Alloimmunization of RhD Following Platelet Transfusion

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Preparation of blood for transfusion in a blood bank consists of checking a patient’s blood type and screening for alloantibodies in their plasma. Blood typing is performed for the ABO blood group and Rhesus D antigen (RhD). ABO typing is important because of naturally occurring antibodies, called isohemagglutinins, that occur against A and B antigens not present on one’s own red blood cells (RBC). RBCs with A or B antigen transfused into blood recipients who lack these antigens may result in a life-threatening acute hemolytic transfusion reaction. Platelets also have A or B antigens on their surface but can be transfused safely across A and B groups in selected settings, although this may lead to a shortened platelet half-life.

The other routinely typed RBC antigen is RhD, a large transmembrane protein on the RBC surface. Red blood cells bearing the Rhesus D antigen are commonly referred to as “Rh positive,” while those lacking RhD are “Rh negative.” Excluding the ABO system, RhD is the strongest antigen for red cell alloantibody formation. A transfusion from a blood donor who has RhD on his or her RBC can easily stimulate anti-D in a blood recipient who lacks RhD. The prevalence of people who are RhD negative varies between races. (Table 1) An initial exposure to RhD positive RBC is required for developing RhD antibodies, which typically occurs in the context of blood transfusion or during the pregnancy of an RhD negative mother, carrying an RhD positive fetus. After the initial exposure, RhD positive RBCs can lead to life-threatening hemolytic transfusion reactions or hemolytic disease of the fetus and newborn (HDFN) in RhD negative persons.

The incidence of alloimmunization to RhD when RhD negative persons are exposed to RhD positive RBCs has historically been reported as high as 80 to 85 percent. Recent studies demonstrated varying rates of sensitization that are not as high. Observed rates of alloimmunization differ based on the patient population described; for example, 0 percent in a small group of AIDS patients and liver transplant patients, up to 19 percent in patients with hematologic malignancy, and 0.6 percent in hemorrhagic trauma. Yazer et al reported an alloimmunization rate to RhD of 22 percent in immune competent critically ill patients in the emergency department or operating room, who received at least one unit of RhD positive leukoreduced RBC for urgent bleeding.

The primary reason for RhD typing in the blood bank is to identify RhD negative patients and prevent RhD sensitization. In an ideal world, two things would always occur: 1) every transfusion recipient would be typed and if a patient were RhD negative, he or she would receive RhD negative blood components; and 2) all pregnant women would be typed and RhD negative mothers would receive RhIg antepartum and postpartum to minimize maternal sensitization from fetal maternal hemorrhage. Unfortunately, the ideal does not always exist; emergency transfusion may be necessary prior to RhD typing, pregnant women may get late or no prenatal care, and
Alloimmunization of RhD, continued

RhD negative blood products may be available only in limited quantities. With a limited supply of RhD negative blood products, choices need to be made by the transfusion service medical directors and clinicians for best utilization of these products. These decisions are based on evidence based medicine or best practice determined by expert opinion. For RBC transfusion, current standard practice is transfusion of RhD negative patients and patients with an unknown blood type with RhD negative RBC when there is sufficient RhD negative RBC inventory available. If there are limited RhD negative RBCs available, RhD negative RBCs are reserved for RhD negative women of childbearing potential or those patients with existing RhD antibody.

Since RhD is exclusively located on RBCs, and is not present on white blood cells, platelets, or as a plasma protein, whether RhD negative platelets or plasma products are required for RhD negative recipients has been an ongoing debate. The concern has been that residual red blood cells (rRBC) or RBC microparticles in platelet or plasma products, may lead to RhD alloimmunization in RhD negative persons. rRBCs are present in apheresis platelets (0.1-32.5 uL RBC).4,5 rRBCs have also been documented as present and a rare cause of RhD alloimmunization in plasma products. In platelet and plasma products, the risk for RhD alloimmunization is thought to be overall low, but there is little biological data or evidence-based medicine to identify populations at risk. A recently published retrospective analysis of 1,014 RhD negative patients receiving RhD positive platelets examined RhD sensitization four weeks following platelet transfusion has been the most comprehensive to date. The study showed a 1.9 percent RhD sensitization rate in immunocompetent individuals with higher rates of RhD alloimmunization in individuals with frequent platelet transfusions for a hematologic or oncologic diagnosis. (Table 2)6 No RhD sensitization occurred in patients who received only apheresis platelets.

The ideal standard of care is to transfuse RhD negative platelets into RhD negative recipients. However, that is not possible in the setting of inventory shortages, and alternative transfusion plans are necessary. If RhD positive platelets must be used for RhD negative patients, IV RhIg may be administered to minimize the risk of RhD sensitization. Follow manufacturers recommendations for dosing; i.e. Win-Rho® 1500 IU (300 mcg) protects against 17 ml RBC.

References


Table 1. Prevalence of RhD negative phenotype

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>White</th>
<th>Black</th>
<th>Asian</th>
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<tbody>
<tr>
<td>RhD negative</td>
<td>15-17%</td>
<td>3-5%</td>
<td>&lt;0.1%</td>
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Table 2. RhD sensitization in RhD negative patients transfused RhD positive platelets (Cid et al, Transfusion 2011)

<table>
<thead>
<tr>
<th># RhD sensitized (%)</th>
<th>Hematologic</th>
<th>Oncologic</th>
<th>Immunocompetent</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td>RhD positive platelets to RhD negative recipients</td>
<td>177 (6%)</td>
<td>31 (12.9%)</td>
<td>107 (1.9%)</td>
<td>315 (3.8%)</td>
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