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Observational Study

Matrix metalloproteases and their tissue inhibitors in non-alcoholic liver fibrosis of HIV-infected patients

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1 What did this study explore?

The relationships among diverse *MMPs* SNPs, MMPs and TIMPs serum levels and non-alcoholic liver fibrosis, evaluated by means of different non-invasive markers, in HIV-infected patients with and without HCV coinfection.

2 How did the authors perform all experiments?

HIV and HCV serologies were determined by enzyme immunoassay. HIV and HCV RNA by quantitative PCR and HCV genotypes by a line probe assay. Routine laboratory parameters were measured by standard methods. Laboratory-derived liver fibrosis indexes were calculated from AST and platelets (APRI index), age, platelets, total cholesterol and GGT (Forns index), and age, AST, ALT and platelets (FIB-4 Index). In addition the Yearly Fibrosis Progression Index (YFPI) was also calculated in HCV-infected patients as follows: YFPI =TE value/years of estimated HCV infection.

Liver fibrosis was assessed by transient elastometry using Fibroscan (EchoSens, Paris, France). MMPs and TIMPs serum levels were measured by the Quantibody™ Human MMP Array 1 (RayBiotech, Parkway Lane, Norcross, GA, USA).

DNA for SNPs genotyping was obtained from peripheral white blood cells and stored at -20ºC before use. Oligonucleotide primer sequences, PCR conditions and restriction enzymes used for genotyping and sequencing of the different SNPs studied have been described previously.

3 How did the authors process all experimental data?

MMPs and TIMPs serum levels were logarithmically transformed for analysis, because their values showed a markedly non-Gaussian distribution. Univariate (chi-square, t-test, one-way analysis of variance and Pearson's correlation coefficient) and multivariate tests (stepwise logistic and multiple regressions) were used for statistical analysis.

4 How did the authors deal with the pre-study hypothesis?

We hypothesized that some MMPs, TIMPs and SNPs might be related to liver fibrosis development and, consequently, their determination could be helpful to evaluate the degree of fibrosis.

Our results confirmed that some of these parameters (MMP-2, TIMP-2 and MMP-9) were independent predictors of the degree of fibrosis, as evaluated by different non-invasive methods.

5 What are the novel findings of this study?

We excluded patients with excessive alcohol intake in order to homogenize the study population and to minimize the possible confounding effect of different etiologies of fibrosis. We also evaluated several markers of fibrosis to assess the reliability of the results.

Our study supports the implication of these substances in the generation of liver fibrosis, and their value as predictors of the degree of fibrosis in HIV-infected patients with non-alcoholic liver disease. The determination of these parameters, particularly MMP-2, could be useful for the development of non-invasive indexes of fibrosis, in order to improve the accuracy of the current tests.