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Effect of pre-S2 mutation of hepatitis B virus subgenotype B3 the endemic strain in Indonesia on hepatocellular carcinoma: Observation on transcription factor NF-κB expression and activation

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Published: 19 December 2015

Aim/Background: More than 50% of hepatocellular carcinoma (HCC) cases worldwide and 70–80% of HCC cases in highly hepatitis B virus (HBV) endemic regions are attributable to HBV. Indonesia has high prevalence of hepatitis B with subgenotype B3 as the major and endemic strain. Cross sectional study on hepatitis B patients in Indonesia showed association of pre-S2 start codon mutation with severity liver disease which was dissimilar with studies from
other population where pre-S2 deletion mutation was more prevalent. The different mutation pattern was attributed to the different HBV subgenotype of each population study. HBV surface proteins were reported to induce the activation of NF-κB, a transcriptional factor known to involve directly in many aspects of chronic liver disease such as cirrhosis and HCC. Hence this study aimed to observe the effects of different HBs mutant variants of Hepatitis B Virus (HBV) subgenotype B3 as the endemic strain in Indonesia on the expression and activation of NF-κB.

**Methods:** HBs genes of HBV subgenotype B3 isolated from three hepatitis B patients with HCC were amplified and cloned to pcDNA3.1, and were transfected using lipofectamine into Huh7 cell line. Expressions on mRNA level for HBs, IκB-α and NF-κB (p50) were evaluated using real-time PCR. IκB-α expression which is regulated by NF-κB was used as parameter to measure NF-κB activation.

**Results:** HBs mRNA expressions were decreased after 48 to 72 hours. HBs protein expression detected using ELISA were increased at 72 hours for pre-S2 start codon mutation and pre-S2 deletion. NF-κB activation was higher for HBs wild type compared to the two mutant variants, however pre-S2 deletion mutant showed higher NF-κB activation after longer period of incubation. NF-κB (p50) expression was higher for pre-S2 start codon mutation.

**Conclusions:** Pre-S2 mutations had no effect to the increment of NF-κB activation, however pre-S2 start codon mutation might associated to increased expression of NF-κB (p50). This suggests that preS2 start codon mutation and pre-S2 mutation may utilize different pathway in liver disease progression.

**Disclosure:** All authors have declared no conflicts of interest.

**Topic:** second heart sound, s2, mutation, carcinoma, hepatocellular, indonesia, hepatitis b virus, transcription factor
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