PO-01
How to differentiate acute hepatitis B from chronic hepatitis B with acute exacerbation

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Background/Aims: Although distinguishing acute hepatitis B (AHB) from chronic hepatitis B (CHB) with acute exacerbation (AE) is difficult, it is extremely important considering their prognosis and treatment strategy. Therefore, simple, effective and inexpensive methods are required for differentiating between these conditions. This study aimed to evaluate factors distinguishing AHB from CHB with AE.

Methods: Sixty-eight patients, who were positive to hepatitis B surface antigen (HBSAg) and IgM anti-HBc during the AE, were analyzed. These patients were divided into two groups based on their clinical diagnosis. The AHB group was defined as patients having AE without evidence of positive HBSAg before this episode of acute hepatitis and with loss of HBsAg within 6 months after onset of acute hepatitis. AE was defined as elevation of serum ALT levels more than 5-fold upper limit of normal. Known CHB patients with AE (CHB-AE) during the same period were recruited as a control group. Biochemical and virological profiles were compared between AHB group and CHB-AE group. Then, parameters with great differences were selected to assess diagnostic power for differentiating between AHB and CHB-AE.

Results: 40 patients were in AHB and 28 in CHB-AE. There were significant difference in platelet count, AST, ALT, LDH, albumin, α-fetoprotein, HBV DNA levels and IgM anti-HBc titer between the AHB and the CHB-AE group. IgM anti-HBc titer and HBV DNA levels were more predictive than other factors. HBV DNA levels < 6 log (copies/mL) had sensitivity, specificity, PPV and NPV of 87.5%, 89.3%, 92.1% and 83.3%, respectively, and IgM anti-HBc titer > 5 (index) had 97.5%, 82.1%, 88.6%, and 95.8%, respectively for diagnosing AHB. The combination of HBV DNA levels and IgM anti-HBc titer had sensitivity, specificity, PPV and NPV of 100%, 71.4%, 83.3% and 100%, respectively.

Conclusions: HBV DNA levels and IgM anti-HBc titer might differentiate patients with AHB from CHB-AE.

Keyword: Acute hepatitis B, Chronic hepatitis B

PO-02
Changes in serum creatine kinase level and clevudine induced myopathy

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Background: The aim of this study was to evaluate the predictable clinical factors and to assess the elevation in serum creatine kinase (CK) levels as a predictable marker of clevudine-induced myopathy.

Methods: Treatment-naïve chronic hepatitis B patients with compensated liver disease treated with 30 mg clevudine once daily for more than 6 months were studied consecutively from Konkuk University Hospital. Clinical factors were assessed according to medical history, physical examination, HBeAg and HBV DNA level. Adverse events and laboratory abnormalities—AST, CK, creatine-related with myopathy were monitored baseline and every 3 months throughout treatment period.

Results: A total of 99 patients (M:F=61:38, mean age 44.7 yr) with chronic hepatitis B were included. Mean duration of clevudine treatment was 18 months. Fifteen patients developed myopathy related with clevudine therapy. There was no difference in age, gender, alcohol, diabetes, medications, cirrhosis, antiviral response between non-myopathy group and myopathy group. Elevation of CK level was frequently observed in the patients with clevudine therapy. At least one episode of elevation of CK were 57.1% in non-myopathy group and 100% in myopathy group (p=0.001). At least two episodes of elevation of CK were 40.5% in non-myopathy group and 93.3% in myopathy group (p=0.001). At least one episode of toxic grade above 3 of CK were 15.5% in non-myopathy group and 40.0% in myopathy group (p=0.026). Toxic grade above 3 of CK was not observed in the both groups. Fluctuations in CK level during treatment with clevudine were frequently observed in both groups.

Conclusions: The elevation in serum CK level occurs frequently during the long-term treatment with clevudine. It could be a predictive marker for developing clevudine-induced myopathy. Muscle-related symptoms and serum CK level should be carefully monitored during treatment of clevudine.

Keyword: Chronic hepatitis B, Clevudine, Myopathy, Creatine kinase

PO-03
Clonal evolution of hepatitis B virus resistant to lamivudine, adefovir and entecavir during therapy with lamivudine and adefovir

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Background: Multi-drug resistant hepatitis B virus (HBV) has been reported in hepatitis B patients who received sequential antiviral therapy. This study aimed to determine whether mutations conferring resistance to multiple antiviral agents co-locate on the same HBV genome in vivo and to describe the evolution of these mutations.
PO-04

Antiviral efficacy of adefovir dipivoxil in lamivudine-resistant chronic hepatitis B: the optimal duration of lamivudine overlap

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Backgrounds: The antiviral response of adefovir dipivoxil (ADV), the predictors of its response, and optimal duration of lamivudine (LAM) overlap were studied in patients with LAM-resistant chronic hepatitis B (CHB).

Methods: Retrospective analysis on the antiviral efficacy of ADV was performed in the 175 LAM-resistant CHB patients who were treated with ADV for more than 12 months either as the switch therapy from LAM, or as the add-on therapy with LAM. The mean duration of ADV treatment was 34 months.

Results: The subjects showed mean age of 48.1 years, 72.6% of male, 37.1% of compensated cirrhosis, 75.4% of HBeAg positivity, mean ALT level of 258, and mean pretreatment HBV DNA level of 6.33 log_{10} copies/mL. The overall virologic response rate (VR) at the last follow-up was 57.1%, and virologic breakthrough rate (BT) was 12.6%, and HBeAg loss rate was 29.1% among the 175 patients, in whom 45 patients (25.7%) were ADV switch group and 130 patients (74.3%) were ADV add-on group. The add-on group showed significantly higher VR (61.5%) and lower BT (4.6%) at the last follow-up than those of switch group (42.2% and 35.6%, respectively). The undetectable HBV DNA level at 12 months of treatment was a significant predictor of VR. As a subgroup analysis, the add-on group was divided into 2 subgroup, LAM-discontinuation group and LAM-continuation group at 12 months after achieving VR. The LAM-discontinuation group showed similar VR (93.3%) and BR(0%) to the LAM-continuation group (85.7% and 0%, respectively).

Conclusions: LAM should be added to ADV therapy for the LAM-resistant CHB patients to get a better VR. However, LAM may be discontinued when LAM and ADV combination was administered for 12 months after achieving VR. Further studies are warranted to investigate the optimal duration of ADV and LAM combination for the LAM-resistant CHB.

Keyword: Adefovir, Lamivudine resistance, Chronic hepatitis B, Combination therapy

PO-05

Antiviral efficacy of entecavir monotherapy in adefovir-resistant chronic hepatitis B; focus on genotypic mutation patterns

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Background: Despite of limited evidence, entecavir (ETV) has been thought as an effective agent to adefovir (ADV) resistance. However, its antiviral efficacy and safety, especially in terms of ADV signature mutation types, have not been elucidated so far. An antiviral effect of ETV to multidrug-resistant mutation of A181V/T remains unclear.

Methods: We assessed consecutive 57 patients on ETV monotherapy due to sequential lamivudine (LAM)- and ADV-resistant CHB. For sub-analysis, an antiviral efficacy was evaluated according to ADV resistant mutation patterns as follows; A181V/T (n=33), N236T (n=9) and A181V/T+N236T (n=15).

Results: The median baseline viral load was 4.94 log_{10} IU/mL (range 1.78-8.23) and the median duration of follow-up was 22 months (range 6-60). The A181V/T mutation showed a significantly higher reduction of HBV DNA level at 24 weeks (-2.24±0.38 log_{10}copies/mL, p<0.0001), while the drop was significantly greater in the A181V/T+N236T group (-2.24±0.61 log_{10}copies/mL, p=0.0004) at 48 weeks. Four (14%) patients with A181V/T mutation showed virologic breakthrough and there was no significant differences in virologic response among the three subgroups (21% vs. 12% vs. 27%, p=0.749). Serum alanine aminotransferase normalization was higher in