High effectiveness of peginterferon alfa-2a plus ribavirin therapy in Korean patients with chronic hepatitis C in clinical practice

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Background/Aims: Identifying the impact of a patient’s ethnicity on treatment responses in clinical practice may assist in providing individualized treatment regimens for chronic hepatitis C (CHC). The effectiveness of standard peginterferon plus ribavirin therapy and the need for triple combination therapy with protease inhibitors in Koreans remain matters of debate. These issues were investigated in the present study.

Methods: The clinical data of 272 treatment-naïve Korean CHC patients who were treated in a community-based clinical trial (Clinical Trial group; n=51) and in clinical practice (Cohort group; n=221), were analyzed and compared. All were treated with standard protocols of peginterferon alfa-2a plus ribavirin therapy.

Results: For patients with hepatitis C virus (HCV) genotype 1, the sustained virological response (SVR) rates in the Clinical Trial and Cohort groups were 81% (21/26) and 55% (58/106), respectively, by intention-to-treat (ITT) analysis (P=0.02), and 100% (13/13) and 80% (32/40), respectively, in treatment-adherent patients (P=0.18). For patients with HCV genotype 2, the SVR rates in these two groups were 96% (24/25) and 88% (101/115), respectively, by ITT analysis (P=0.31). Adherence and treatment duration were independent predictors of SVR for genotypes 1 and 2, respectively (P<0.01 for each). Korean patients with CHC achieved high SVR rates with peginterferon alfa-2a plus ribavirin in both the clinical trial and clinical practice settings.

Conclusions: Measures to raise adherence to standard therapy in clinical practice may improve the SVR rates in these patients as effectively as adding protease inhibitors, thus obviating the need for the latter. (Clin Mol Hepatol 2013;19:60-69)

Keywords: Medication adherence; Hepatitis C; Peginterferon alfa-2a; Ribavirin
INTRODUCTION

Chronic hepatitis C virus (HCV) infection is one of the major causes of chronic hepatitis, cirrhosis, and hepatocellular carcinoma. The prevalence of HCV infection varies geographically, with the majority of infected people (about 90 million) originating from Asian countries. Despite the high burden of HCV disease among Asians, very little is known about the treatment outcomes in these patients because most of the pivotal studies only included small numbers of Asian patients.

The standard-of-care treatment for patients with chronic hepatitis C (CHC) has been combination of peginterferon (PEG-IFN) and ribavirin (RBV), which induces sustained virological response (SVR) rates of 40-50% in cases with HCV genotype 1, and of 80% or more in cases with genotype 2 or 3 infections. The recent development of protease inhibitors has substantially improved the SVR rates of patients with genotype 1. However, given the high cost and the more frequent occurrence of adverse events associated with triple combination therapy with PEG-IFN, RBV, and protease inhibitor, it is important to identify who would benefit the most from this therapy.

Although the HCV genotype is known to be the strongest predictor of SVR, several host genetic factors have also been found to affect the response to treatment. Recent studies have revealed that the likelihood of achieving an SVR with PEG-IFN and RBV depends on the nucleotide sequence near the interleukin (IL) 28B gene. Interestingly, the frequency of the favorable IL 28B allele is substantially higher in East Asians. Notably, several earlier studies have demonstrated that Asian patients are more likely to achieve SVR than Caucasians. However, contradicting the earlier reports described above, several recent studies have found that Asians have similar or even inferior SVR rates compared to Caucasian patients with the same HCV genotype.

When comparing data from different studies, the study design and methods of analysis should be considered. Real-world effectiveness data derived from ordinary clinical practice settings often differ markedly from the efficacy data obtained in the settings of randomized controlled registration trials.

We assessed the effectiveness of PEG-IFN α-2a and RBV therapy in treatment-naïve Korean patients with CHC and who had accurately diagnosed HCV genotype 1, 2, or 3.

PATIENTS AND METHODS

Patients

The study population was recruited from two groups of treatment-naïve patients with CHC who were treated with the PEG-IFN α-2a plus RBV combination. One group consisted of 100 patients in a prospective, industry-sponsored, open-label, uncontrolled, community-based clinical trial (Pegasys Expanded Access Program) conducted at six tertiary referral centers in Korea between 2003 and 2004 (Clinical Trial group). The second group consisted of 522 patients who were treated in a single tertiary referral hospital (Asan Medical Center, Seoul, Korea) between 2004 and 2008 (Cohort group).

Eligible patients were previously untreated adults aged 18-70 years who had polymerase chain reaction (PCR)-detectable HCV ribonucleic acid (RNA) and compensated liver disease. Patients were excluded if they had any of the following: a HCV genotype other than 1, 2, or 3; acute hepatitis C; decompensated cirrhosis; hepatocellular carcinoma; other forms of liver disease. Patients with human immunodeficiency virus, pre-existing severe depression or other psychiatric disease, previous organ transplantation, absolute neutrophil count (ANC) <1,000 cells/mm³, platelet count <75,000 cells/mm³, or hemoglobin (Hb) <13 g/dL for men or <12 g/dL for women were also excluded. Cirrhosis was based on the histological diagnosis in Clinical Trial group, and on histological or radiological diagnosis in Cohort group. All study patients were of Korean ethnicity. This study was approved by the Institutional Review Board at each participating center.

Treatment protocol

The HCV genotype was determined by using the restriction fragment mass polymorphism (RFMP) assay. Patients with genotype 1 were treated with PEG-IFN α-2a (Roche, Basel, Switzerland) 180 μg/week and a daily RBV (Roche for the Clinical Trial group; Shin-poong, Korea for the Cohort group) dose of 1,000 mg (for patients with body weight <75 kg) or 1,200 mg (for patients with body weight ≥75 kg) for 48 weeks. Patients with genotype 2 or 3 were treated with PEG-IFN α-2a 180 μg/week and a daily RBV dose of 800 mg for 24 weeks. All study medications for the patients in the Clinical Trial group were provided by Roche, whereas the Cohort group patients purchased their medications. HCV RNA was quantified (Roche AMPLICOR HCV Test v2.0) at pretreatment, weeks 12, 24 and 48 for both genotypes and at week 72 for genotype 1.