ORT_01 - Genetic variability of hepatitis B virus: influence on the course of infection in patients with acute and chronic hepatitis B

Camilla Rodrigues de Almeida Ribeiro[1]*; Katrini Guidolini Martinelli[2]; Vinícius da Motta de Mello[1]; Natália Spitz Toledo Dias[1]; Oscar Rafael Carmo Araújo[1]; Lia Laura Lewis Ximenez[1]; Vanessa Salete de Paula[1].
[1]Fiocruz/IOC;
[2]Universidade Federal do Espírito Santo.

Introduction: Several viral HBV factors, including viral load, genotype and genome mutations have been reported to be associated with different risks of progression of liver disease.

Objective: The aim of this study was to investigate the influence of genetic variability of HBV in association with the progression of hepatitis B virus infection in acute and chronic conditions.

Methodology: All samples (acute n=22 and chronic n=49) of the study were tested for the presence of HBV DNA by real-time and nested-PCR, positive samples were purified, sequenced and genotyped for phylogenetic tree construction and mutation search.

Results: Four genotypes were found (A, D, E and F) and the isolates obtained were mostly of genotype A, subgenotype A2. We analyzed 190 mutations in the pre-S/S gene region of these we found 53 nucleotide mutations and 110 amino acid mutations divided between the L, M and S regions of the pre-S/S. For the viral polymerase (RT) region, 17 amino acid mutations were found. For the Pre-core and Core regions, 2 and 8 amino acid mutations were found, respectively. The acute profile showed more statistically significant nucleotide mutations in the Pre-S / S region compared to the chronic one; Immune escape mutations were found distributed between the two profiles. The A7T and A7Q mutations, which may be associated with an increased risk of hepatocellular carcinoma (HCC), were related to the chronic and acute profile, respectively. Mutations D42*, C69* and W179* were found more frequently in the acute and W182* more frequently in the chronic ones, it is known that stop mutations in the pre-S/S region are found in patients with progressive liver diseases; In the pre-core region, a mutation was found in nucleotide G1896A, replacing tryptophan with a stop codon at position 28 (W28*), this mutation has been associated with an increased risk of liver fibrosis in combination with mutations in the core region and more prevalence of HCC. In general, most of the mutations that obtained statistical difference between the genotypes were associated with the non-A genotype (D, E and F), indicating that these genotypes are more susceptible to the appearance of mutations. Of the 17 mutations analyzed in the region of RT, the secondary mutation L180M of resistance to Lamivudine and Entecavir showed a statistical difference between the mutant and the wild type.

Conclusion: The search for resistance mutation before starting treatment is necessary due to the natural occurrence of these mutations for best therapeutic choices.

Keywords: Hepatitis B infection; Acute and chronic Hepatitis B; Mutation