Clinical, immunologic, and technical factors affecting recovery of platelet count after platelet transfusion

We evaluated the recovery of platelet count after 348 platelet transfusions administered to 98 patients with hematologic diseases. The aim of the study was to evaluate the effects of detrimental factors impairing a good recovery of the platelet count. We found that: (1) despite the rates of patients with immune or clinical detrimental factors being similar (7.1% vs 9.1%), alloimmunized patients received up to 40.5% of all platelet concentrates; (2) autoantibody-like antibodies do not cause refractoriness; (3) apheresis- and buffy coat-derived platelet concentrates have quite similar clinical effects.

haematologica 2002; 87:893-894
(*http://www.haematologica.ws/2002_08/893.htm*)

The failure of platelet concentrates to induce a significant increase of the platelet count in patients may have adverse clinical effects. A variety of clinical detrimental factors, alloimmunization, and technical aspects may counteract the clinical usefulness of platelet transfusion.[1] Preventive measures such as leukodepletion and/or irradiation of blood components have reduced the prevalence of alloimmunization.[2] In patients who still develop alloimmunization, platelet selection or cross-matching increases the rate of successful transfusions.[3-4] A real efficacy–related higher quality of platelet apheresis (PA-PC) over buffy-coat-derived platelet concentrates (BC-BC) still needs convincing demonstration.[5-6]

The aim of this prospective survey was to evaluate the relevance of factors affecting the recovery of platelet count after transfusion. Between November 1999 and January 2002, one hundred and twenty-three consecutive hematologic patients were enrolled. Twenty-five did not receive platelet transfusions and were dropped from the study. Ninety-eight patients, who received 348 platelet transfusions, were evaluated. Transfusions were delivered in the absence of complications to thrombocytopenic patients with a platelet count lower than 10×10^9/L; the 20×10^9/L cut-off limit was used for hemorrhagic patients.

One hundred and fifty-seven on-line leukodepleted (LRS-6, Pall) platelet aphereses (MCS+, Haemonetics) and one hundred and ninety-one leukodepleted buffy-coat-derived platelet concentrates were transfused (five pooled buffy-coats, platelets suspended in T-Sol Baxter and filtered through SephacelI PLX-5A Ashai).

In vivo recovery was evaluated computing the corrected count increment (CCI), using the patients' blood samples collected within one hour after transfusion completion. Antibody screening for platelet reactive antibodies was performed using ELISA (GTI Pack-Plus) and/or SPRCA assay (Capture-P RS, Immucor). Non-cytotoxic anti-HLA antibodies were investigated by ELISA assay (QUIK-ID, GTI). Class I HLA typing was performed by lymphocytotoxicity (Lymphotype ABC 144, Biotest AG). The presence of clinical detrimental factors (fever, bacteremia, hemorrhage, coagulopathy, progenitor cell transplantation, toxic medications) was recorded. Alloimmunized refractory patients were provided with either HLA selected or cross-matched platelets, or unselected random platelets according to the inventory availability. Five groups of patients were clustered: group 1, absence of any detrimental factor; group 2, alloimmunized patients transfused with incompatible platelets; group 3, the same patients as group 2 but transfused with compatible platelets; group 4, patients transfused while having clinical detrimental factors; group 5, the same patients as group 4 but transfused in the absence of clinical detrimental factors. Statistical significance was determined using analysis of variance and t-tests.

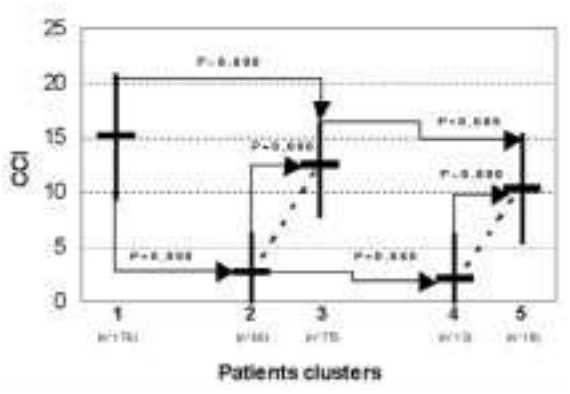

Figure 1. Platelet recovery (CCI) following platelet transfusions. Median value ± standard deviation, and *p* value (t-test). Lane 1: responding patients without detrimental factors; lane 2: alloimmunized patients transfused with incompatible (retrospective) platelet concentrates; lane 3: alloimmunized patients transfused with compatible (prospective or retrospective) platelet concentrates; lane 4: patients with clinical detrimental factors present; lane 5: patients with clinical detrimental factors no longer present.

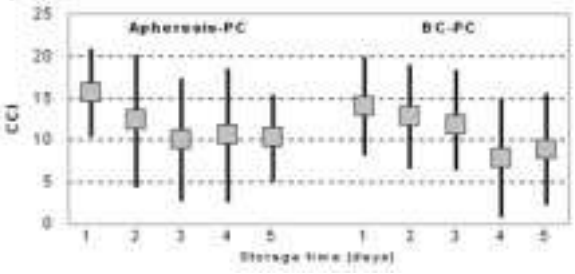

Figure 2. Platelet recovery (CCI) following platelet transfusions. Median value ± standard deviation. Left: apheresis-derived platelet concentrates; right: pooled buffy coat-derived platelet concentrates. X axis: storage time from the day of preparation (day 1) up to the last day of the shelf-period (day 5).

Of the 348 transfusions, 176 (50.5%) resulted in optimal recovery of the platelet count (group 1, median CCI: 15.1±5.67). Sixty-six incompatible transfusions (18.9%) were given to 7/98 alloimmunized patients: the post-transfusion recovery was poor (group 2, median CCI: 2.6±3.67). These patients also received 75 transfusions (21.5%) which were biologically compatible (group 3, median CCI: 12.5±4.73). Thirteen transfusions (3.7%) were given to 9/98 patients while temporary clinical detrimental factors were present: the recovery was poor (group 4, median CCI:

2.1±4.03). These patients also received 18 transfusions (5.1%) in the absence of clinical detrimental factors, exhibiting good increments (group 5, median CCI: 10.35±4.93). These results are summarized in Figure 1.

Only one patient had anti-HPA (anti-HPA-5b) antibodies coexistent with anti-HLA antibodies. Two patients with anti-HLA antibodies each received two random platelet transfusions which were effective. Antibodies with broad reactivity against non-allelomorphic platelet glycoprotein epitopes (autoantibody-like) were found in 9 out 98 patients. These patients were given 13 transfusions overall, all resulting to be effective (median CCI, 12.0±3.08).

The overall post-transfusion recovery, clustered according to the kind of preparation and the age of the platelet concentrate prior to transfusion (from day 1 up to day 5), is depicted in Figure 2. Recovery decreased over storage time. The difference between day 1 and the following days was not significant until day 3 for AP-PC (p=0.009) and day 4 for BC-PC (p=0.019). The day-by-day recovery difference between AP-BC and BC-PC was never statistically significant. Albeit insignificant, the slight recovery difference observed at day 1 between PA-PC and PC-BC could be because HLA compatible PA-PC are administered more frequently to the immunized patients on day 1 after collection.

The prevalence of patients with immune (7.1%) or clinical (9.1%) refractoriness was similar. The detrimental effect of clinical and immunologic factors on post-transfusion recovery was identical. When clinical detrimental factors were absent, or when compatible platelets were administered to alloimmunized patients, a similar recovery was obtained. The few alloimmunized patients (7.1%) received as many as 40.5% of the platelet concentrates. Taken together these data strongly support the need to provide compatible platelet concentrates to alloimmunized patients. No recovery at all can be expected when patients with active clinical detrimental factors are transfused, thus the clinical value of these transfusions remains to be ascertained.

Autoantibody-like antibodies do not affect the recovery after platelet transfusion. Anti-HPA antibodies seem to have minor effects on refractoriness. The presence of anti-HLA antibodies does not necessarily equate to platelet transfusion refractoriness. Platelets from pooled random donors and single donor apheresis have quite similar effects. These two last conclusions confirm the results reported in the TRAP study.[7]

Considering the very low infection risk now achieved, the efficacy of the means to reduce alloimmunization, and the insignificant difference of the recovery provided by PA-PC and BC-PC, the putative advantage of providing hematologic patients by default with platelet-aphereses, should be critically reconsidered.

Daniela Inverardi, Chiara Bocchio, Lucia Rossi, Laura Mazzucco, Lorella De Paoli, Piero Borzini

Department of Hematology and Transfusion Medicine, Ospedale SS Antonio e Biagio, Alessandria, Italy

Key words: refractoriness, platelet transfusion, detrimental factors, compatible platelets, corrected count increment.

Correspondence: Piero Borzini, MD, Ospedale SS Antonio e Biagio, Department of Hematology and Transfusion Medicine; via Venezia 15, 15100 Alessandria Italy. Phone: international +39.0131.206963. Fax: international +39.0131.206859. E-mail: pborzini@ospedale.al.it

Manuscript processing
This manuscript was peer-reviewed by two external referees and by Professor Mario Cazzola, Editor-in-Chief. The final decision to accept this paper for publication was taken jointly by Professor Cazzola and the Editors. Manuscript received January 29, 2002; accepted June 11, 2002.

References

1. Delaflor-Weiss E, Mintz PD. The evaluation and management of platelet refractoriness and alloimmunization. Transfus Med Rev 2000; 14:180-96.
2. Brand A. Alloimmune platelet refractoriness: incidence declines, unsolved problems persist. Transfusion 2001; 41: 724-6.
3. Gelb AB, Leavitt AD. Crossmatch-compatible platelets improve corrected count increments in patients who are refractory to randomly selected platelets. Transfusion 1997; 37:624-30.
4. Schiffer CA. Diagnosis and management of refractoriness to platelet transfusion. Blood Rev 2001; 15:175-80.
5. Krailadsiri P, Seghatchian J. Are all leucodepleted platelet concentrates equivalent? Comparison of Cobe LRS Turbo, Haemonetics MCS+ LD, and filtered pooled buffy-coat-derived platelets. Vox Sang 2000; 78:171-5.
6. Botchway AN, Flores NA, Sheridan DJ, Cohen H. Storage pool defect in pooled buffy coat platelet concentrates within the shelf-life period. Clin Lab Haematol 2000; 22:21-8.
7. Anonymous. Leukocyte reduction and ultraviolet B irradiation of platelets to prevent alloimmunization and refractoriness to platelet transfusions. The Trial to Reduce Alloimmunization to Platelets Study Group. N Engl J Med 1997; 337:1861-9.

Results of an allogeneic non-myeloablative stem cell transplantation program in patients with chronic myelogenous leukemia

Chronic myelogenous leukemia (CML) is a deceptive leukemia because in its chronic phase it evolves with a rather benign phenotype; however, its invariable transformation to the acute blast crisis endows the disease with its true malignant character. The ultimate goal of the treatment of CML is to induce cytogenetic and molecular remissions; cytogenetic remissions can be obtained with interferon, but molecular remissions can only be achieved with allogeneic bone marrow transplantation (BMT).[1] We present here the results of allografting a group of 21 patients with CML, using non-myeloabative stem cell transplants (NST).

haematologica 2002; 87:895-896
(*http://www.haematologica.ws/2002_08/895.htm*)

All patients with Philadelphia (Ph1) chromosome and/or BCR/ABL (p210) positive CML allografted in both the Centro de Hematología y Medicina Interna de Puebla (Puebla, Mexico) and in the Hospital Universitario de Monterrey (Monterrey, Mexico) were prospectively accrued in the study. All patients were transplanted within one year after diagnosis, all had received hydroxyurea and 10 had also received interferon. The donor was an HLA-identical sibling in all instances. A simplification of the low intensity conditioning regimens used by Giralt *et al.*[2] and Slavin *et al.*[3] was employed as previously described[4-5] using oral busulphan, iv cyclophosphamide, iv fludarabine, oral cyclosporin and iv methotrexate. Donor lymphocyte infusions were used 100 days after the allografts only if no evidences of GVHD were present or if there were data of leukemic activity or relapse. Twenty one patients with CML were allografted; eleven in chronic, six in blastic and four in accelerated phase. Median age of the patients was 43 years, with a range of 20 to 61; 13 were 40 or more years-old (Table 1). All patients engrafted successfully. Patients developed chimerism 15-51 days (median 30) after the