Evolution of Hepatitis B virus genome in the post antiviral era: Increasing prevalence of the G1899A mutation and its association with liver cirrhosis

Statement of the Problem: Replication of Hepatitis B virus (HBV) depends on an error prone reverse transcriptase encoded by the viral polymerase gene. Mutations developed along the clinical course of chronic infection. Following widespread use of antivirals, lifelong administration of polymerase inhibitors posted a serious threat to the virus, forcing it to execute further adaptation. To date, there was no study monitoring the changes of HBV genomes over time in the post antiviral era.

Methodology & Theoretical Orientation: Recently, we analyzed basal core promoter (BCP)/precore sequences in 1224 treatment-naive chronic Hepatitis B patients in the post antiviral era. The prevalence of all BCP/precore mutations were compared year-on-year. Subsequently, we analyzed age-dependent correlation between BCP/precore mutations and liver cirrhosis.

Findings: Overall, the prevalence of HBeAg-negative chronic Hepatitis B was increasing (P<0.001) and the patients’ age was also increasing (P=0.001), independent of HBeAg status. Additionally, the prevalence of both G1896A and G1899A mutations was increasing (from 67.50% to 74.45% (P=0.003) and 20.00% to 26.81% (P=0.019), respectively). In HBeAg-positive subgroup (n=398), only the prevalence of G1899A mutation and HBV-DNA levels were increasing yearly (from 2.50% to 17.44% (P=0.038) and 7.74 to 8.30 Log10 copies/mL (P=0.013)). These two factors were also independent to each other. In HBeAg-negative subgroup (n=826), a significant decrease in the prevalence of A1752G mutation was found (P=0.022). Subsequent study showed that the G1899A mutation was associated to liver cirrhosis development in old age patients. In fact, in patients >65 years of age, G1899A was the only associated mutation when evaluating all BCP/precore mutations.

Conclusion & Significance: HBV continued to evolve in the post antiviral era. The prevalence of G1899A mutation was increasing associated with liver cirrhosis in old age patients.

Biography
Chau-Ting Yeh has obtained his MD from National Taiwan University and PhD from Department of Molecular Microbiology and Immunology, University of Southern California. He is the Director of Liver Research Center, Chang Gung Memorial Hospital, Taiwan, since 2007. His research interests focus on HBV antiviral drug-related mutants and their oncogenic potential and new strategies applying precision medicine to treat hepatocellular carcinoma. He has published more than 200 papers in SCI indexed journals.

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