ORT_05 - Evaluation of mutations in ABCB1 and ABCB11 genes by qPCR and their impact on the clinical evolution of hepatitis C

Leticia Bomfim Campos[1]; Nathália Alves Araújo de Almeida[1]; Marcia Amendola Pires[2]; Carlos Eduardo Brandão Mello[2]; Livia Melo Villar[3]; José Júnior França de Barros[1]; Vanessa Salete de Paula[1].
[1]Laboratory of Molecular Virology and Parasitology - IOC/Fiocruz
[2]Gastroenterology Service - Gaffrée and Guinle University Hospital – UNIRIO
[3]Laboratory of Viral Hepatitis - IOC/Fiocruz

Introduction: Many factors are associated with susceptibility to hepatitis C virus (HCV) infection and progression to cirrhosis and hepatocellular carcinoma (HCC). Mutations 1236C>T (p.G412G), 2677G>T (p.A893S) and 3435C>T (p.I1145I) in the ABCB1 gene that synthesize the drug export pump (P-glycoprotein) were associated with the plasmatic concentration and the efficacy of drugs used in the treatment of HCV. The 1331T>C (p.V444A) mutation in the ABCB11 gene encoding the bile salt export pump is associated with cholestasis and with significant changes in total bilirubin levels after antiviral therapy. These mutations can be an aggravating factor for liver tissue damage and can lead to a worse clinical prognosis of the infection for HCV.

Objectives: This study aimed to investigate the frequency and correlation of genetic polymorphisms C1236T, G2677T, C3435T and T1331C in chronic HCV patients.

Methodology: Samples from 241 patients with chronic hepatitis C referred to Gaffrée e Guinle University Hospital were analyzed by qPCR using TaqMan SNPs Genotyping Assays.

Results: In the ABCB1 gene, the C3435T mutation was found in 14.9% (TT), 40.7% were wild-type (CC) and 44.3% were heterozygous (CT). The frequency for C1236T wild type (CC) was 48.6%, heterozygotes (CT) 40.7% and mutants (TT) 10.8%. For G2677T, 8.7% were mutants (TT), 55.6% were wild type (GG) and 35.7% were heterozygous (GT). For T1331C, 53.5% were heterozygous (TC), followed by mutant - CC (32.0%) and wild type - CC (14.5%). ABCB1 mutant genotypes were more frequent in the white population (self-declared) and 2677TT in males ($p<0.05$). Individuals with genotypes 2677TT and 1236TT had lower cholesterol levels when compared to 2677GG and 1236CC ($p<0.05$). Patients with the 1331CC genotype had a higher AST level than 1331TT ($p<0.05$).

Conclusion: We observed a greater presence of heterozygous genes in the studied population, which may be a characteristic of a mixed population such as the Brazilian one. It is important to establish the risks associated with these mutations in patients with chronic HCV to understand their influence on the clinical feature and evolution of these individuals, mainly due to the association with cholestatic damage and the efficacy and safety of antivirals. Support: CAPES, CNPq and FAPERJ.

Keywords: Hepatitis C, ABCB1 and ABCB11, drug resistance