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Editorial

# Is peginterferon and ribavirin therapy effective in Korean patients with chronic hepatitis C?

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Chronic hepatitis C (CHC) affects approximately 170 million people worldwide, and over 3 million individuals are newly infected each year.[1] Kim et al[2] reported that the adjusted prevalence rate of hepatitis C virus (HCV) infection in the general Korean population is approximately 0.78%, and the prevalence has been increasing.[3]

HCV is an important cause of liver diseases, such as liver cirrhosis and hepatocellular carcinoma (HCC). When it is not treated properly, patients diagnosed with CHC may progress to liver cirrhosis within 20 years and the 5-year risk of non-cirrhotics developing HCC was 4.8%.[4,5] The standard treatment for CHC is a combination of pegylated interferon and ribavirin (PEG-IFN/RBV). The purpose of this antiviral therapy is to achieve sustained virologic response (SVR), which is defined as negativity for HCV RNA by real time PCR at 24 weeks after completing treatment.[6,7] Previous reports have shown that HCV genotype, serum HCV RNA level before treatment, age, gender, body mass index, fibrosis, and ethnicity affect the outcome of antiviral therapy, and more recently, genome wide association studies (GWAS) showed that polymorphisms near the interleukin 28B (IL28B) gene might have a profound effect on treatment outcome.[8,9]

According to surveys conducted in the West, the SVR rate for HCV genotype 1 is 40-50% and for HCV genotype non-1 is 70-80%. In Korean patients, the SVR rate of HCV genotype 1 is about 70% and for HCV genotype non-1 is 80-90%.[10] Although it is not conclusive yet, it seems that ethnicity may have strong influence on treatment response. Our review of the literature showed that Asians CHC patients have better treatment responses than patients in the West. In special consideration of the Korean studies, Park et al by pooled analysis, found that Korean HCV genotype 1 patients had a better SVR rate than corresponding Western patients (62.7% vs. 42.4%) (Table 1).[11]

A recent GWAS showed that single nucleotide polymorphisms (SNPs) near IL28B are associated with virologic response in patients with genotype 1, and also prevalence of good response SNPs was high in Asian CHC patients.[12,13] Lyoo et al[14] and Jeong et al[15] reported, CHC patients with the rs12979860 CC and rs8099917 TT genotypes showed significantly higher SVR than patients with the CT and TG/GG genotype (70.2% and 68.6% vs. 25% and 33.3%, respectively),[14] provided convincing evidence supporting that ethnicity importantly determines treatment response in CHC patients.

According to Heo et al,[16] the clinical trial group had a significantly higher SVR rate than the cohort group for patients with

**Abbreviations:**

CHC, chronic hepatitis C; HCV, hepatitis C virus; HCC, hepatocellular carcinoma; SVR, sustained virologic response; PEG-IFN/RBV, pegylated interferon and ribavirin; GWAS, genome wide association studies; IL28B, interleukin 28B; SNPs, single nucleotide polymorphisms; DAA, direct-acting antiviral agent

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**Table 1.** Summary of data of chronic hepatitis C with peg-interferon and ribavirin treatment in Korea during 2006-2012

| Study (yr) | No. | M/F | EVR 1/non-1 | Mean age (yr) | Pretreatment HCV RNA (IU/mL) | EVR* 1/non-1 | ETR* 1/non-1 | SVR* 1/non-1 |
|---|---|---|---|---|---|---|---|---|
| Lee et al. (2006) | 75 | 39/36 | 29/46 | 50.8 | $4.0\times10^5$ | 86.2/n-a | 58.6/84.8 | 55.2/80.4 |
| Lee et al. (2008) | 70 | 46/24 | 49/21 | 50.4 | $28\times10^5$ | n-a | n-a | 67.3/76.1 |
| Kang et al. (2008) | 141 | 90/51 | 59/82 | 47.7 | $8.0\times10^5$ | 69.5/86.6 | 83.1/96.3 | 69.5/89.0 |
| Kim et al. (2008) | 97 | 58/39 | 46/51 | 51.2 | $18.9\times10^5$ | 84.8/94.1 | 69.6/88.2 | 58.7/86.3 |
| Kim et al. (2008) | 64 | 33/31 | 23/41 | 50.2 | $5.8\times10^5$ | 87.0/n-a | 82.6/97.6 | 69.6/90.2 |
| Kim et al. (2009) | 50 | 26/24 | 50/0 | 49.5 | $19.2\times10^5$ | n-a | 98.0/n-a | 74.0/n-a |
| Jeong et al. (2009) | 92 | 56/36 | 59/33 | 56.1 | $8.1\times10^5$ | n-a | n-a | 62.7/81.8 |
| Kim et al. (2009) | 74 | 29/45 | 51/23 | 46.4 | $4.4\times10^5$ | n-a | n-a | 35.3/57.0 |
| Sinn et al. (2011) | 314 | 143/171 | 139/175 | 50.3 | $12\times10^5$ | n-a | n-a | 64.7/85.0 |
| Goh et al. (2011) | 82 | 48/34 | 38/34 | 52.4 | $3.2\times10^5$ | n-a | n-a | 68.4/86.4 |
| Park et al. (2012)[18] | 758 | 456/302 | 461/293 | 50.2 | $3.2\times10^6$ | n-a | n-a | 56.6/71.4 |

Values are presented as number or percentage (*)
EVR, early virologic response; ETR, end-of-treatment response; SVR, sustained virologic response; n-a, not available.
This table was adapted from Park SY, et al.[11] and Park SH et al.[18] was added.

genotype 1 (80.8% vs. 54.7%, *P*=0.02), although patients with genotypes 2 and 3 in a clinical and cohort study had similar SVR rates. The clinical trial group also had a significant higher proportion of patients treated for the duration (96.2% vs. 69.8%, *P*=0.01). By per-protocol analysis, the SVR rate of HCV genotype 1 patients for 48 weeks treatment in the clinical trial group was 100%.

Treatment with PEG-IFN/RBV requires a complex regimen of subcutaneous injection, twice daily oral administration, and frequent monitoring for adverse effects, such as flu-like symptoms, depression, anemia, neutropenia, and thrombocytopenia. Consequently, not all patients complete planned treatment regimens. Previously conducted studies showed that good adherence to combination treatment enhanced SVR rate, as was demonstrated in a clinical trial, in which >80% of patients complied with >80% of PEG-IFN/RBV doses.[17]

In a study by Heo et al,[16] 12 of 51 clinical trial patients (37.3%) and 102 of 221 cohort patients (50.7%) did not adhere to combination treatment due to treatment related complications, such as, anemia and neutropenia. However, in genotype 1 patient in the Clinical Trial, the SVR rate increased from 66.7% to 100% among the patients showed good adherence. Thus, in multivariate analysis of predictive factors for SVR, adherence was found to be independently associated with SVR (OR=4.47, CI=1.82-12.0, *P*<0.01). According to this result, increasing adherence to combination treatment in Korean CHC patients appears to offer a more cost effective way of improving SVR rates than adding direct-acting antiviral agent (DAA).

This study investigated virological response among Korean CHC patients treated with PEG-IFN/RBV in a clinical trial group and in a cohort group. However, because this study was conducted retrospectively using a cohort model in a Korean patient population, the results obtained cannot be generalized. Nevertheless, the study does identify some significant points. First, it highlights the importance of ethnicity and genetic features regarding response to tailored treatment approaches in CHC. Second, Korean patients with HCV genotype 1 that adhered to PEG-IFN/RBV seemed to achieve better SVR rates at lower cost than Caucasian patients treated with PEG-IFN/RBV adding DAA. It is thought that PEG-IFN/RBV therapy is more effective in Korean CHC patients than that of the Western, and a positive attitude is required in HCV treatment.

## Conflicts of Interest

The authors have no conflicts to disclose.

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