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Post-Transfusion Non-A, Non-B Hepatitis after Cardiac Surgery

Prospective Analysis of Donor Blood Anti-HBc Antibody as a Predictive Indicator of the Occurrence of Non-A, Non-B Hepatitis in Recipients

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Abstract. We prospectively studied the incidence of post-transfusion non-A, non-B hepatitis in 64 cardiac surgery patients: 4 (6.25%) developed non-A, non-B hepatitis after an incubation period of 4–10 weeks. Units of blood products from donors seropositive for antibody to hepatitis B core antigen (anti-HBc) were not associated with a greater risk of non-A, non-B hepatitis in recipients than units from seronegative donors. Our data indicate that donor blood anti-HBc testing is of no value as a screening method to reduce the incidence of post-transfusion non-A, non-B hepatitis.

Introduction

Since blood donors were routinely tested for hepatitis B surface antigen (HBs Ag), the incidence rate of post-transfusion hepatitis B has dropped. Consequently, the prevalence rate of non-A, non-B (NANB) hepatitis among post-transfusion hepatitis raised to about 90% [1]. Specific tests for NANB virus infection are still lacking, and antibody to hepatitis B core antigen (anti-HBc) has been proposed as an indirect marker predictive of the occurrence of NANB hepatitis in recipients [2–4]. In the present study, we aimed at defining the effectiveness of donor blood anti-HBc screening to predict the occurrence of NANB hepatitis in recipients.

Materials and Methods

Patients

64 patients undergoing cardiac surgery with extracorporeal circulation participated in this study: 46 (72%) were men, 18 (28%) were women. Their mean age (±1SD) was 52±13 years (range 19–72 years). Blood samples were taken from each patient just before operation and at 2weekly intervals during 5months after operation. All samples were tested for HBs Ag (AusriaII 125®, Abbott Laboratories, North Chicago, USA), anti-HBs (Ausab®, Abbott), anti-HBc (Corab®, Abbott), HBe Ag and anti-HBe (Abbott-HBe, Abbott), anti-hepatitis A virus IgM (anti-HAV, Havab®, Abbott), anti-cytomegalovirus (anti-CMV; Enzygnost-Cytomegalie®, Behringwerke AG, Marburg, FRG), anti-Epstein Barr virus (anti-EBV; Institut Virion, Rüschlikon, Zürich, Switzerland), bilirubin, alanine aminotransferase (ALAT; UV test, Boehringer-Mannheim, FRG; upper normal limit 22IU/l at 25°C), aspartate aminotransferase (ASAT; UV test, Boehringer-Mannheim; upper normal limit: 18IU/l at 25°C), γ-glutamyltransferase (γ-GT; colorimetric method, Boehringer-Mannheim; upper normal limit 28IU/l at 25°C).

Patients were transfused during the preoperative and early postoperative periods only (none of them was transfused after a 1-week period following operation). A diagnosis of NANB hepatitis was made if, at least 30days after operation, (a) there were elevated ALAT serum levels (>100IU/l in 2 consecutive samples or >40IU/l in 4 consecutive samples) without any serologic evidence of recent HBV, HAV, CMV or EBV infection, and (b) no obvious alternative diagnosis was found, such as alcoholic or drug-induced hepatitis.

Blood donors

All blood product units transfused to the 64patients came from a group of 447volunteer donors. All of them fulfilled the clinical qualification criteria commonly accepted in France and were seronegative for HBs Ag testing. All were tested for anti-HBc (Corab®, Abbott): 427 (95.5%) were seronegative for anti-HBc testing and 20 (4.5%) were seropositive. Transfused blood products were red blood cells diluted in saline-adenine-glucose medium (RBC-SAG) and fresh frozen plasma (FFP) exclusively.

Table I. Numbers of blood product units received by the patients

Blood product units	Patients (n=64)	Patients without NANB hepatitis (n=60)	Patients with NANB hepatitis (n=4)
RBC-SAG			
Total	269	259	10
Mean ± 1 SD	4.2 ± 3.1	4.3 ± 3.1 — NS —	2.5 ± 1.3
Range	0–17	0–17	1–4
FFP			
Total	204	191	13
Mean ± 1 SD	3.2 ± 1.5	3.2 ± 1.6 — NS —	3.25 ± 0.5
Range	0–10	0–10	3–4

NS = Not significant ($p > 0.05$; Wilcoxon's rank sum test).

Table II. Donor anti-HBc status and NANB hepatitis in recipients

Donor anti-HBc status	Donors (n=447)	Incriminated donors[a] (n=23)	Recipients with NANB hepatitis
Negative	427 (95.5%) (RBC-SAG 255 units; FFP 193 units)	23 (RBC-SAG 10 units; FFP 13 units)	4/64 (6.25%)
Positive	20 (4.5%) (RBC-SAG 14 units; FFP 11 units)	0 (RBC-SAG 0 units; FFP 0 units)	0/64 (0%)

[a] Incriminated donors refers to donors of at least 1 blood product unit (RBC-SAG or FFP) transfused to a patient who developed NANB hepatitis.

Results

Post-Transfusion Hepatitis

During the 5-month follow-up period, 5 patients (7.8%) developed post-transfusion hepatitis: 1 patient had clinical and serological evidence of CMV hepatitis, while 4 patients, in whom no other causal agent could be incriminated, were considered as having NANB hepatitis. The incubation periods of the disease were 4 weeks (3 patients) and 10 weeks (1 patient). Among the 4 patients, jaundice was absent in 1 case and remained mild in 2 (maximum bilirubin levels: 25.6 and 32.5 µmol/l).

Amounts of Transfused Blood Product Units

Table I shows that patients who developed NANB hepatitis had not received significantly different numbers of RBC-SAG and FFP units as compared to those who did not.

Anti-HBc-Positive Donors and NANB Hepatitis in Recipients

25 blood product units (14 RBC-SAG and 11 FFP) from seropositive donors were transfused to 24 patients: none of them developed NANB hepatitis. As can be seen in table II, all blood products transfused to the patients who developed NANB hepatitis came from 23 anti-HBc seronegative donors.

Discussion

In our group of 64 patients, we found 4 cases of post-transfusion NANB hepatitis, giving an incidence rate of 6.25%. This figure is within the range of those found in other studies [5–8]. This incidence of 6.25% may be an underestimation, since follow-up was discontinued after 5 months. The prevalence rate of NANB hepatitis among post-transfusion hepatitis was 80% (4/5), similar to those found elsewhere [6, 7, 9].

Several data indicated that recipients of blood products from donors seropositive for anti-HBc testing were at greater risk to develop NANB hepatitis than recipients of blood products from seronegative donors [3, 4]. Therefore, anti-HBc could serve as an indirect screening test for donors who are likely to transmit NANB hepatitis. Our study failed to confirm the association between the donors' anti-HBc seropositivity and enhanced risk of NANB hepatitis in recipients, since no case of NANB hepatitis developed among the 24 patients who received blood products from anti-HBc positive donors (the 4 patients with NANB hepatitis received blood product units from anti-HBc seronegative donors exclusively). Thus, 20 donors (4.5%) would have been discarded without any reduction of the incidence of NANB hepatitis in recipients. It appears from this study that the donors' anti-HBc seropositivity has no predictive value for the

development of NANB hepatitis among recipients. Therefore, we cannot recommend anti-HBc testing as a screening method to reduce the incidence of post-transfusion NANB hepatitis. Larger studies, however, are needed to clearly assess this point.

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