ABO Compatibility and Platelet Transfusions of Alloimmunized Thrombocytopenic Patients

By René J. Duquesnoy, Alfred J. Anderson, Peter A. Tomasulo, and Richard H. Aster

With data on 91 alloimmunized thrombocytopenic patients and 389 donor-recipient pairs matched or selectively mismatched for HLA antigens, it was observed that ABO incompatibility significantly reduced the effectiveness of platelet transfusions. The mean 24-hr recovery of platelets from histocompatible donors and from donors selectively mismatched for cross-reactive HLA antigens was decreased by approximately 23% if the donor typed for blood group A and/or B not found in the recipient. Thus, the reduction in platelet recovery associated with ABO incompatibility is not of a magnitude that would contraindicate transfusion of ABO-mismatched platelets.

PLATELET TRANSFUSIONS matched for antigens of the HLA system are frequently effective for the treatment of bleeding in alloimmunized thrombocytopenic patients who are unresponsive to pooled platelet concentrates from random donors.\(^1\)\(^2\) Strict histocompatibility between donor and recipient is not always an absolute requirement for successful transfusions of refractory patients because platelets mismatched for cross-reactive and even certain non-cross-reactive HLA antigens may also be effective.\(^3\)\(^5\) However, a significant proportion of these platelet transfusions (up to 30%) are unsuccessful. Poor responses to such platelets could reflect incompatibility between donor and patient for platelet antigens other than HLA. Although ABO blood group antigens are undoubtedly present on platelet membranes,\(^6\)\(^8\) the importance of ABO compatibility in platelet transfusion therapy has been questioned.\(^2\)\(^3\)\(^11\) We report studies of the role of ABO compatibility in platelet transfusion therapy of alloimmunized thrombocytopenic patients utilizing two different methods of statistical analysis.

MATERIALS AND METHODS

More than 1500 platelet transfusions administered to 91 patients with documented refractoriness to random platelets were evaluated. These patients had a history of multiple platelet and blood transfusions and showed unresponsiveness to transfusions with pooled platelet concentrates from random donors (24 hr posttransfusion platelet recovery of less than 10%) on at least two occasions. Patients with splenomegaly, sepsis, fever, or documented consumption coagulopathy were not considered because these conditions may alter the response to platelet transfusions through nonimmunologic mechanisms. All patients had thrombocytopenia as a result of bone marrow failure or suppression induced by chemotherapy. Twenty-four patients had aplastic anemia, and 67 had leukoproliferative disease. Twenty-five patients were transfused outside the Milwaukee metropolitan area with platelets shipped from Milwaukee by air express.

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A simplified classification of three HLA match groups was used for analysis purposes. The first group consisted of donors whose HLA type did not show detectable antigens that were incompatible with those of the recipient. The second group was comprised of donors mismatched for HLA antigens that cross-react serologically with those of the recipient. In the third group, the donor typed for one or more non-cross reactive HLA antigen(s) not present in the recipient (major mismatch). ABO compatibility was not considered in the selection of platelet donors.

Single donor platelets were obtained by plateletpheresis using a Haemonetics Model 30 Processor (Haemonetics, Natick, Mass.). Transfusion responses were expressed as percent platelet recovery 1 and 24 hr after transfusion, as previously described. Platelet transfusions were considered ABO incompatible if blood group A and/or B was present in the platelet donors but not in the patient (for instance, A to B, A to O, etc.). Transfusions of ABO-compatible platelets included all other ABO matches and mismatches (for example, A to A, O to A, etc.).

When a donor was used more than once for the same patient (usually because of good transfusion responses), the results of these transfusions were averaged for use in analysis to avoid biasing the data towards single donor-recipient pairs.

All platelet transfusion data were stored on a computer file. Significances of differences between groups were determined by multifactorial analysis of variance.

RESULTS

Table 1 shows the results of 389 observations on 91 refractory patients. The data, expressed as mean platelet recoveries (± SEM), showed that ABO-incompatible platelet transfusions were less effective than those from ABO-compatible donors. The effect of ABO incompatibility was noted both 1 hr and 24 hr after transfusion and was most pronounced with platelets from donors matched for HLA or selectively mismatched for cross-reactive HLA antigens. In these HLA-match categories, the mean 24-hr posttransfusion recovery with ABO-incompatible platelets was about 77% of that of ABO-compatible platelets (28.9/37.4 = 77.3%; 28.1/36.7 = 76.6%). The effect of ABO incompatibility was less with platelets selectively mismatched for noncross-reactive HLA antigens. As previously reported in a smaller study, HLA-compatible platelets and platelets from donors selectively mismatched for cross-reactive HLA antigens, had similar posttransfusion platelet recoveries, both at 1 and 24 hr after transfusion. Platelets mismatched for noncross-reactive HLA antigens survived less well.

A second statistical approach was used to avoid possible bias toward individual

Table 1. Influence of ABO Compatibility on Percent Recovery of Transfused Platelets of Different Degrees of HLA Compatibility

<table>
<thead>
<tr>
<th></th>
<th>Platelets</th>
<th>Platelets</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HLA-Compatible</td>
<td>Selectively Mismatched for Non-Cross-Reactive HLA Antigens</td>
</tr>
<tr>
<td>After 1 hr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABO-compatible</td>
<td>72.8 ± 4.4 (79)*</td>
<td>67.0 ± 5.5 (89)</td>
</tr>
<tr>
<td>ABO-incompatible</td>
<td>54.6 ± 5.2 (51)</td>
<td>58.3 ± 4.8 (81)</td>
</tr>
<tr>
<td>After 24 hr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABO-compatible</td>
<td>37.4 ± 3.0 (84)</td>
<td>36.7 ± 4.5 (83)</td>
</tr>
<tr>
<td>ABO-incompatible</td>
<td>28.9 ± 3.7 (51)</td>
<td>28.1 ± 3.9 (88)</td>
</tr>
</tbody>
</table>

*Mean ± SE (number of observations between parentheses).
Table 2. Influence of ABO on Recovery of Transfused Platelets Calculated as Differences From the Mean Response of Each Individual Patient

<table>
<thead>
<tr>
<th></th>
<th>Platelets Selectively Mismatched for Cross-Reactive HLA Antigens</th>
<th>Platelets Selectively Mismatched for Non-Cross-Reactive HLA Antigens</th>
<th>Significance of Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HLA-Compatible Platelets</td>
<td>ABO-compatible</td>
<td>ABO-compatible</td>
</tr>
<tr>
<td>After 1 hr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>+12.7 ± 3.6 (79)*</td>
<td>+6.0 ± 4.6 (89)</td>
<td>−12.3 ± 4.1 (42)</td>
</tr>
<tr>
<td></td>
<td>−2.4 ± 4.4 (51)</td>
<td>−2.6 ± 4.1 (81)</td>
<td>−20.3 ± 4.6 (34)</td>
</tr>
<tr>
<td>After 24 hr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>+8.3 ± 2.5 (84)</td>
<td>+6.0 ± 3.1 (83)</td>
<td>−6.7 ± 2.9 (40)</td>
</tr>
<tr>
<td></td>
<td>−0.2 ± 2.8 (51)</td>
<td>−5.1 ± 3.4 (88)</td>
<td>−10.9 ± 2.9 (43)</td>
</tr>
</tbody>
</table>

*Mean ± SE (number of observations between parentheses).

patient characteristics. For each patient, the mean platelet recovery of all transfusions was calculated. The difference from the mean was determined for each transfusion given to that patient and classified according to HLA and ABO compatibility. The mean values of these differences were calculated for each compatibility group, and a multifactorial analysis of variance was done to determine significance levels of differences. The results in Table 2 indicate that ABO-compatible platelets were more effective than ABO-incompatible platelets in each match category, both at 1 and 24 hr posttransfusion. For instance, the 24 hr posttransfusion recovery of platelets compatible for both HLA and ABO was 8.3% above the mean recovery of all platelet transfusions. In contrast, recovery of HLA-compatible but ABO-incompatible platelets was 0.2% below the mean platelet recovery. For platelets from donors mismatched for cross-reactive HLA antigens, the 24-hr platelet recovery with ABO-compatible platelets was 6.0% above the mean, but with ABO-incompatible platelets, it was 5.1% below the mean. Table 2 also shows that histocompatible, but ABO-incompatible, platelets may be less effective than ABO-compatible platelets but mismatched for cross-reactive HLA antigens. As was expected, platelets selectively mismatched for non-cross-reactive HLA antigens survived less well than those of the other HLA match groups, and the 24-hr platelet recovery was even less when such platelets were also ABO incompatible (−10.9% versus −6.7%).

**DISCUSSION**

These observations demonstrate that ABO incompatibility reduces the effectiveness of platelet transfusions in alloimmunized thrombocytopenic patients. In the case of platelet transfusions from donors who were HLA-compatible or selectively mismatched for cross-reactive HLA antigens, the 24-hr platelet recovery with ABO-compatible platelets was 6.0% above the mean, but with ABO-incompatible platelets, it was 5.1% below the mean. Table 2 also shows that histocompatible, but ABO-incompatible, platelets may be less effective than ABO-compatible platelets but mismatched for cross-reactive HLA antigens. As was expected, platelets selectively mismatched for non-cross-reactive HLA antigens survived less well than those of the other HLA match groups, and the 24-hr platelet recovery was even less when such platelets were also ABO incompatible (−10.9% versus −6.7%).

Although the recovery of ABO-incompatible platelets has been shown to be reduced in several reports,12-14 in which 51Cr-tagged platelet concentrates were transfused to normal subjects, many investigators believe that ABO compatibility between donor and recipient does not influence the outcome of platelet transfu-
sions,\textsuperscript{9-11,15,16} at least when large numbers of platelets are transfused to thrombocytopenic patients. Freireich and coworkers studied an apparently nonrefractory pediatric patient who received six platelet transfusions from a blood group B incompatible donor and three platelet transfusions from a blood group A incompatible donor.\textsuperscript{9} Although this patient developed hemolytic antibodies against both A and B, the data on platelet recovery were interpreted to indicate that ABO compatibility did not influence platelet survival. Using data with 19 blood group A or B incompatible donors, Lohrmann et al. were unable to show a significant effect of ABO compatibility on the effectiveness of HLA-compatible platelet transfusions in refractory patients.\textsuperscript{2} These investigators were also unable to demonstrate any correlation between recipient titers of isoagglutinins against A or B and the posttransfusion platelet increments with ABO-incompatible platelets. From a study on 393 platelet transfusions given to 30 pediatric patients, Van Eys and coworkers concluded that ABO differences between donor and recipient had no effect on platelet increments.\textsuperscript{10} These authors did not indicate how many patients were refractory at the time of transfusion nor did they define ABO type differences.

Recently, Tosato and coworkers concluded from their studies on 84 ABO-incompatible and 172 ABO-compatible platelet transfusions given to 11 refractory patients with aplastic anemia that ABO compatibility between donor and recipient did not influence the outcome of platelet transfusions.\textsuperscript{11} In the latter study, in four of the five HLA-match groups, ABO-incompatible platelets gave lower increments than ABO-compatible platelets, but the differences were not considered statistically significant. Failure to demonstrate statistical significance in some of these studies may be related to the high degree of variation in platelet increments observed in single donor–recipient pairs. From the data of Tosato et al.,\textsuperscript{11} (shown on their Table 5) we have calculated that for the combined HLA-match groups, the posttransfusion increments with ABO-incompatible platelets was 23.5\% lower than those with ABO-compatible platelets (4.46 versus 5.83 $\times$ BSA $\times 10^{-3}$), a difference consistent with that observed in our studies.

Although our observations suggest that ABO compatibility should perhaps be considered in platelet donor selection for refractory patients, it may be difficult to demonstrate a statistically significant ABO effect in any individual patient. Indeed, in our group of patients it was not possible to clearly identify patients in whom unsuccessful platelet transfusions could be explained by ABO incompatibility alone. This is presumably due to the aforementioned problems of statistical analysis of small samples, but also to factors as yet poorly understood, such as the relative importance of the $A_1$ (strong) and $A_2$ (weak) blood group phenotype and the strength of anti-A and anti-B isoagglutinins/isochemolysins in the recipients. We believe that these data show that ABO incompatibility significantly reduces the recovery of single donor platelet concentrates in alloimmunized patients, but that this reduction is not sufficient to consider ABO-mismatched platelets to be contraindicated.

**ACKNOWLEDGMENT**

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ABO EFFECT ON PLATELET TRANSFUSIONS

REFERENCES


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