PLASMA HBsAg LEVELS CORRELATE WITH LIVER cccDNA IN TOLERANT CHILDREN WITH INFANCY ACQUIRED CHRONIC HEPATITIS B INFECTION

doi:10.1136/gutjnl-2012-302514b.156
I Carey,* Y Zen, M J Bruce, M Horner, S Bansal, D Vergani, G Mieli-Vergani. Institute of Liver Studies and Transplantation, King’s College Hospital, London, UK

Introduction Plasma HBsAg reflects the transcriptional activity of covalently closed circular (ccc) DNA within the liver rather than the absolute amount of cccDNA copies. Higher plasma HBsAg levels are reported among tolerant than immuno-active HBeAg positive chronic hepatitis B (CH-B) patients. Only limited information is available on the interaction of plasma HBsAg, expression of HBsAg and HBcAg within the liver and liver relaxed circular (RC) HBV DNA and cccDNA in patients with infancy-acquired CH-B.

Aims To evaluate whether there is a relationship between plasma HBsAg and HBV DNA levels and HBsAg/HBcAg expression within the liver and liver RC HBV DNA and cccDNA in tolerant children with infancy-acquired CH-B.

Patients 23 children (eight males, median age 10.2 yrs) with infancy-acquired CH-B (all HBeAg+) in tolerant stage underwent liver biopsy prior to antiviral therapy with lamivudine and interferon-α.

Methods Plasma HBsAg and HBV DNA levels were measured at therapy baseline by Abbott ARCHITECT® assay and real-time TaqMan PCR [both log10 IU/ml]. Baseline liver RC HBV DNA and cccDNA was quantified by real-time TaqMan PCR [copies/ng genomic DNA]. Immunostaining of formalin-fixed, paraffin-embedded liver specimens assessed HBsAg and HBcAg expression (# of positive cells per 1000 hepatocytes). Results are presented as median, range.

Results Baseline plasma HBsAg levels were 4.67 (3.7–5.1), HBV DNA was 8.2 (7.1–8.9) both log10 IU/ml and ratio HBsAg/HBV DNA 0.57 (0.44–0.65). Liver RC HBV DNA was 4.41 (2.5–5.3) log10 copies/ng genomic DNA and cccDNA was 365 (303–5632) copies/ng genomic DNA. HBsAg is predominantly expressed in cytoplasm focally associated with membranous staining. 2.9 (0–56.9) positive cells/1000 hepatocytes, in contrast to HBcAg expressing predominantly in the nucleus, 83 (0.5–83.6) positive cells/1000 hepatocytes. There were positive bivariate Spearman correlations between plasma HBsAg levels and liver cccDNA (r=0.41, p=0.05), HBcAg liver expression and cccDNA (r=0.44, p=0.05), liver RC HBV DNA and cccDNA (r=0.67, p=0.04) and a trend towards correlation between plasma HBsAg and HBcAg liver expression (r=0.38, p=0.07).

Conclusion Plasma HBsAg levels correlate with liver cccDNA in tolerant children with infancy-acquired chronic hepatitis B infection suggesting that plasma HBsAg levels acts as a surrogate marker of cccDNA within the liver in tolerant patients.

Competing interests I Carey grant/research support from: BMS, Gilead, Y Zen: None declared, M Bruce: None declared, M Horner: None declared, S Bansal: None declared, D Vergani: None declared, G Mieli-Vergani: None declared.

RS12979860 CC GENOTYPE IS ASSOCIATED WITH BASELINE HIGH NUMBERS OF CD56BRIGHT NK-CELLS, LOW NUMBERS OF CD3-CD56-CD16+ CELLS, LOW IL-10 HCV-SPECIFIC PRODUCTION IN CH-C THERAPY RESPONDERS

doi:10.1136/gutjnl-2012-302514b.158
I Carey,* M J Bruce, D Joshi, D Vergani, K Agarwal. Institute of Liver Studies and Transplantation, King’s College Hospital, London, UK

Introduction IL28B gene single nucleotide polymorphisms (SNPs) rs12979860 and rs8099917 help to predict treatment response in chronic hepatitis C (CH-C). Strong immune responses control HCV infection. Little is known on the association between IL28B SNPs, innate/adaptive immune responses in relation to Peg-IFN/ribavirin sustained virologic response (SVR) in CH-C.

Aims To evaluate the relationship between rs12979860 and rs8099917, pre-treatment frequency/phenotype of natural killer (NK) cells (innate immunity), HCV-specific immune responses (adaptive immunity), and SVR.