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**PP-112** Analysis of five HBeAg-positive patients with Chinese herb Kuanxiongjiedu grain anti-HBV infection treatment

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**Background and objectives:** The objectives of the research are to observe the efficacy of the Chinese Herb Kuanxiongjiedu Grain (CHKG, consists of 12 ingredients) treatment for the patients whose HBV DNA levels over  $10^6$  copies/mL and analysis the variations of the patients' hepatocyte.

**Methods:** Five patients with HBeAg-positive are selected. They have baseline ALTs: 22.3~285U/L, HBV DNAs:  $2.1 \times 10^6 \sim 2.8 \times 10^8$  copies/mL. The patients received CHKG two times daily (24g each time) for 32 weeks. The ALT and HBV DNA tests were implemented every two weeks in the first three months, and taken every four weeks in the following months. A Ultrasound Scanner was used to scan the patients and a normal person's livers. The mean and standard deviation of the gray levels of the normal person's scanned liver image are selected as the standard of normal liver.

**Results:** At the week 32, one patient's HBV DNA was below 1000 copies/mL and had normal ALT; three patient's HBV DNAs and ALTs have no significant changes; one patient's HBV DNAs have significant changes. Except the first patient, the patients' normal liver pixels increased 14% ~ 51%.

**Conclusion:** The CHKG may help to recovered the chronic HBV patients' damaged hepatocyte even the patients' virus levels were not be suppressed during the therapy. Further investigation should be implemented.

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**PP-113** Sequence analysis and replication fitness of the complete hepatitis B virus genome in patients with chronic hepatitis B

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**Objective:** To analyze the complete HBV genome in patients and evaluate its replication capacity.

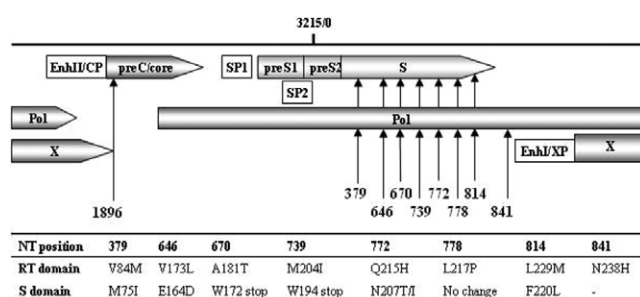


Fig. 1. Schematic diagram of the point mutations analyzed in the study. In the first part of the figure, the number on the top of the full HBV genome refers to the EcoRI site (3215/0). Position of the four open reading frames (ORFs) encoding preC/core, preS1/preS2/S, polymerase (Pol), and X protein are shown by the gray rectangle and the arrow indicates the transcription direction. The four cis-elements (enhancers and promoters) are indicated by the open triangle. The numbers under the full HBV genome represent the nucleotide positions of the studied mutations. In the second part of the figure are listed amino acid mutations in both polymerase (RT domain) and envelope genes-associated domains (S domain).

**Methods:** The full-length HBV genome amplification, cloning, and sequencing were preformed. Genotype and mutation sites related to antiviral agents were analyzed, and site-directed mutagenesis was performed on interested sites. The full-length HBV genomes were transfected into HepG2 and Huh-7 cell lines. 72 h after transfection, expression of HBsAg was detected with ELISA, quantitation of intracellular HBV replicative intermediates were examined by qPCR.

**Results:** 12 different clones were obtained. several mutation sites, such as A181V/S, V84M, were identified, and the better management of 5 patients was developed.

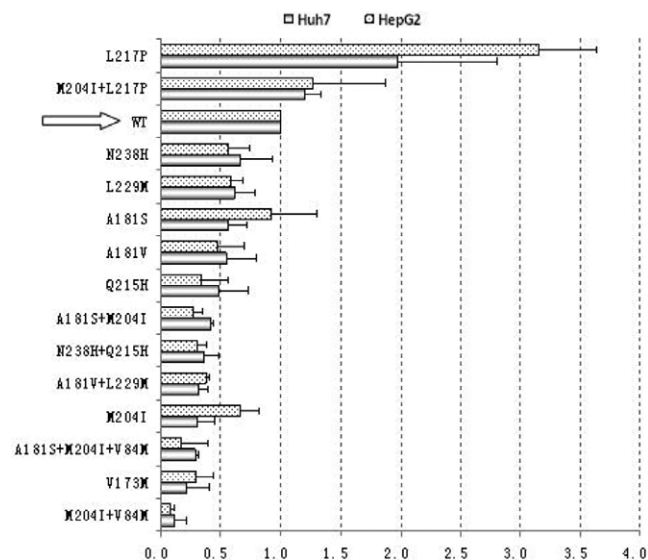


Fig. 2. Relative replication yield of HBV mutants.

**Conclusion:** Vector-free replication assay is an approach to determine the phenotype of clinical HBV strains, which could become an important tool for the management of patient infected with HBV.

**PP-114** Correlation factors involved in therapeutic efficacy of adefovir dipivoxil for chronic hepatitis B with YMDD mutation

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**Background:** To investigate the correlation factors associated with the therapeutic efficacy of adefovir dipivoxil for chronic hepatitis B with YMDD mutation.

**Methods:** 92 patients were enrolled and treated with adefovir dipivoxil for 48 weeks, Logistic regression analysis was used to identify some possible correlation factors associated with therapeutic efficacy.

**Results:** Patients who achieved undetectable HBV DNA at week 48 of the treatment were found to have a lower baseline HBV DNA levels compared with those who did not achieve, and the same result in patients who achieved HBeAg seroconversion and serum alanine aminotransferase (ALT) normalization. There were significant difference between patients whose baseline ALT levels  $\leq 1$  ULN, HBV DNA levels  $\leq 5.0$  lgcopies/mL and patients whose baseline serum ALT levels  $> 1$  ULN, HBV DNA levels  $> 5.0$  lgcopies/mL in undetectable HBV DNA ( $\chi^2=17.321$ ,  $P<0.001$ ), HBeAg seroconversion ( $\chi^2=3.88$ ,  $P=0.049$ ) and ALT normalization rates ( $\chi^2=25.526$ ,  $P<0.001$ ) after 48-week treatment. Logistic regression analysis indicated the baseline HBV DNA levels, undetectable serum HBV DNA by PCR at week 24, and undetectable serum YMDD mutation at week 12 were correlation factors of therapeutic efficacy at week 48.

**Conclusion:** Better response at week 48 has significantly asso-

ciated with the lower baseline serum HBV DNA levels, HBV DNA negativity at week 24 and undetectable serum YMDD mutation at week 12 compared with non-response. Early treatment with adefovir dipivoxil for the patients with YMDD mutation who had virological breakthrough and without biochemical breakthrough can reach for better curative effect.

**PP-115 Hepatitis B vaccination of chronic HBV infected cases who lost HBsAg during follow-up**

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**Background:** Over time, the levels of HBsAg in some chronic HBV infected individuals declines and is not detectable in the serum. The purpose of this study was to assess the efficacy of HBV vaccine in subjects who lost their HBsAg with not seroconversion to anti-HBs.

**Methods:** From April 1993 to December 2007, among 1603 chronic HBV infected individuals, 34 subjects (22 males, 12 females) became HBsAg negative with no detectable anti-HBs and HBV DNA in their sera. They received HBV vaccine at 0, 1 and 6 months (case group). Fifty-two subjects (30 males, 22 females) who were negative to HBsAg, anti-HBs and anti-HBc received HBV vaccine like the above schedule (control group). Anti-HBs was assessed one month of the last dose in these two groups.

**Result:** The mean age of the case group was 38±12.7 and the control group was 33.4±8.6 years ( $p=0.07$ ). The distribution of sexes between these two groups were equal ( $p=0.652$ ). The mean year of follow-up for the case group was 7.6±4.5 years. Anti-HBs levels  $\geq 10$  IU/l was developed in 8 (23.5%) subjects in the case group and in 45 (86.5%) of the control group ( $p=0.0001$ ). The mean anti-HBs levels in the case group was 68±32.66 and in the control group was 344.6±38.9 IU/l ( $p=0.00001$ ).

**Conclusion:** The results show that nearly 24% of chronic HBsAg positive subjects, who lost their HBsAg responded to hepatitis B vaccine and the remaining cases need to be followed for occult HBV infection.

**PP-116 Profile of occult hepatitis B virus infection in an area with intermediate prevalence of HBV infection**

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**Background & Aim:** Hepatitis B virus (HBV) infection with undetectable levels of hepatitis B surface antigen (HBsAg) is called an occult infection, which although has been described among subjects with chronic hepatitis C liver disease in the western world, it's prevalence and clinical significance are still ambiguous in the Indian subcontinent.

**Methods:** We investigated HBV-DNA PCR in serum samples of 260 HBsAg negative subjects with chronic HCV-related liver disease, and 70 apparently healthy volunteers negative for HBsAg and anti-HCV as control.

**Results:** Serum samples found positive by at least two independent PCR assays were considered HBV DNA positive. HBV-DNA was detected among 19 HCV-related chronic liver disease (CLD) patients (7.3%), which was higher ( $p=0.2$ ) as compared with the control volunteers (4.3%). It was more frequent (37.5%) in 24 anti-HBs negative/anti-HBc positive patients than in 180 anti-HBs/anti-HBc positive (5%,  $p<0.05$ ). HCV RNA by qualitative PCR was significantly ( $p<0.001$ ) higher in occult HBV compare to

non-occult. HCV genotype 1b was predominantly associated with occult HBV (73%), especially among subjects with hepatocellular carcinoma (HCC) ( $p<0.05$ ) as compared to non-occult HBV cases. Though not significant, frequency of occult HBV infection was higher than healthy controls and HCV 1b genotype was significantly associated in patients with HCC.

**Conclusion:** This study suggests that in all HBV-endemic areas, the possibility of occult HBV in patients with HCV should be considered and HBV-DNA should be performed.

**PP-117 Thymosin alpha-1 therapy in Chinese patients with chronic hepatitis B: results from a randomized controlled clinical trial**

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**Objective:** To observe the efficiency of Thymosin- $\alpha$ 1 treatment in patients with chronic hepatitis B.

**Methods:** Fifty-six HBeAg-negative and sixty-two HBeAg-positive patients were randomly divided two groups, received Thymosin- $\alpha$ 1 or Interferon alpha for six months respectively.

**Results:** At the end of treatment, complete response (CR) occurred in 8 of 26 and 9 of 29 in T- $\alpha$ 1 group and in 14 of 30 and 15 of 33 in IFN- $\alpha$  group in HBeAg-negative and HBeAg-positive patients respectively ( $p>0.05$ ). After a 6-month follow-up period, a CR was observed in 11 of 26 HBeAg-negative and 14 of 29 HBeAg-positive in T- $\alpha$ 1 group and in 7 of 30 HBeAg-negative and 9 of 33 HBeAg-positive patients in IFN- $\alpha$  group ( $p>0.05$ ). Compared with the results observed in untreated patients, the rate of CR was significantly higher in IFN- $\alpha$  group at the end of therapy ( $p<0.001$ ) and in T- $\alpha$ 1 group at the end of follow-up ( $p<0.001$ ). Ten of the 12 T- $\alpha$ 1 responders experienced sustained non-detectable HBVDNA after the 6-month treatment period. Six of the 14 T- $\alpha$ 1 non-responders showed delayed response of non-detectable HBVDNA during the follow-up period. In HBeAg-positive patients, it is 87.5% and 53.8%. However, the data were 50% and 0%, 59.1% and 0% in IFN- $\alpha$  group, respectively. The rate of delayed response was significantly higher in T- $\alpha$ 1 group ( $p=0.010$ ) and the rate of flare was higher in IFN- $\alpha$  group ( $p>0.05$ ) during the follow-up period.

**Conclusion:** A 6-months course of T- $\alpha$ 1 therapy is effective in CHB patients with a gradual and more sustained ALT normalization and HBVDNA loss.

**PP-118 Adefovir genotypic resistance in chronic hepatitis B patients with virological breakthrough during adefovir treatment**

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**Objectives:** To investigate the genotypic resistance profiles in chronic hepatitis B patients who underwent virological breakthrough during adefovir treatment.

**Methods:** Serum samples and clinical data were collected from adefovir treated patients (10mg/d) who underwent virological breakthrough (HBV DNA increase  $1\log_{10}$  copies/ml from the Nadir). Adefovir genotypic resistance was detected with PCR product pyrosequencing. HBV genotypes were identified by phylogenetic tree analysis of PCR product di-deoxy sequencing