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## ABC Publications

### ABC Blood Bulletin

#### ABO Incompatible Platelet Transfusions

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#### Introduction

In contrast to red blood cell transfusion—where ABO incompatibility has potentially lethal implications—ABO matching has historically been considered less critical for platelet transfusion. Nonetheless, platelets bear ABO blood group antigens and the plasma contained in platelet concentrates results in passive transfer of anti-A or anti-B antibodies.<sup>1</sup>

In day-to-day transfusion practice, inventory management stress associated with the limited 5-day storage period for platelets results in the provision of many type-compatible, as opposed to type-specific, platelet transfusions. These include transfusion of platelets from type A or B donors to type O recipients. Several studies found mild or no difference in post-transfusion platelet increments following infusion of group A or B platelets to group O recipients. On occasion, infusion of plasma from O donors causes red cell hemolysis in group A recipients. Accordingly two major issues arise: (1) what is the impact of providing out-of-group platelets, *e.g.*, group A platelets to a group O recipient, and (2) what is the risk associated with infusion of ABO incompatible plasma?

#### Background

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Studies in recipients of major ABO mismatched transfusions conducted in refractory, alloimmunized patients report decreases in post-transfusion platelet count increments. Several studies evaluated the effect of transfusing ABO mismatched platelets to patients who were refractory due to HLA alloimmunization. Decreases in post-transfusion platelet count increments were found, although the results were not always statistically significant.<sup>2,3,4</sup> A recent study, which compared the percentage of platelet recovery following various methods of selecting platelet transfusions for refractory patients, analyzed multiple covariates. ABO blood group match and minor ABO incompatibility were not significant factors.<sup>5</sup>

However, some group O patients consistently have poor post-transfusion increments when they receive platelets from group A donors.<sup>6,7</sup> Ellinger *et al.*, using a radio-labeled crossmatch test, also demonstrated the importance of O recipients with high titer anti-A or anti-B receiving A or B platelets and the potential impact on platelet increments.<sup>8</sup> Heal *et al.*, using a different assay, found Group O plasma to be crossmatch-incompatible 52% and 17% of the time against group A platelets and group B platelets, respectively.<sup>1</sup> In contrast, group A platelet donors versus group B recipients and vice versa rarely produced a positive crossmatch. An additional explanation for poor response may be that some donor platelet units have an extra strong expression of blood group A and B antigens. This may make these platelets more susceptible to destruction by anti-A and anti-B antibodies.<sup>9</sup> Post-transfusion platelet count increments should be monitored specifically for this effect.

Severe immune-mediated red cell hemolysis following passive transfer of naturally occurring IgM or IgG ABO antibodies contained in platelet concentrates causes hemolysis in 1 per

6,600 to 9,000 transfusion episodes.<sup>10,11</sup> In general, the infusion of incompatible plasma has little effect on circulating hemoglobin levels. Nevertheless, fatalities associated with out-of-group platelet transfusions and resultant hemolytic transfusion reactions have been reported to the Food and Drug Administration.<sup>9</sup>

### Key Messages

- The most significant risk is associated with infusion of ABO incompatible plasma. Infants may be at greatest risk.
- Incompatible apheresis platelets represent greater risk than random platelets if ABO antibody titers are high.
- Patients should be observed for hemolytic reactions when receiving blood components containing incompatible plasma.
- An ABO-matched pool of whole blood-derived platelet concentrates may be preferable to an apheresis unit with incompatible plasma.
- If there is significant concern about infusing incompatible plasma, volume-reduced or washed red cell and platelet components may be considered.
- Little, if any, risk is associated with infusion of plasma contained in group

Because severe hemolytic reactions can occur with infusion of small plasma volumes in instances where the titer of donor ABO antibodies is high, the safe volume of ABO-incompatible plasma infusion is unknown. In practice, 300 to 500 mL of incompatible plasma is given to adult patients receiving ABO-incompatible transfusions. There are few practical screening methods and no uniform criteria

for excluding donors who may pose a risk.

### **Pediatric Transfusion Practice**

A recent report discussed three infants who experienced delayed hemolytic transfusion reactions after receiving incompatible plasma from platelets and plasma during surgery for congenital cardiac or facial defects.<sup>9</sup> Infants may be at greater risk from incompatible plasma because the amount transfused, relative to their blood volume, is greater than for adults and they have lower levels of circulating A or B substance, decreasing the buffering capacity in their plasma to adsorb the antibody. Finally, such infants are more likely to receive an unpooled transfusion, i. e., a single platelet concentrate from a donor with high titer anti-A, B would not be diluted - as it would be in a pooled transfusion provided to larger patients. (A similar risk occurs when an apheresis platelet with high titer anti-A or anti-B is given to a group A or group B recipient.)

### **Other Adverse Outcomes Attributed to Incompatible Plasma Infusion**

Another effect of incompatible plasma is a positive direct antiglobulin test (DAT) acquired from passive infusion of anti-A or B antibody. Among 11 non-group O bone marrow transplant recipients who routinely received pooled platelets from group O donors,<sup>9</sup> subsequently manifested positive DATs-as opposed to 0/15 patients receiving only blood components containing compatible plasma.<sup>13</sup>

Benjamin and Antin<sup>14</sup> reported decreased survival among patients receiving bone marrow transplants for acute myelogenous leukemia (AML) or myelodysplastic syndrome (MDS) from ABO-major or minor mismatched allogeneic donors who also received platelet transfusions containing plasma incompatible with the recipients' original ABO-types. They changed the transfusion policy to avoid infusion of

incompatible plasma and subsequently observed improved survival among those recipient subsets. This observation has been cited as an example of an untoward effect of infusing ABO-incompatible plasma. However, the authors stated that their practice was unusual and their observation was not confirmed by International Bone Marrow Transplant Registry data or by investigators at the University of Michigan.<sup>15</sup> Clouding interpretation of the results, survival declined among recipients of ABO-compatible bone marrow transplants after the transfusion protocol changed.

A report from France shows a greater incidence of veno-occlusive disease (VOD) in young children undergoing autologous stem cell transplants given ABO-incompatible plasma with platelet transfusions.<sup>16</sup> The higher incidence of VOD observed may relate to the conditioning regimen chosen—because infusion of any ABO-incompatible plasma was used to assign recipients to the ABO-incompatible group. That is, no analysis was performed to demonstrate a relationship between volume of infused incompatible plasma and an adverse outcome, making it difficult to interpret the data.

### **Summary/Recommendations**

Although infusion of blood products containing incompatible plasma is not the preferred option, inventory constraints may require use of ABO-mismatched platelet concentrates. In practice, the most significant risk is associated with infusion of incompatible plasma.

The growing use of single donor apheresis platelets may increase the frequency of severe hemolytic reactions because it increases the dose of incompatible plasma. Patients should be observed for hemolytic reactions when receiving products with incompatible plasma (e.g., look for evidence of anemia, hyperbilirubinemia,

and a positive DAT). Alternatively, an ABO-compatible pool of whole blood-derived platelet concentrates may be preferable than providing an apheresis unit with incompatible plasma. Also, an incompatible plasma volume limit might be useful in preventing hemolytic or putative immunomodulatory effects in chronically transfused patients such as bone marrow transplant recipients. However, this is speculative at this time. In addition if there is significant concern about infusing incompatible plasma, volume-reduced or washed red cell and platelet components may be considered. Of note, little, if any, risk is associated with infusion of plasma contained in group A or B platelets provided to group O recipients.

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