Eur. J. Epidemiol. 0392-2990
September 1990, p. 326-328

EUROPEAN JOURNAL OF EPIDEMIOLOGY

Vol. 6, No. 3

BRIEF REPORTS

ANTIBODIES TO HEPATITIS C VIRUS IN BLOOD DONORS

P. FERRONI*[1], A. TAGGER*, M.L. RIBERO**, A. GROSSI*, F. PREGLIASCO*, M.L. PASQUALI*** and S. SALVANESCHI****

*Istituto di Virologia, Università di Milano, Via C. Pascal, 38 - 20123 Milano, Italy.

**Istituto di Igiene, Università di Milano, Italy.

***Servizio di Immunoematologia, Istituto Nazionale dei Tumori, Milano, Italy.

****Centro Trasfusionale A.V.I.S., Pavia, Italy.

Key words: Hepatitis C virus - Hepatitis B virus - Antibody - Blood donors

Recently a recombinant polypeptide of hepatitis C virus (HCV) has been developed by the Chiron Corporation in California. This antigen has been used to develop an ELISA test (Ortho Diagnostic Systems for serum anti-HCV antibodies. Preliminary data have shown that this virus is the major cause of NANB hepatitis in the world. We examined differences in anti-HCV prevalence among subgroups of blood donors (total sera examined 639) classified for past or present exposure to HBV or not, and for ALT levels. The anti-HCV prevalence found in regular blood donors with normal ALT levels and no antibody to HBcAg was 1.2%. No significant difference in the anti-HCV prevalence was found among other subgroups of blood donors except that a higher prevalence (10%) was found in a group with both elevated ALT and HBV markers.

These preliminary findings suggest that the policy of blood supply should take into account the advent of HCV antibody test.

For over a decade efforts to develop a suitable test for detecting markers associated with non-A, non-B hepatitis (NANBH) have been frustrated. Recently, researchers at the Chiron Corporation in California have isolated a cDNA clone from a parenterally transmitted NANBH viral genome. This virus has been named hepatitis C virus (HCV) (1). A polypeptide antigen containing 363 viral amino acids was expressed in yeast as a fusion protein with human superoxide dismutase and used to establish first an RIA and then an ELISA test to detect antibodies to HCV. The specificity of the prototype test was established by testing sera from patients with chronic post-transfusional NANBH (PT-NANBH) and from blood donors implicated in the transmission of PT-NANBH (4). High prevalences of anti-HCV were found in prospectively followed patients with PT-NANBH, in patients with chronic hepatitis or cirrhosis and a history of blood transfusion (2, 5).

We report here the prevalence of anti-HCV in regular blood donors and in donors suspended from donation because of previous exposure to HBV or elevated ALT levels.

We tested 639 serum samples belonging to four groups of individuals:

Group 1: 427 regular blood donors randomly selected with normal ALT values (< 45 IU/l), 85 of whom were anti-HBs and anti-HBc positive.

Group 2: 60 regular blood donors with normal ALT values who had been suspended from donation because of anti-HBc or anti-HBc plus anti-HBe positivity.

Group 3: 102 regular blood donors with ALT values > 45 IU/l, 30 of whom were anti-HBs and anti-HBc positive.

Group 4: 50 regular donors found to be HBsAg-positive from 1983 to 1988 in routine pre-donation testing. It was not possible to ascertain parenteral exposure to blood for these donors, and their ALT remained normal throughout follow up.

[1] Corresponding author.

All sera were tested for antibody to HCV by an ELISA method provided by Ortho Diagnostic Systems.

The cut-off value was calculated by adding 0.400 to the mean O.D. value of negative controls. All reactive samples were confirmed by repetition of the test.

Before the sample examination we evaluated the sensitivity and specificity of the test with "proficiency and reproducibility panels" provided by the manufacturer.

Hepatitis B virus markers (HBsAg, anti-HBs, anti-HBc and anti-HBe) were detected by commercially available kits (Abbott Labs., USA).

The significance of the differences in the prevalence of antibody against HCV was estimated by the Fischer exact test.

Group 1: the prevalence of anti-HCV antibody among these 427 donors was 1.4% (Table 1); the mean O.D. value was 0.038 (s.d. 0.039). However, for 11 donors the O.D. values ranged from 0.200 to 0.400.

TABLE 1. - Anti-HCV prevalence among 427 blood donors.

HBV Serological status	No.	anti-HCV positive (%)
anti-HBc − anti-HBs −	342	4 (1.2)
anti-HBc + anti-HBs +	85	2 (2.3)
Total	427	6 (1.4)

The difference between the prevalence of anti-HCV in the 85 donors with anti-HBc and anti-HBs (2.3%) and the 342 donors without HBV markers (1.2%) was not statistically significant ($p > 0.05$). No previous parenteral exposure was found in the 6 anti-HCV-positive donors. Four of these had had normal ALT levels for the past 3 years, while the other 2 had shown transient ALT elevations (2.5 times the normal value) in one of the samples donated.

Group 2: the difference between the prevalence of anti-HCV among donors with anti-HBc alone (2.6%) and those with anti-HBc plus anti-HBe (9.1%) was not statistically significant ($p > 0.05$) (Table 2).

TABLE 2. - Anti-HCV prevalence in 60 anti-HBc positive donors with or without anti-HBe.

HBV Serological status	No.	anti-HCV positive (%)
anti-HBc + anti-HBe +	22	2 (9.1)
anti-HBc +	38	1 (2.6)
Total	60	3 (5.0)

Group 3: the donors included in this group had ALT values ranging from 46 to 145 IU/1; only 3 subjects had ALT values higher than 100 IU/1. The only anti-HCV-positive donor among the 72 anti-HBc and anti-HBs-negative subjects had an ALT of 122 IU/1. The other 3 anti-HCV-positive donors, who were also anti-HBs and anti-HBc positive, had ALT values of 48, 71 and 75 IU/1 respectively (Table 3.).

TABLE 3. - Anti-HCV prevalence in 102 donors with abnormal ALT levels.

HBV Serological status	No.	anti-HCV positive (%)
anti-HBc − anti-HBs −	72	1 (1.4)
anti-HBc + anti-HBs +	30	3 (10.0)
Total	102	4 (3.2)

The difference in anti-HCV prevalence between two subgroups with or without anti-HBc/anti-HBs markers was at the limit of 95% significance.

Group 4: the prevalence of anti-HCV in the 50 healthy HBsAg carriers was 2%.

The prevalence of HCV antibody in regular donors from Milan with normal ALT levels and no antibody to HBcAg was 1.2% (4/342), a frequency higher than that found in donors from the U.S.A. (0.5%) (4) and West Germany (0.4%) (3), but comparable to that reported by Esteban (2) in Spanish donors (1.2%). This frequency rose to 3% in the 195 donors with normal ALTs with past or present exposure to HBV. However, the difference in prevalence was not statistically significant when compared to that found in the above subgroup without previous HBV exposure.

The proportion of HCV antibody among donors with elevated ALT levels (1/72, or 1.4%) and without HBV exposure was similar to that found in donors with normal ALT without HBV markers.

The highest prevalence of HCV antibody was found in donors with both elevated ALT levels and antibody to HBcAg and HBsAg (3/30, or 10%). This proportion is lower than that observed among a group of blood donors with high ALT elevation implicated in PT-NANBH cases (5).

Statistically significant difference emerged only between this latter group and that of donors with normal ALT levels and no antibody to HBcAg ($p < 0.05$).

At the present the lack of a confirmatory test has not allowed us to verify whether all reactive samples were truly positive or to establish whether samples with O.D. values 5-10 times above the mean of negative donors were truly negative.

These preliminary findings suggest that blood donor screening policies should take into account the advent of HCV antibody test.

In addition, a test (e.g. polymerase chain reaction) is now needed to distinguish anti-HCV positive subjects with ongoing infections in order to reduce the risk of HCV transmission among donor contacts as well.

REFERENCES

1. *Choo Q.L., Kuo G., Weiner A.J., Overby L.R., Bradley D.W.* and *Houghton M.* (1989): Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome. - Science *244:* 359-362.
2. *Esteban J.I., Esteban R., Viladomiu L., Lopez-Talavera J.C., Gonzales A., Hernandez J.M., Roget M., Vargas V., Genesca J., Buti M., Guardia J., Houghton M., Choo Q.L.* and *Kuo G.* (1989): Hepatitis C virus antibodies among risk groups in Spain. - Lancet *ii:* 294-297.
3. *Kuhnl P., Seidl S., Stangel W., Beyer J., Sibrowski W.* and *Flik J.* (1989): Antibody to hepatitis C virus in German blood donors. - Lancet *ii:* 324.
4. *Kuo G., Choo Q.L., Alter H.J., Gitnick G.L., Redeker A.G., Purcell R.H., Miyamura T., Dienstag J.L., Alter M.J., Stevens C.E., Tegtmeier G.E., Bonino F., Colombo M., Lee W.S., Kuo C., Berger K., Shuster J.R., Overby L.R., Bradley D.W.* and *Houghton M.* (1989): An assay for circulating antibodies to a major etiologic virus of human non-A, non-B hepatitis. - Science *244:* 362-364.
5. *Van der Poel C.L., Reesink H.W., Lelie P.N., Leentvaar-Kuypers A., Choo Q.L., Kuo G.* and *Houghton M.* (1989): Anti-hepatitis C antibodies and non-A, non-B post-transfusion hepatitis in the Netherlands. - Lancet *ii:* 297-298.