CLINICAL IMPACT OF HFE MUTATIONS IN PORTUGUESE PATIENTS WITH CHRONIC HEPATITIS C

Joana Ferreira1,2,3, Clímena Baldaia2,4, Ângela Inácio1, Manuel Bicho1,5, José Velosa4, Paula Faustino3 and Fátima Serejo2,4

1. Laboratório de Genética, Faculdade de Medicina de Lisboa; 2. Instituto de Medicina Molecular 3. Departamento de Genética Humana, Instituto Nacional de Saúde Dr. Ricardo Jorge; 4. Departamento de Gastroenterologia e Hepatologia, Hospital de Santa Maria, Centro Hospitalar Lisboa Norte; 5. Instituto Bento da Rocha Cabral; Lisboa, Portugal

Introduction

Chronic hepatitis C (CHC) is often associated with alterations in iron and lipid metabolisms, which may affect the long-term prognosis and the response to antiviral treatment (1,2). Some studies have suggested that the occurrence of HFE mutations may contribute to modulate these metabolisms in CHC (3,4). In this study, the prevalence of two common HFE mutations (C282Y and H63D) was determined in a group of Portuguese CHC patients and the findings were correlated with their clinical, histological and virological features.

Methods

• Clinical parameters were measured by standard techniques: AST, ALT, GGT, lipid profile (LDL, HDL, total cholesterol and triglycerides), iron, ferritin, transferrin and transferrin saturation, insulin, glucose, HOMA-IR and peptide-C.
• 82 patients were treated with SOC (Pegyferferon + Ribavirin).
• HCV-RNA was determined by PCR and genotype by Inno-Lipa.
• Liver steatosis, fibrosis stage and degree of inflammation (grading) were assessed by liver biopsy (Peter Scheuer score).
• HFE polymorphisms, H63D and C282Y, were analyzed by PCR-RFLP.
• Antioxidant potential (tGSH/GSSG Ratio) was evaluated by spectrophotometry.
• Statistical analysis was performed by SPSS 19.0 (level of significance p<0.05). Clinical data results were corrected for age and BMI using a General Linear Model – Univariate.

Population

• One hundred and eighty three CHC patients were enrolled in this study.
• Population clinical parameters, liver histology, virus genotype and type of anti-viral response are described in Tables 1-4.
• Patients exclusion criteria: other chronic liver diseases, alcohol ingestion >40g/day, HIV infection, metabolic and autoimmune diseases.

Results

✓ HFE polymorphisms frequency
HFE_H63D and C282Y genotype frequency in the CHC studied population is summarized in Table 5.

✓ HFE polymorphisms and the type response to antiviral therapy
No significant difference was found comparing HFE polymorphisms and the type of antiviral response.

✓ HFE polymorphisms and clinical or histological data:
• HFE_H63D: regarding all the clinical and histological data, we observed a decrease in the degree of inflammation (Table 6) and in tGSH/GSSG ratio, and an increase in total cholesterol (Table 7; Fig. 1 and 2) in CHC patients presenting the H63D mutant allele (HD/DD) comparing to HH individuals.

✓ HFE_C282Y: Our study revealed that heterozygous C282Y had lower Total Cholesterol (p=0.0011) and higher iron and Transferrin Saturation levels (p=0.0001 and 0.006, respectively); (Table 8; Fig. 3-5).

Conclusions

✓ In this CHC population, the C282Y polymorphism was associated to higher serum iron levels. This biochemical phenotypic was in turn observed in patients with higher fibrosis stages.
• C282Y was also found associated with lower total cholesterol, which in turn was observed in patients with more severe liver inflammatory and steatosis grade.
• On the other hand, the H63D polymorphism was found associated with higher total cholesterol levels and less noninflammation. In addition, it was also associated with a decreased antioxidant potential (tGSH/GSSG ratio).
• These data suggest a relevant role of HFE_H63D and C282Y polymorphisms in CHC progression (liver fibrosis, inflammation and steatosis).
• We did not find association between these two HFE polymorphisms and the type of response to the anti-viral therapy (Pegyferferon + Ribavirin).

References

1. [List of references]

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