INTRODUCTION

Chronic hepatitis B (CHB) is a worldwide health problem. More than 400 million people around the world are chronically infected despite the hepatitis B virus (HBV) vaccination, and those patients have increased risk for complications of CHB, including liver cirrhosis and hepatocellular carcinoma (HCC).1 An increased serum HBV DNA level (>10,000 copies/mL) is a strong risk factor for HCC and liver cirrhosis independent of hepatitis B e-antigen (HBeAg) status and the serum alanine aminotransferase (ALT) level.2,3 Therefore,
one of primary goals in treatment of CHB is suppressing HBV replication and reducing complications, such as the development of HCC and cirrhosis.

Entecavir (ETV) is a potent and selective guanosine analogue with a high genetic barrier to resistance and strong suppression of HBV replication. Long-term observation has revealed low rates of resistance in nucleoside-naive patients during 5 years of ETV therapy, with a 5-year cumulative probability of ETV resistance of 1.2%. Also, treatment with ETV showed improved histologic, virologic, and biochemical efficacy after 48 weeks of treatment compared to lamivudine (LAM) in HBeAg-positive and HBeAg-negative patients with CHB. ETV has been recommended as a primary therapy for CHB with potent HBV DNA suppression and low resistance, because the proportion of patients with a documented LAM-resistant mutation increased from 23% in year 1 to 65% in year 5 of treatment with LAM. Therefore, ETV is currently used worldwide as primary drug in nucleoside-naive CHB patients.

However, factors influencing the antiviral effect of ETV have not yet been widely studied. In particular, obesity and alcohol consumption are major factors that have a harmful impact on the liver. A longitudinal cohort study suggested that a higher body mass index (BMI) was associated with transition from healthy HBV carrier state to HCC and liver-related death among men. Alcohol is also associated with the development of both alcoholic cirrhosis and HCC. A report demonstrated that chronic ethanol consumption stimulates HBV gene expression and replication in transgenic mice, and one prospective study found that obesity and alcohol synergize to increase the risk of incident HCC in men.

In this retrospective study, we analyzed the association between alcohol consumption, obesity, and treatment outcomes in naive CHB patients receiving ETV.

PATIENTS AND METHODS

Patients

The most of data were extracted from a retrospective cohort study previously performed in our institution. Additionally, we retrospectively analyzed the medical records of treatment-naive patients with CHB who received 0.5 mg ETV once daily for >12 months at our institution between March 2007 and September 2009. ETV was commenced according to the Korean Association for the Study of the Liver. Liver cirrhosis was clinically diagnosed (varix, ascites, reasonable result on radiologic method). The exclusion criteria included a co-infection with hepatitis C virus or human immunodeficiency virus, a history of taking other antiviral agents for CHB, decompensated liver cirrhosis, HCC, and a concurrent use of immunosuppressive drugs or corticosteroids and underlying medical diseases accompanied by ascites such as congestive heart failure.

The study protocol was approved by the Institutional Review Board for Human Research at Kangbuk Samsung Hospital. Written, informed consent was obtained from all participating patients.

Laboratory assays

Serum biochemical parameters, including total bilirubin, ALT, aspartate aminotransferase, gamma glutamyl transpeptidase, alkaline phosphatase, HBeAg, anti-HBeAg, and HBV DNA were measured at baseline. Total bilirubin, ALT, aspartate aminotransferase, albumin, gamma glutamyl transpeptidase, alkaline phosphatase, HBeAg, anti-HBeAg, and HBV DNA were accessed at 3, 6, and 12 months during treatment. Serum levels of HBV DNA were quantified with a real-time polymerase chain reaction (PCR) assay by a Cobas TaqMan 48 analyzer (Roche Molecular Systems, Branchburg, NJ, USA). Treatment response was evaluated at 3, 6, and 12 months after initiation of ETV. Complete virologic response (CVR) was defined as an HBV DNA level by a real-time PCR assay of <300 copies/mL, and biochemical response (BR) was defined as normalization of the ALT level (ALT level ≤1×the upper normal limit) in subjects with an abnormal baseline ALT level at 6 months after initiation of ETV treatment. Non virologic response was defined as an HBV DNA decline of <2 log10 copies/mL at 6 months after initiation of ETV treatment. Virologic breakthrough was defined as an increase in HBV DNA levels to >1 log10 copies/mL above the treatment nadir during the follow-up period.

Measurement of obesity and alcohol use

Weight and height were measured by a trained nurse at 6 months after initiation of ETV treatment. BMI was calculated using weight divided by height squared (kg/m²), and subjects were categorized into the normal group (BMI <25 kg/m²) and the high BMI group (BMI ≥25 kg/m²).

At 6 months after initiation of treatment, we interviewed enrolled patients using the alcohol use disorder identification test (AUDIT) questionnaire of the World Health Organization (WHO) to investigate the status of alcohol intake. The AUDIT questionnaire