in hepatitis B treatment and in predicting HBsAg seroconversion. Although there are certain limitations, with the advancement of technology and the establishment of standardization, we anticipate that the clinical application of HBV-pgRNA detection in the treatment of hepatitis B will grow.

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Disclosure statement

The authors declare no conflict of interest.

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