Incidence of Anti-Hepatitis C Virus Antibodies in Non-A, Non-B Post-Transfusion Hepatitis in an Area of Northern Italy

Summary: A total of 210 patients consecutively submitted to heart surgery at the Parma University Hospital and transfused with 1,898 units of blood were followed after transfusion in order to evaluate both the incidence of anti-hepatitis C virus (HCV) seroconversion in non-A, non-B post-transfusion hepatitis (PTH-NANB) cases and the usefulness of the screening for anti-HCV in comparison with that for serum glutamic pyruvic transaminase (SGPT) values in preventing PTH-NANB transmission. Fifteen recipients developed PTH-NANB (group A); ten of them (66.6%) showed anti-HCV seroconversion within 3–12 months. Eight of the ten anti-HCV positive patients developed chronic hepatitis, but none of the five PTH-NANB anti-HCV negative did. None of the 15 controls (group B) randomly chosen among the patient population showed anti-HCV seroconversion. A close correlation with the transmission of PTH was showed by anti-HCV positivity but not by SGPT elevation in blood donors. Eleven of 172 blood products transfused to group A but none of 139 products transfused to group B were anti-HCV positive. The incidence of elevated SGPT values was similar between the two groups of the transfused blood products. Nevertheless, the correlation observed between anti-HCV positivity and SGPT levels in the blood products involved in PTH confirms the need to exclude blood donors with abnormal SGPT values. On the whole, anti-HCV screening of donors showed a predictive value higher than that of SGPT (100% vs. 53.3%), allowing a minor blood donation exclusion. The percentage of anti-HCV seroconversion observed in PTH-NANB is probably underestimated because of the limits of the ELISA method we used for the detection of anti-HCV.


Introduction

It is well known that 80–90% of post-transfusion hepatitis (PTH) is of the non-A, non-B (NANB) type [1–9]. After the recent cloning of the hepatitis C virus (HCV) genome and the later development of specific serologic tests, it has been possible to attribute a large proportion of PTH to this virus [10]. The percentages of anti-HCV seroconversion in PTH-NANB reported by various authors are not always
were reasonably excluded. Chronic hepatitis was defined as a normal values within 3 weeks after the discovery of the original rise in SGPT values of at least 2.5 times the upper normal limit. ii) doubling of SGPT levels with respect to 2 to 6 weeks after transfusion in subjects with previous normal transaminase values; iii) exclusion of alternative viral causes of PTH based on the negativity of IgM antibodies against HBCAg, hepatitis A virus, cytomegalovirus and Epstein-Barr virus. Other non-viral causes of SGPT elevation, such as drug toxicity, anesthesia, alcoholism, shock, congestive heart failure and sepsis, were reasonably excluded. Chronic hepatitis was defined as a persistent elevation of SGPT values higher than the upper limit lasting at least 12 months after the acute onset.

Patients and Methods

A total of 210 patients consecutively submitted to open heart surgery at the Heart Surgery Unit of the Parma University Hospital from November 1987 to December 1988 were included in the study. The patients had been transfused with 1,898 units of blood products obtained from volunteer donors of the Transfusion Center of Parma. The subjects admitted to donations were HBsAg negative, with SGPT activity < 1.5 times the upper limit (45 IU/I) of the method employed (automatic method with optimised kinetics at 37°C and spectrophotometric reading).

In order to ascertain the onset of acute hepatitis, SGPT levels were tested weekly for the first 2 months and monthly for a further 4 months after transfusion; in case of transaminase elevation, the patients were referred to the Department of Infectious Diseases.

According to other authors [3,14,17-19], acute PTH-NANB was diagnosed in 15 patients (7.1%) using the following criteria: i) rise in SGPT values of at least 2.5 times the upper normal limit 2 to 26 weeks after transfusion in subjects with previous normal transaminase values; ii) doubling of SGPT levels with respect to normal values within 3 weeks after the discovery of the original SGPT rise; iii) exclusion of alternative viral causes of PTH based on the negativity of IgM antibodies against HBCAg, hepatitis A virus, cytomegalovirus and Epstein-Barr virus. Other non-viral causes of SGPT elevation, such as drug toxicity, anesthesia, alcoholism, shock, congestive heart failure and sepsis, were reasonably excluded. Chronic hepatitis was defined as a persistent elevation of SGPT values higher than the upper limit lasting at least 12 months after the acute onset [1-3.14].

Serum samples from the patients who developed PTH-NANB (group A) and from 15 randomly chosen controls who did not show transaminase increase during the follow-up period (group B) were stored (at -20°C) before surgery in both groups and at the 1st, 3rd, 6th, 9th, and 12th month after transfusion, respectively. In addition, the serum samples of 172 blood donors involved in the donors involved in PTH. No significant difference was concordant, ranging from 23 to 90% [11-17]. In addition, the incidence of anti-HCV positive PTH has not been extensively studied so far.

The aim of this study was to analyze the incidence of anti-HCV seroconversion in a group of patients who underwent open heart surgery and received blood products. In addition, the efficacy of the screening for anti-HCV was compared with that of the serum glutamic pyruvic transaminase (SGPT) determination in preventing PTH.

Finally, the cost-benefit ratio of both anti-HCV and SGPT screenings has been analyzed in terms of loss of blood donations.

The Chiron recombinant immunoblot assay (Chiron RIBA HCV Test System, manufactured by Chiron Corp., Emeryville, California, distributed by Ortho Diagnostic Systems Inc., Johnson & Johnson Co., Raritan, New Jersey) was used to test the ELISA-positive sera of blood donors. Blood donors' sera were also tested for anti-HBC (Corzyme Diagnostic Kit, Abbott Laboratories, Illinois). Fisher's exact test, chi-square, chi-square for independent samples, and Student's t-test for unpaired data were used for statistical analysis.

Results

None of the 30 patients studied was anti-HCV positive before surgery. Ten of 15 patients with PTH (66.6%) but none of the 15 transfused controls showed anti-HCV seroconversion (p<0.0001, Fisher's exact test). Eight of the ten patients with anti-HCV positive PTH but none of five anti-HCV negative PTH showed evidence of chronic hepatitis at the end of the follow-up period (p<0.01, Fisher's exact test).

After transfusion, anti-HCV seroconversion occurred in three patients within 3 months, in five within 6 and in two within 12.

Amongst the ten patients who developed anti-HCV positive PTH, seven had received at least one anti-HCV positive blood transfusion and three had received only anti-HCV negative blood products. On the other hand, among the patients who developed anti-HCV negative PTH, two had received at least one anti-HCV positive blood product. As shown in Table 1, group A received a total of 11 anti-HCV blood units, while no anti-HCV positive blood products were transfused to group B. Conversely, the incidence of anti-Hbc antibodies and of SGPT values > 45 IU/I was not different between the two groups of donors.

All anti-HCV positive blood products showed a ratio of ELISA optical density/cut-off of >2 and were reactive for both 5-1-1 and C 100-3 antigens in the Chiron recombinant immunoblot assay.

The SGPT levels were higher in the anti-HCV positive than in the anti-HCV negative blood products implicated in PTH cases (43 ± 14 vs. 27 ± 10 IU/I, p<0.01; data not shown).

The percentage of SGPT values >45 IU/I was higher in the anti-HCV positive than in the anti-HCV negative sera of the donors involved in PTH. No significant difference was

Table 1: Relationship between features of the transfused blood products (presence of anti-HCV, anti-HBc, SGPT values >45 IU/I) and development of PTH-NANB in recipients.

<table>
<thead>
<tr>
<th>Transfused blood products</th>
<th>PTH patients</th>
<th>Controls</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-HCV positive</td>
<td>11/172 (6.4%)</td>
<td>0/139 (0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SGPT &gt; 45 UI/I</td>
<td>15/172 (8.7%)</td>
<td>6/139 (4.3%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Anti-HBc positive</td>
<td>7/172 (4.0%)</td>
<td>6/139 (4.3%)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

*Chi-square test.


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