treatment-naive and other nucleoside-experienced patients with chronic hepatitis B

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Background: Entecavir (ETV) is a first-line agent in the treatment of chronic hepatitis B (CHB) because of its potent antiviral effect and low rate of viral resistance. Although the efficacy of ETV in treatment-naive CHB is well established, there are few data regarding its efficacy in other nucleoside-experienced CHB without resistant mutants. The aim of this study was to assess the efficacy of ETV in treatment-naive and other nucleoside-experienced CHB.

Methods: A total of 225 patients, who were treated with ETV 0.5 mg daily for at least 1 year, were included in this study. Patients were classified into two groups: treatment-naive (group 1, n=125) and other nucleoside-experienced (without resistant mutants at the start of ETV therapy, group 2, n=100). Group 2 patients had previous history of lamivudine or clevudine treatment with inadequate virologic response. There were significant differences between the two groups in pretreatment AST, ALT, HBV DNA level, and HBeAg positivity. The parameters including normalization of ALT, HBeAg loss, HBeAg seroconversion, undetectable HBV DNA, virologic breakthrough, and genotypic resistance were assessed.

Results: Mean age was 46.9 years and 144 (64.0%) patients were men. HBeAg was positive in 145 (64.4%) patients. After 1 year of ETV treatment, serum HBV DNA became undetectable (<400 IU/mL) in 109 (87.2%) and 90 (90.0%) patients of group 1 and 2, respectively, and HBeAg seroconversion occurred in 14 (15.2%) and 8 (15.1%) patients of group 1 and 2, respectively. There was significant difference in resistance rate between group 1 and 2 (0.8% vs. 7.0%, respectively). There was significant difference in resistance rate between group 1 and 2 (0.8% vs. 7.0%, respectively). There was significant difference in resistance rate between group 1 and 2 (0.8% vs. 7.0%, respectively).

Conclusions: This study showed that the genotypic resistance after ETV therapy for at least 1 year was more frequent in other nucleoside- experienced patients than treatment- naïve CHB patients. Nevertheless, because of its low resistance rate, switch to ETV therapy is recommended in CHB with inadequate virologic response to other nucleoside therapy.

Keyword: Entecavir, Chronic hepatitis B

PE-009

Efficacy of three years of continuous entecavir therapy in treatment-naive chronic hepatitis B patients

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Background: Entecavir (ETV) is a potent, selective inhibitor of HBV DNA polymerase. The aims of our study are to evaluate the efficacy of ETV and to explore useful predictors for efficacy of ETV treatment in treatment-naive patients with CHB.

Methods: A total of 105 treatment-naive patients with CHB, who visited Chung-Ang University Hospital between January 2007 and January 2008, were enrolled in this study (77 males, and 64 HBeAg positive). Mean age, baseline serum ALT level and serum HBV DNA level were 49 years (range, 21-78), 220.0 IU/L (range, 11-898) and 7.5 log10copies/mL (range, 5.4-9.9), respectively. They were treated with ETV 0.5 mg/dL. The mean duration of treatment was 39 months (range, 24-60). All patients were assessed for virological response (HBV DNA <140 copies/mL), biochemical response (ALT < 40 IU/mL), and HBeAg seroconversion. Serum HBV DNA was quantified using the real time PCR assay (Roche Diagnostics).

Results: 72 patients were followed more than 3 years. 14 patients were followed less than 3 years, 13 patients were follow-up loss, 5 patients died of HCC, and 1 patient was developed ETV resistance. In 45 HBeAg- positive and 27 HBeAg-negative ETV-treated patients, the rates of virological response were 51.1% (23/45) and 85.2% (23/27) at 3 years, respectively. The rates of biochemical response were 59.4% (38/65) and 85.2% (23/27). Mean reduction of baseline HBV DNA was -5.3, and -4.9 log10copies/mL. The rate of HBeAg seroconversion was 24.4% (11/45). We experienced one case of genotypic ETV resistance with viral rebound during ETV treatment. The ETV-resistance-related substitution (T184A), along with L180M and M204V, was detected by sequence analysis at week 96, simultaneously.

Conclusions: This study showed that genotypic resistance after ETV therapy for at least 1 year was more frequent in other nucleoside- experienced patients than treatment- naïve CHB patients. Nevertheless, because of its low resistance rate, switch to ETV therapy is recommended in CHB with inadequate virologic response to other nucleoside therapy.

Keyword: Chronic hepatitis B, Entecavir

PE-010

The rates of viral breakthrough and myopathy during clevudine therapy

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Background: Clevudine (CLV) has potent and sustained antiviral activity against hepatitis B virus (HBV). However, relatively frequent chances of viral resistance and myopathy are the major limitation of long-term CLV therapy. We intended to evaluate the rates and the clinical features of viral breakthrough (VR) and CLV-related myopathy during CLV therapy.

Methods: Eighty-five patients (69 CHB, 14 LC, 2 HCC, 65 male, mean age 43) were treated with 30 mg of CLV per day for > 6 months (median; 16 months, range; 6-36 months). VR was defined as an increase in serum HBV DNA by > 1 log10copies/mL above nadir in at least two consecutive tests. The frequency and features of myopathy and the changes of muscle enzyme levels were examined.

Results: 10 patients (12.9%) experienced VR. The rates of VR at 1, 2, and 3 years were 4.1%, 25.0%, and 43.7%, respectively.
6 of 10 with VR were tested for genotypic mutation. Among them, rtM204I was detected in one patient and rtM204I+rtL180M was detected in 5 patients. At the time of VR, 9 patients (90%) switched from CLV to the entecavir 1mg, and 1 patient (10%) to adefovir. CLV-related myopathy occurred in 12 patients (14.1%). The rates of myopathy at 1, 2, and 3 years were 3.7%, 21.8%, and 41.0%, respectively. Myalgia occurred in 7 (8.2%), upper limb and lower limb weakness occurred in 5 (5.9%). Myopathy symptom and sign were accompanied by muscle enzyme elevation in 9 of 12 patients. When CLV was stopped or changed to the other nucleos(t)ide analogues, myalgia and muscle weakness were improved in all cases.

Conclusions: 10 patients (12.9%) experienced viral breakthrough during therapy. The frequency of myopathy increased with each year of therapy, however, myopathy completely recovered after stopping or changing the medication.

Keyword: Chronic hepatitis B, Clevudine, Viral breakthrough, Myopathy

PE-011
Five years’ experience of Entecavir treatment in Korean chronic hepatitis B patients

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Background: Entecavir is one of the highly potent and commonly prescribed oral antiviral agent for treating chronic hepatitis B virus infection. Here, an experience in the use of Entecavir in Korean patients with chronic hepatitis B is reported.

Methods: The patients who have taken 0.5 mg/d of entecavir to control hepatitis B virus between January, 2006 to December, 2010 were retrospectively studied. The virologic response during the medication, and the DNA status after the cessation were observed.

Results: Among 1367 patients prescribed with entecavir, 128 patients discontinued the drug before December 31th, 2010. Of these 128 patients, HBeAg was positive in 63 (49.2%), negative in 47 (36.7%), and not identified in 18 (14.1%) patients. Among 111 patients whose DNA level was detected at least once after the first prescription, 87 (78.4%) patients showed undetectable levels of HBV DNA (< 300 copies/mL) on a median of 139 days, and underwent treatment for a median of 410 days. 48 patients were followed up after the end of treatment, and 38 (79.2%) patients showed relapse on a median of 128 days. In the 10 patients whose consolidation duration was under 365 days, the virologic relapse was at a median of 99 days and none of the patients showed sustained suppression of the viral DNA, while in 38 patients who underwent consolidation for at least one year, the virologic relapse was in 29 patients at a median of 134 days and 9 patients are showing sustained DNA suppression till now.

Conclusion: These data are compatible to previous reports on the good virologic responses of entecavir in chronic hepatitis B virus, and also may support the idea that the longer the consolidation treatment duration (at least one year) after undetectable levels of HBV DNA, the longer will the virologic response sustain.

Keyword: Chronic hepatitis B, Entecavir, Durability

PE-012
The analysis of early virologic response in combination treatment with pegylated interferon and nucleoside analogue in patients with chronic hepatitis B

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Background: For the treatment of chronic hepatitis B, a long-term use of oral nucleoside analogues have been mainly used. However, drug-resistant virus and the low response rate of interferon are problematic. Recently, the new clinical studies have reported, which oral antiviral agents is administered for lowering viral load and, then pegylated interferon treatment is followed, sequentially. In this study, we aimed to compare the treatment efficacy between pegylated interferon monotherapy and pegylated interferon, entecavir combination therapy in chronic hepatitis B.

Methods: All enrolled patients were 57, which divided into two groups, Group A (pegylated interferon alone, n=35) and Group B (pegylated interferon plus entecavir, n=22). In both group, pegylated interferon alpha-2a (pegasys, ROCHE) 180 mcg/wk was administered. In combination group, oral nucleoside analogue, Entecavir, was administered for 2-12 weeks. The results were analyzed by intention to treat population.

Result: Age, sex, AST/ALT, BMI, HBV DNA copies were no difference between two Groups. Total 11 patients were dropped out, 6 of whom were non-responders. Although EVR were statistically no difference, Group A (45%) and Group B (68.8%) (p=0.163), it seems to be higher in Group B. In 48 weeks, response rates were Group A (58.3%) and Group B (81.8%) (p=0.222), and HBV DNA negativity’s rates were Group A (25%) and Group B (27.3%) (p=0.635). In 34 patients, liver biopsy was performed before treatment. Although there were no significant factors to influence the virologic response, Inflammation score seems to be higher in EVR group.

Conclusion: Our data suggest that combination therapy of pegylated interferon and oral nucleoside analogues shows the tendency of raising EVR. Further study is needed for the evaluation of the factors associated EVR and SVR.

Keyword: Pegylated interferon, Entecavir, Chronic hepatitis B

PE-013
Entecavir and lamivudine in patients with decompensated chronic hepatitis B liver disease

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