Conflicting Results of Hepatitis C Virus Serological Tests in Haemodialysis Patients

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Dear Sir,

Non-A, non-B hepatitis (NANBH) is now the most common form of hepatitis in haemodialysis (HD) units both in patients and staff [1]. Recently, it has been clarified that hepatitis C virus (HCV) is a major cause of NANBH [2], but only indirect diagnosis is routinely available. In fact, with the advent of recombinant technology it has been possible to develop assays (first-generation ELISA assays) to detect antibodies to a non-structural part of this virus. Recent studies, utilizing first-generation assays, indicate that antibodies to HCV are present in a high proportion of HD subjects [3]. However, because first-generation assays show limited specificity and sensitivity, we used second-generation ELISA assays which include polypeptides representing structural and on-structural antigens. In spite of that, as with the first-generation tests, the second-generation ELISA can yield false-positive reactions. A new four-antigen RIBA (4-RIBA) [4] has been developed by Chiron (Emeryville, Calif., USA), in which two additional HCV-recombinant antigens were added to the C-100 RIBA. 4-RIBA is a confirmatory assay which provides a method for identifying genuine anti-HCV reactivity. However, it can be 'indeterminate' (reacting with one RIBA antigen) and in our present state of knowledge of HCV infection, such a finding is uninterpretable.

The proportion of 4-RIBA indeterminate patients is variable: in our population of 207 HD subjects, we found 13 4-RIBA indeterminate subjects (26% of positive patients by second-generation assays) [unpubl. data].

Some authors [5] suggest that about half of HCV 4-RIBA indeterminate results are false positive reactions, but others [6] disagree on this subject. We used a new screening test 'Innotest HCV (Innogenetics) to evaluate serum samples that had been tested by ELISA and 4-RIBA. This test uses five synthetic bands: c33, c22, c100, 5-1-1 and NS5.

Of 53 serum-repeated samples HCV positive by ELISA (Ortho, second generation), and analyzed by 4-RIBA, 27 were indeterminate. The results are given in table 1.

Most subjects of this group were HD patients or kidney graft recipients and had been transfused several times.

The 19 c22 4-RIBA indeterminate samples reacting with Innatest had a high intensity (c22 band was always 3 + or above). Innatest reactivity was strong (OD 0.67-2.5; OD/CO mean ratio 5.7).

The 5 c22 4-RIBA indeterminate samples not reacting with Innatest had a c22 band with a low intensity (4 samples were 1 + , only 1 was 2 +).

Our data show that c22 band with a strong intensity seems to be highly specific, that is partially in contrast with other authors [7]. Our results suggest that 4-RIBA indeterminate samples with a c22 band of weak intensity and negative by Innatest should be considered negatives, but a single and strong c22 band should prompt more thorough investigations and follow-up.

On the other hand HCV testing HD patients or donors is influenced by the screening tests used. We have to wait for the development of a more satisfactory serological technique since at present polymerase chain reaction [8] to detect circulating HCV RNA is not routinely available in most clinical laboratories.

Table 1. Results

Innotest (positive/negative)

4-RIBA band Total pattern

0/1

19/5

0/2

24

2

c33 c22 c100

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