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Citation	The 22nd Conference of the Asian Pacific Association for the Study of the Liver (APASL 2012), Taipei, Taiwan, 16-19 February 2012. In Hepatology International, 2012, v. 6 n. 1, p. 7, abstract PS03-01
Issued Date	2012
URL	http://hdl.handle.net/10722/153091
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PS03-01

Effect of nucleos(t)ide analogues therapy on HBsAg, intrahepatic HBV DNA and covalently closed circular DNA levels

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BACKGROUND: We aimed to study 1) the effects of 1-year nucleos(t)ide analogue (NA) therapy on HBsAg and covalently closed circular DNA (cccDNA) levels; and 2) the possible use of HBsAg reduction as a marker for cccDNA reduction. METHODS: We recruited 124 NA-treated patients with baseline and 1-year sera and liver biopsies. The NAs were categorized into the more potent (entecavir, telbivudine, and clevudine; n = 71) and less potent groups (lamivudine and adefovir; n = 53). cccDNA and HBsAg levels were measured by real-time PCR and the Elecsys HBsAg assay, respectively. RESULTS: At year 1, there were approximately 5 log(IU/ml), 2 log(copies/cell), and 1 log(copies/cell) reductions in serum HBV DNA, intrahepatic total HBV DNA, and cccDNA, respectively. Only a small reduction of HBsAg (mean: 0.18 log[IU/ml]) was observed. There were no significant differences between the more and less potent NAs in the reduction of HBsAg, intrahepatic total HBV DNA and cccDNA. Although 88/124 (71%) patients had undetectable serum HBV DNA, all had detectable HBsAg and intrahepatic total HBV DNA. Logarithmic reductions of HBsAg and cccDNA correlated weakly ($r = 0.183$, $p = 0.042$). Patients with cccDNA reduction. CONCLUSIONS: Despite the profound serum HBV DNA reduction after 1 year of therapy, reduction in HBsAg level was minimal, and reduction in intrahepatic total HBV DNA and cccDNA was relatively mild. HBsAg reduction may be a potential marker for the monitoring of cccDNA reduction during NA therapy.