Cipla

Hep B SPECTACLES

Issue 3

MANAGEMENT OF CIRRHOSIS AND DECOMPENSATED CIRRHOSIS: APPRAISING THE ROLE OF ENTECAVIR

Introduction

Hepatitis B virus (HBV) infection is considered as one of the most important global public health concerns; this potentially life-threatening infection damages the liver and can contribute to a wide spectrum of liver disorders. Approximately 400 million people are estimated to be chronically infected with HBV which may result in serious complications, such as liver cirrhosis, hepatic decompensation and hepatocellular carcinoma (HCC) in about 15-40% of these individuals.[1,2]

Cirrhosis and decompensated liver cirrhosis in CHB: An overview

Chronic hepatitis B (CHB) is a dynamic state of interactions among HBV, hepatocytes, and the host immune system. CHB results in varying degrees of predominantly lymphocytic infiltration in the portal tracts associated with portal inflammation, interface hepatitis, and spotty lobular inflammation. Inflammation can lead to liver damage, including fibrosis (light to medium scarring of the liver), cirrhosis (extensive scarring of the liver), and liver cancer. If left untreated, 6–20% of CHB patients will develop cirrhosis over five years. Following development of fibrosis or compensated cirrhosis in patients with CHB, liver disease may continue to progress and decompensation or HCC may occur, especially in those with active viral replication. According to studies of the natural course of cirrhosis, every year, 2-5% patients with HBV-related compensated cirrhosis develop decompensation. The prognosis of patients with decompensated HBV-related cirrhosis is poor, with a 5-year survival rate of 14-35% compared to 84% in patients with compensated cirrhosis. The clinical presentation of decompensated cirrhosis includes jaundice, ascites, hepatic encephalopathy (HE) or bleeding esophageal varices.[3-5]

> **The prognosis of patients with decompensated HBV-related cirrhosis is poor, with a 5-year survival rate of 14-35% compared to 84% in patients with compensated cirrhosis**

> **CHB is a dynamic state of interactions among HBV, hepatocytes, and the host immune system**

Management of patients with HBV-related decompensated cirrhosis: Appraising the role of entecavir (ETV)

Oral antiviral agents are found to be effective in restoring liver functions and improving survival in these patients by preventing the development of complications from HBV-related cirrhosis, particularly, decompensation and acute-on-chronic liver failure (ACLF).[6] Nucleos(t)ide analogue therapy is widely used in the management of patients with decompensated liver. Among the nucleos(t)ide analogue therapy, ETV has been reported to achieve the HBV DNA suppression, biochemical and histological improvement in HBV-related liver cirrhosis.[7] The European Association for the Study of the Liver (EASL) has recommended ETV as first-line therapy for HBV-decompensated cirrhosis owing to its high efficacy, potential antiviral activity and high barrier to resistance.[8] A plethora of clinical studies have reported the efficacy of ETV therapy in the management of HBV-related cirrhosis

Assessing the treatment outcomes of ETV in participants with hepatitis B decompensated cirrhosis[7]

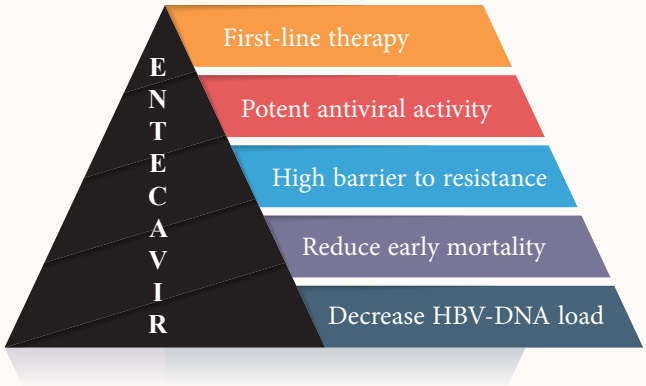
- Meta-analysis including 26 studies (involving 2040 patients) showed that ETV treated patients had significant HBV-DNA loss and normalized alanine aminotransferase levels (ALT) (P=0.003 at 24 weeks, P=0.02 at 48 weeks), and low mortality rate at 24 weeks (P=0.003). Hence, ETV therapy can be used as a first-line therapy in patients with hepatitis B decompensated cirrhosis as it reduced the early mortality and attenuated HBV DNA load.

To evaluate ETV therapy as a treatment for patients with HBV-related compensated and decompensated cirrhosis[9]

- Study involved ETV treated compensated (n=46) and decompensated cirrhotic patients (n=51) for 96 weeks. Results showed significant improvements in serum levels of HBV DNA (P=0.002), albumin (P=0.014), cholinesterase (CHE; P=0.001), HBV DNA negativity rate (P=0.004), Child-Turcotte-Pugh score (P=0.030), normalized ALT rate (P=0.039), and the degree of esophageal varices liver stiffness (P=0.002) in both the groups. The complement component (C)3 and C4 levels were also significantly increased in the compensated patients compared with the decompensated patients at weeks 24, 48 and 96 (P<0.05). Thus, treatment with 96-week ETV therapy produced similar clinical outcomes in compensated and decompensated cirrhotic patients via inhibiting HBV-DNA viral load and recovering complement C3 and C4.

EASL has recommended ETV as first-line therapy for HBV-decompensated cirrhosis owing to its high efficacy, potential antiviral activity and high barrier to resistance

ETV in decompensated cirrhosis



Sources: **1.** Wang FY, Li B, Li Y, et al. Entecavir for Patients with Hepatitis B Decompensated Cirrhosis in China: a meta-analysis. *Scientific Reports. 2016;6:32722.* **2.** European Association For The Study Of The Liver. EASL clinical practice guidelines: Management of chronic hepatitis B virus infection. *J Hepatol. 2012 Jul;57(1):167-85.*

To conclude

Following development of liver cirrhosis in patients with CHB, it may continue to progress and decompensation or HCC may occur, especially in those with active viral replication. The clinical application of ETV as a treatment for CHB-related liver cirrhosis results in reduced HBV DNA viral load, increased liver function, extended years of life and improved quality of life. Thus, making ETV an effective treatment for patients with compensated and decompensated cirrhosis.

References

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JOURNAL SCAN

SHORT- AND LONG-TERM OUTCOMES OF TREATMENT IN PATIENTS WITH CHB AND DECOMPENSATED CIRRHOSIS

There is dearth of data regarding the effects of antiviral therapy on short- and long-term survival of patients with HBV-related decompensated cirrhosis. A study was conducted to determine whether a maintained virologic response (MVR, defined as persistent undetectable HBV DNA during therapy) associates with short-term (6 mo) and long-term (6-120 mo) survival of patients with decompensated cirrhosis. It was a 10-year observation analysis comprising data from the Epidemiology and Natural History of Liver Cirrhosis study of patients with decompensated liver cirrhosis in Korea. The study comprised 295 patients out of the entire cohort who immediately began treatment with ETV (n=179) or lamivudine (LMV) (n=116) after decompensation. Laboratory test results, data on HCC development, and Child-Turcotte-Pugh and model for end-stage liver disease (MELD) scores were collected. The mean follow-up time was 62.3 ± 36.5 months. The primary end point was time of liver transplant-free survival.

> **In patients with HBV-related decompensated cirrhosis the baseline MELD score and MVR to ETV or LMV associates with short- and long-term transplant-free survival**

The study reported median survival time of 7.7 years; 60.1% of patients survived for 5 years and 45.7% survived for 10 years without liver transplantation. An MVR was also observed in 116 patients (39.3%); patients reported significantly longer times of transplant-free survival than patients without MVR. In addition, survival of patients without HCC was excellent if they survived the first 6 months after initiation of antiviral therapy, whereas the survival rates of patients with HCC decreased persistently over time. Moreover, a baseline MELD score above 20 and multiple complications were associated with short-term mortality. Additionally, MVR was strongly associated with long-term transplant-free survival. A larger number of patients who received ETV survived for 10 years unlike those who received LMV. Patients with MVRs showed improvement in hepatic function over time, but not marked reductions in risk of HCC or HCC-related mortality.

Hence, the study showed that in patients with HBV-related decompensated cirrhosis the baseline MELD score and MVR to ETV or LMV associates with short- and long-term transplant-free survival. Benefits of MVR were maintained for up to 10 years even after decompensation, but patients are still at risk for HCC.

Source: Jang JW, Choi JY, Kim YS, Yoo JJ, Woo HY, et al. Effects of Virologic Response to Treatment on Short- and Long-Term Outcomes of Patients With Chronic Hepatitis B Virus Infection and Decompensated Cirrhosis. *Clin Gastroenterol Hepatol. 2018. pii: S1542-3565(18)30471-3.*

GUIDELINES

EASL CLINICAL PRACTICE GUIDELINES FOR THE MANAGEMENT OF PATIENTS WITH DECOMPENSATED CIRRHOSIS - 2018

The research panel decided to cover all those complications of cirrhosis which remained untouched by previous EASL guidelines, namely: gastrointestinal (GI) bleeding, bacterial infections other than spontaneous bacterial peritonitis (SBP), acute-on-chronic liver failure (ACLF), adrenal failure, hepato-pulmonary syndrome (HPS), portopulmonary hypertension (PPHT) and cirrhotic cardiomyopathy (CCM).

Management of decompensated cirrhosis

- In patients with decompensated cirrhosis, the etiological factor, should be removed, particularly alcohol consumption and hepatitis B or C virus infection as this strategy is associated with decreased risk of decompensation and increased survival.
- Strategies based on targeting abnormalities in gut-liver axis by antibiotic administration (i.e. rifaximin), improving the disturbed systemic circulatory function (i.e. long-term albumin administration), decreasing the inflammatory state (i.e. statins), and reducing portal hypertension (i.e. beta-blockers) decrease cirrhosis progression among patients with decompensated cirrhosis. Further clinical research is warranted with these strategies to validate safety and potential benefits of these therapeutic approaches.

Management of ACLF

- At present, there is no specific therapy for ACLF aside from antiviral therapy in patients with ACLF due to reactivation of HBV infection.
- Treatment of ACLF should be based on organ support and management of precipitants and associated complications.
- Early identification and treatment of precipitating factors of ACLF, particularly bacterial infections, are recommended.
- In patients with ACLF due to HBV infection it is recommended to start nucleoside analogues (tenofovir, ETV) as early as possible.
- Early referral of patients with ACLF to liver transplant centres for immediate evaluation.
- Patients who are not candidates for liver transplant, with four or more organ failures after one week of adequate intensive treatment, a withdrawal of ongoing intensive care support can be suggested.

Source: European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu; European Association for the Study of the Liver. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. *J Hepatol. 2018 Aug;69(2):406-460*