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Genotypes and reverse transcriptase variability in asymptomatic chronic hepatitis B virus

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Background: Genomic mutations presented during hepatitis B virus (HBV) reverse transcription could explain its genetic diversity and account for genetically distinct eight genotypes which show distinctive geographically distribution. The main objectives of this study were to determinate the prevalence of hepatitis B virus genotypes in asymptomatic chronic hepatitis B patients without treatment, and to identify mutations associated to nucleos(t)ides analogues.

Methods: Twenty two serum samples from asymptomatic chronic hepatitis B patients without treatment were analyzed using INNO-LIPA HBV Genotyping assay and INNO-LIPA HBV DRv2 assay (Innogenetics). Nucleic acid was isolated and quantified using real time PCR assay COBAS Taqman HBV test. HBsAg, anti-HBs, HBeAg and anti-HBe were determined by ADVIA Centaur.

Results: Genotype D was the most prevalent (45.5%) followed by genotype A (27.3%) and genotype E (9%). There were four coinfection cases (18.2%) (two D/H, one E/F and one A/D genotypes). Both patients infected with genotype E were from sub-Saharan area. In our study, all the patients were positive for HBsAg and negative for HBeAg. HBV-DNA levels were quantified and the mean was 3.4 log10 copies/ml (minimum 1.07 and maximum 7.04). Among the twenty two HBV chronic inactive carriers, in only one case was detected a single mutation in rtV214A position, which has been associated to adefovir dipivoxil treatment. In this case, patient was infected with genotype D. In the remaining patients no mutations were identified at reverse transcriptase domain. Risk factors for HBV acquisition were as follow: vertical (27.3%), transfusion (13.6%), sexual (9.1%), tattoos (4.5%), interfamilial (4.5%) and unknown (41%).

Conclusion: INNO-LIPA is a convenient tool for detection HBV genotype and resistance mutation. Genotype D was the most prevalent accompanied with genotype A in asymptomatic patients, but also coinfection genotypes are frequent. A resistant mutation is rare in asymptomatic patients but it was detected in one patient, indicating a possible predisposition to adefovir dipivoxil therapy resistance. HBV reverse transcriptase gene sequencing analysis provides additional insight as part of monitoring program that includes genotypic analysis and quantification of circulating virus.

Antiviral treatment with interferon alpha and ribavirin influences serum markers of liver fibrosis in children with chronic hepatitis C

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Background: Liver fibrosis largely influences the course and prognosis of chronic hepatitis C (CHC). Although percutaneous liver biopsy is a valuable tool in the evaluation of liver injury, it posses significant drawbacks that limit repeated use of this technique. The aim of this study was to assess chosen serum markers of liver fibrosis − laminin (LAM), hyaluronic acid (HA) and transforming growth factor beta 1 (TGF-beta-1) with their relation to histopathological findings as well as their alterations after antiviral treatment with recombinant interferon alpha (IFN-alpha) and ribavirin (Rib) in children with CHC.

Methods: Study group included 68 children, age range 6−18 years (mean 13,34 ± 3,27 years) with diagnosed CHC. History data were analysed. Diagnosis was confirmed by the presence of HCV-RNA in serum by RT-PCR. All children underwent histopathological evaluation of liver biopsy specimen according to Ishak scoring system. Serum sample and liver biopsy specimen were collected the same day. LAM, HA and TGF-beta-1 were measured in serum by enzyme linked immunosorbent assay kits. Children were treated with IFN-alpha (3 MU/m2 3 x/week in s.c. injections) and Rib (orally, twice daily) for 48 weeks. Serum markers of fibrosis were also assessed at the end of the treatment.

Results: Length of infection was 7.34 ± 4.03 years (range 2−13.5 years). Mean ALT activity was 60,82 ± 65,02 IU/l. Increasing mean serum TGF-beta-1 ($p = 0.029$) and decreasing mean LAM level ($p = 0.039$) was found in the groups of children with increasing stage of fibrosis. Level of LAM was defined a risk factor of significant fibrosis (95%CI 18.05; 67.87, $p = 0.001$), while level of TGF-beta -1 of significant (95%CI: -33.51;-1.73, $p = 0.030$) and progressed liver fibrosis (95%CI -36.09; -3.37, $p = 0.019$). Conducted antiviral treatment with IFN-alpha and Rib resulted in significant decrease of TGF-beta-1 (51.42 ± 30.68 vs. 35.24 ± 31.50 ng/ml, $p = 0.032$) and increase of LAM (60.26 ± 52.38 vs. 83.70 ± 46.25 ng/ml, $p = 0.002$) in serum. No significant alterations were detected in the control group of untreated children.

Conclusion: Level of liver injury in children with CHC varies in severity. TGF-beta-1 and LAM are not only proportional to the stage of fibrosis but also seem to be a good risk factor for the development of significant and advanced fibrosis. Their alterations during antiviral treatment allow monitoring the progression of liver fibrosis.