

ABSTRACT

FACTORS THAT INFLUENCE THE SEVERITY OF FIBROSIS IN CHRONIC VIRAL HEPATITIS

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Hepatitis C and B viruses are the main causes leading to cirrhosis. Worldwide there are over 300 million people infected by hepatitis B virus and over 170 million infected by hepatitis C virus. Viral C infection is a problem of public health concerning all the countries. Seventy percents of chronic hepatitis are attributed to viral C infection, but also 40% of liver cirrhosis with functional failure, 60% of hepatocellular carcinoma. Almost half of the indications for liver transplantation are due to chronic C viral infection.

The first part of the thesis is dedicated to hepatic fibrogenesis, enlisting the modulating factors of fibrosis in hepatitis B and C. It deals also with means of evaluating liver fibrosis, the progression to cirrhosis and liver carcinoma, detailing the management intended for hepatitis C.

The second part of the thesis comprises several studies (run on patients from Romania and France) inspired by the above topic.

The first study aimed at identifying the factors able to predict the evolution of chronic infection with hepatitis C virus to severe fibrosis using elastography to assess liver fibrosis (FibroScan). Severe fibrosis was assessed according to the Metavir scale as stages F3 and F4. The study was run on a number of 126 patients. It was a retrospective observational study, as all the studies comprised in this research.

The main factors identified as predictive for the progression to severe fibrosis were: the age over 50 years at the moment of the diagnosis of chronic hepatitis C, but also GOT and GPT values higher than normal at the moment of the diagnosis. Interesting enough, viremia over 4 000 000 at the moment of diagnosis did not appear to be a risk factor for severe fibrosis, nor did 1a, 2 and 3 genotypes, or BMI (body mass index) over 25, or high values of triglycerides or cholesterol.

The 2nd study focused on the evaluation of some factors involved with the severity of viral C infection relapse and progression to liver fibrosis of the transplanted grafts. We used GraphPad Prism 6 to statistically analyze our data. We came up with the following results:

- The factors that failed to predict evolution to liver fibrosis were: the age over 40 at the moment of transplantation, the GOT values at the relapse of HCV to the patients with a viremia of >1 million, as well as both genotypes 1a and 1b.

- There was no significant difference as to the time elapsed from transplantation to fibrosis between the patients having a viremia over or under 1 million at the moment of transplantation

- Diabetes diagnosed at transplantation and steroids used to prevent rejection were not predictive as to the severity of fibrosis

The 3rd study tried to identify possible correlations between demographic parameters, serum biochemistry and the incidence of hepatocellular carcinoma on cirrhosis due to HVC, as well its different treatment possibilities. There is no significant decrease or increase in the following biochemical markers – transaminase between the diagnosis of cirrhosis and hepatocarcinoma, thus precluding their use. The decrease in albumin and viral and the prolonged TQ are significantly different between the two time points.

Fibrosis's evolution in patients with co-infection with HIV-VHC/VHB and specific treatment and complications was treated in the 4th study.

The last study included 36 patients diagnosed with chronic viral B type hepatitis. It tried to identify possible correlations between demographic parameters, serum biochemistry and the severity of fibrosis as assessed histologically by liver biopsy at the moment of diagnosis. Three patients had no fibrosis, 7 scored 1; 19 scored 2 and 7 scored 3; three of the patients with severe fibrosis had to some extent fat liver – steatosis.

We could not make any significant correlations to these last 36 patients studied as to any of the aforementioned parameters.

To sum up, the final conclusions are:

Viremia, irrespective of the values at the moment of diagnosis of hepatitis C, serum biochemistry or BMI seem to have no predictive value for the evolution to fibrosis or to its' severity.

Neither viremia of >1 million at the moment of transplantation, nor biochemistry or diabetes and steroid use, to say nothing of age over the 4th decade could predict the evolution to fibrosis to patients submitted to liver transplantation for chronic hepatitis C.