

## Liver Histology in Hepatitis B and C Co-Infection on Hemodialysis Patients

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Dear Sir,

Non-A, non-B hepatitis accounts for a substantial proportion of both acute and chronic liver disease in chronic renal failure patients [1]. Hepatitis C virus has been documented to be the major cause of non-A, non-B hepatitis [2], contributing for long-term morbidity in these patients. Using a second generation diagnostic test for hepatitis C virus antibodies (anti-HCV), the prevalence of hepatitis C infection is reported to be as high as 44% among hemodialysis patients [3]. As these patients are also at high risk of developing hepatitis B, the co-infection of both virus might represent more severe liver injury than that caused by infection with a single virus. There are few reports describing the frequency of hepatitis B and C co-infection and liver dysfunction in chronic renal failure patients [3]. Some studies have defined chronic liver dysfunction only biochemically using persistent high alanine aminotransferase values instead of the standard liver histopathologic diagnosis. To clarify this issue, we studied 17 hemodialysis patients hepatitis B virus 'carriers' (HBsAg-positive) with percutaneous liver core biopsy. These patients were selected among 300 patients from 5 hemodialysis units in Porto Alegre, Brazil, for the presence of HBsAg positivity for more than 6 consecutive months. Of them, 7 (41%) were also anti-HCV positive (ELISA second generation, recombinant c22-3 and C200). The patients had a mean age of  $42 \pm 12$  years. 14 were males and 12 white. They had the primary renal diagnosis of systemic hypertension (8), chronic glomerulonephritis (4), urinary obstruction (2), diabetic nephropathy (1) and unknown (2), and were on hemodialysis for more than a year. Plasma samples were collected for evaluation of liver function tests. The liver core biopsy was processed by standard histology and classified in 4 groups: normal, chronic persistent hepatitis, chronic active hepatitis and cirrhosis as described elsewhere [4]. The patients, when divided in anti-HCV negative or positive, did not differ in mean age, sex or duration of dialysis treatment. The biopsy results were: 4 normal, 3 chronic persistent hepatitis and 3 chronic active hepatitis in anti-HCV-negative patients (10 cases), and 3 normal, 1 chronic persistent hepatitis and 1 chronic active hepatitis in the anti-HCV-positive group (5 cases). In 2

anti-HCV-positive cases, the biopsy samples were not adequate for diagnosis. Although 27% of the patients had chronic active hepatitis, the majority of the cases (3 of 4) were from anti-HCV-negative patients. The mean results for liver function tests were not different between the two groups; alanine aminotransferase (IU/l or U/l): 15±7 (n=10) vs. 21±7 (n=7), aspartate aminotransferase (IU/l or U/l): 26 ± 13 (n = 10) vs. 41 ± 3 (n=7), alkaline phosphatase (IU/l or U/l): 122 ± 90 (n = 10) vs. 175 ± 146 (n=7), for anti-HCV-negative and anti-HCV-positive patients, respectively (Student's t test, not significant).

Previous studies of liver biopsy in hemodialysis patients have suggested that non-A, non-B hepatitis is not likely to induce an active and progressive liver disease [5]. Gilli et al. [5], studying 12 hemodialysis patients with non-A, non-B hepatitis and persistently raised serum ALT, half of them being anti-HCV-positive, described only 1 case of chronic active hepatitis. Mild liver damage

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was also found by Marchesi et al. [6]. However, the liver histopathology studies of HBsAg-positive uremic patients have shown a percentage as high as 41% of chronic active hepatitis [7]. At the moment it is not clear for us why hepatitis C virus induces less liver injury than hepatitis B virus in uremic patients. We did not observe worse liver disease in anti-HCV-positive HBsAg-positive uremic patients, although the number of patients studied was not large. The reports of liver injury

with the co-infection of hepatitis B and C virus in uremic patients are scant and difficult to interpret since they used only biochemical liver dysfunction as the means to diagnose chronic liver disease [3]. As described elsewhere [8] and in this study, the liver function tests in chronic renal failure patients did not help to predict the pathologic liver disease detected by a core biopsy. Considering that liver injury in viral hepatitis is immune mediated, the impaired immune function in uremia could be responsible for more chronic liver disease in these patients than nonuremic subjects. However, uremia per se cannot explain the differences in severity of liver lesions in hepatitis B and C infection. The liver damage with co-infection of hepatitis B and C virus does not seem to be additive. It is possible that only hepatitis B virus infection in uremic patients determines the severity of liver damage.

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