Prevalence of Hepatitis C Virus RNA in Hemodialysis Patients: Comparison of Four Antibody Assays

Table 1. Prevalence of HCV RNA in hemodialysis patients

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Dear Sir,

Hepatitis C virus (HCV) infection is the predominant cause of parenterally transmitted non-A, non-B hepatitis, and it is also a common condition among hemodialysis patients [1,2]. In a recent communication, Chan et al. [3], studying a group of hemodialysis patients, found that the results of a second-generation HCV immunoassay correlated well with the presence of HCV RNA determined by nested polymerase chain reaction (PCR). Since viral replication is a marker of infectivity and associated with the development of chronic liver disease, it may strongly influence the management of hemodialysis patients.

In this study, we examined the prevalence of HCV infection in a group of patients on maintenance hemodialysis by two second-generation enzyme immunoassays (EIA II) and two immunoblot assays. The results were compared with the detection of HCV RNA in serum by nested polymerase chain reaction and Southern blot hybridization.

Forty-five patients (28 men and 17 women) with chronic renal failure on maintenance hemodialysis at the Hemodialysis Unit of the Clinical Hospital of the Catholic University Medical School were enrolled. Anti-HCV antibody detection was performed using the EIA II of Ortho Diagnostics (Rari-tan, N.J., USA), which detects antibodies to C100-3, C-33, and C-22 antigens, and the EIA II of United Biomedical (New York, N.Y., USA) which detects antibodies to NS3, NS4, and core antigens. The HCV-antibody-positive samples were also analyzed by two immunoblot assays: RIBA II (Chiron, Emeryville, Calif., USA), which detects antibodies to the 5-1-1, C-100, C-33c, C22-3, and SOD antigens, and LiaTek-HCV (Organon Teknika, Boxtel) which detects NS4, NS5, and four core antigens. Samples were also tested for HBsAg, anti-HBcAg (EIAs of Abbott Laboratories), and serum alanine aminotransferase (ALT). Detection of HCV RNA was performed using the nested cDNA PCR on sera from anti-HCV-positive patients and on sera from 7 anti-HCV-negative hemodialysis patients, as previously described by Bukh et al. [4]. Synthetic oligonucleotides were synthesized using a DNA synthesizer (Applied Biosystems, model 391). The PCR was performed, using 100 µl serum, in duplicate on two different
serum samples. PCR detection of hepatitis C virus was repeated 1 month later using a new serum sample. The specificity of HCV RNA detection was verified by high-stringency Southern blot hybridization using a 5'-end 32P-oligonucleotide hybridization probe (nucleotide positions -95 to -56) labeled with T4 polynucleotide kinase (Gibco/BRL) [4].

Anti-HCV antibody was detected in 5 patients by the United Biomedical EIA II and in 6 patients by the Ortho EIA II. When these samples were tested by two different immunoblot assays, LiaTek-HCV and RIBA II, six samples were anti-HCV positive (table 1). HCV RNA was detected in 3 of 6 anti-HCV-positive patients (50%) and in none of 7 anti-HCV-negative patients. Identical results were obtained upon repetition, using new serum samples, of the reverse transcription PCR assay 1 month later (fig. 1a). We did not find a correlation between HCV viremia and the absorbance value using the two EIAs, nor with the band profile using the two immunoblot assays.

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Fig. 1. HCV RNA in the serum of hemodialysis patients. +=Positive control; -= negative control; a PCR of HCV RNA in anti-HCV-positive hemodialysis patients. Lane M: molecular weight markers (plasmid Phi X 174/Hae III), b Southern blot hybridization of the HCV RNA in anti-HCV-positive hemodialysis patients.

In order to assess the specificity of HCV RNA detection in the samples, the amplified DNA was hybridized on a Southern blot. A HCV DNA band of 259 nucleotides was clearly detected in the three positive PCR samples, and the hybridization signal was not detected in the 3 HCV-antibody-positive patients with persistent negative HCV PCR (fig. 1b).

In our population we found a prevalence of anti-HCV of 13% and one of HCV RNA of 6.5%. These figures are lower than those previously reported [1-3], probably due to the fact that Chile is a low-risk area for HCV and also for HBV infections [5]. A good correlation between the results of an anti-HCV assay (EIA II) and HVC viremia in hemodialysis patients has been previously reported [3]. In that study, HCV RNA was detected in 13 of 15 (86.7%) patients who were anti-HCV positive on EIA II. We found that only 3 of 6 patients with anti-HCV-positive assays on EIA II and also two anti-HCV immunoblot positive assays had HCV RNA detected in serum twice by PCR. In spite of the small number of patients studied, these findings suggest that the immunoassays may not be good predictors of HCV viremia in hemodialysis patients. Considering the fact that ‘true’ healthy carriers of HCV probably did not exist [6], the finding of patients with a positive anti-HCV test and a negative PCR assay could be interpreted as a resolved HCV infection or as intermittent viremia in a patient with chronic HCV infection.

Interestingly, a good correlation between histological findings of chronic hepatitis and HCV RNA detected in serum by the PCR has
been recently reported [6]. This correlation was not predicted by serum ALT values or by the pattern of specificity of anti-HCV. All patients who had HCV viremia had chronic hepatitis at biopsy, and, in contrast, the patients who did not have HCV viremia on PCR had a normal liver [6]. In our study, none of the hemodialysis patients had evidence of chronic liver disease, and all of them had normal ALT values.

In the absence of a better predictor of HCV infection, HCV PCR seems to be a valuable assay to assess the presence of viremia and probably chronic liver disease in hemodialysis patients. Further studies are required to establish an association between HCV RNA in serum detected by PCR and liver histological findings in this group of patients.

References


