Short Communication

Telbivudine in a patient with HBeAg-negative CHB and high viremia

*Mamun-Al-Mahtab[1], Kathleen Covino[2]
[1] Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh,
[2]BlueSpark Healthcare Communications, Basking Ridge, New Jersey, USA 07920

***Correspondence to**
Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, House #109, Road #4, Block #B Banani, Dhaka-1213, Bangladesh, Tel: +880-1711567275, Fax: +880-2-8826840, E-mail: shwapnil@agni.com

Abstract

We report the efficacy of telbivudine in a patient with hepatitis B e antigen (HBeAg)-negative chronic hepatitis B (CHB) who demonstrated high viremia and evidence of liver fibrosis and had no family history of liver disease. The patient was a 21-year-old man. Laboratory studies at the time of diagnosis showed that, in addition to being HBeAg negative, he was positive for hepatitis B surface antigen and negative for antibody to hepatitis B e antigen. His hepatitis B virus (HBV) DNA level was 6.9×10^9 copies/mL and his alanine aminotransferase (ALT) level was 87 IU/L. Liver biopsy showed significant necroinflammation with mild piecemeal necrotic fibrosis. Telbivudine 600 mg QD was started, and the patient underwent monitoring every 24 weeks. The patient's HBV DNA level was reduced to 1.5×10^3 copies/mL at 24 weeks and to <500 copies/mL at 1 year. Corresponding ALT levels were 45 and 25 IU/L. No adverse events were reported and no virologic/biochemical breakthrough was observed. Regular monitoring of HBV DNA and ALT levels was continued. One year of treatment with telbivudine monotherapy produced undetectable HBV DNA and normalized ALT levels in this young patient with high viremia.

Keywords: Chronic hepatitis B; hepatitis B e antigen; telbivudine; viremia; fibrosis.

Introduction

The treatment of patients with hepatitis B e antigen (HBeAg)-negative chronic hepatitis B (CHB) is a serious clinical challenge because of the requirement for lifelong therapy and a poor long-term prognosis [1]. HBeAg-negative CHB, a variant of the immune clearance phase, is associated with the emergence of mutations in the precore and core promoter regions and is most prevalent among men over 30 years of age [1]. Necroinflammatory changes are detected at diagnosis in >50% of patients, with 25% to 40% of patients demonstrating cirrhosis [2–5]. Although it is predominant in the Mediterranean area, an increased incidence of HBeAg-negative CHB has been noted in the Asia-Pacific region. A study of Taiwanese patients with CHB found the cumulative incidence of HBeAg-negative CHB to be 24% after 16 years in patients with spontaneous HBeAg seroconversion [6].

Current liver society guidelines for the management of CHB recommend treatment for patients with HBeAg-negative CHB who have HBV DNA levels >2000 IU/mL (>10,000 copies/mL) and elevated alanine aminotransferase (ALT) levels and/or necroinflammatory changes and fibrosis on liver biopsy [7–10]. Current options for the treatment of patients with HBeAg-negative CHB include pegylated interferon (PegIFN) alfa-2b and oral nucleos(t)ide analog (NA) therapy. PegIFN can be administered as a finite course of therapy and has been shown to be most effective in younger patients with low baseline HBV DNA levels and elevated ALT levels [11–13]. However, it is costly and often associated with unwanted side effects. Oral NAs induce a rapid and profound suppression of HBV DNA levels and have become the mainstay of treatment for CHB. Evidence from long-term follow-up studies suggests that the administration of NAs, either as monotherapy or in sequential combination, inhibits HBV replication in most patients with HBeAg-negative disease for ≥5 years, preventing disease progression, particularly in patients with decompensated cirrhosis [14]. Telbivudine is a potent oral nucleoside analog licensed for the treatment of patients with CHB that has demonstrated superior efficacy to lamivudine and equivalent potency to entecavir in patients with HBeAg-positive and negative disease [15]. In the present case study, we report the efficacy of telbivudine therapy in the management of a patient with HBeAg-negative CHB who had unusually high viremia and evidence of liver fibrosis.

Case Report

A 21-year-old man with no family history of liver disease was found to be positive for hepatitis B surface antigen (HBsAg) during routine clinical screening. Laboratory studies revealed that he was negative for HBeAg and antibody to hepatitis B e antigen (anti-HBe) as well. He had an HBV DNA level of 6.9×10^9 copies/mL (as assessed by TaqMan® [Applied Biosystems, Foster City, CA] real-time polymerase chain reaction [PCR]) and had an ALT level of 87 IU/L. Ultrasound results were normal; however, confirmatory percutaneous liver biopsy revealed significant necroinflammation (Histologic Activity Index–Necroinflammation score, 7) with mild piecemeal necrotic fibrosis (Histologic Activity Index–Fibrosis score, 1). Treatment was initiated with telbivudine 600 mg QD; HBV and ALT levels were monitored every 24 weeks.

At 24 weeks of follow-up, the HBV DNA level was 1.5×10^3 copies/mL and the ALT level was 45 IU/L. At 1 year of follow-up, the HBV DNA level was <500 copies/mL and the ALT level was 25 IU/L. No adverse events or virologic/biochemical breakthrough was observed. The patient continued to receive telbivudine monotherapy.

Discussion

HBeAg-negative CHB is often difficult to diagnose because it can be confused with CHB in its inactive carrier state, as both are characterized by the absence of HBeAg and detectable anti-HBe. In an inactive carrier, ALT levels usually remain normal on serial monitoring with undetectable to low levels ($<10^5$ copies/mL) of HBV DNA. HBeAg-negative CHB may also be marked by periods of quiescence characterized by low or normal ALT levels and HBV DNA levels below the usual threshold. One study of 196 patients with CHB revealed that 10.5% of HBeAg-negative patients had HBV DNA levels <30,000 copies/mL [16]. As in this case, and particularly in a young patient, a liver biopsy can be used to distinguish between HBeAg-negative CHB and the inactive carrier state of the disease in a clinical setting [17].

The case presented here is unique because of the high viremia and young age of the patient, which is not clinically representative of HBeAg-negative CHB. We decided to treat our patient with telbivudine because of the high level of baseline viremia and risk for disease progression. Telbivudine has been shown to induce rapid and profound suppression of HBV DNA in patients with HBeAg and has recently been shown to be more cost-effective than entecavir for the achievement of PCR-undetectable viremia, the current goal of CHB management [8]. Previous studies have shown that baseline HBV DNA levels <7 $\log_{10}$ copies/mL and HBV DNA undetectability at week 24 are associated with optimal outcomes in telbivudine-treated patients with HBeAg-negative CHB [18]. Although the patient in this case did not possess these characteristics, he was able to achieve a reduction in HBV DNA level of ~7 $\log_{10}$ and near-normal ALT levels at week 24, with undetectable HBV DNA and normalized ALT levels after 1 year of telbivudine monotherapy. Long-term follow-up studies of the efficacy and safety of continuous telbivudine monotherapy for up to 4 years in HBeAg-negative patients demonstrate high rates of maintained virologic and biochemical response [18–20]. However, due to the potential risk for the emergence of resistance in patients who do not achieve undetectable viremia with telbivudine at treatment week 24, we will continue to monitor his HBV DNA and ALT levels every 3 months.

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