Transfusion support of autoimmune hemolytic anemia: how could the blood group genotyping help?

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Conventional pretransfusion testing based on hemagglutination assays can be challenging for patients with autoimmune hemolytic anemia (AIHA) because of the presence of auto-antibodies. It has been suggested that deoxyribonucleic acid-based methods could be more efficient in the selection of antigen-matched red blood cell units in those settings. Because of the high risk of alloimmunization of these patients and the labor-intensive nature of adsorption techniques, we decided to evaluate the feasibility of selecting antigen-matched units on the basis of RBC genotyping. We included in our routine RBC genotyping program samples from 7 patients with AIHA presenting a strongly positive direct antiglobulin test. This made the routine compatibility tests difficult. Most patients had previously received transfusions because of warm AIHA. Matched donor units were selected according to the genotype. For all but 1 patient, blood group genotyping could be done on time to allow antigen-matched transfusion. Four patients received antigen-matched red blood cell units based on RBC genotyping and for 1 patient the fact that no matched units were available led us to postpone the transfusion. After each transfusion, the recovery was recorded and considered satisfactory for all transfused patients. (Translational Research 2014;163:36–42)

Abbreviations: AIHA = autoimmune hemolytic anemia; RBCs = red blood cells; DAT = direct antiglobulin test; DNA = deoxyribonucleic acid; EDTA = ethylenediaminetetraacetic acid; G6PD = glucose-6-phosphate dehydrogenase; INR = International normalized ratio; LISS-IAT = low ionic strength solution-indirect antiglobulin

Autoimmune hemolytic anemia (AIHA) is an uncommon disease characterized by an increased destruction of red blood cells (RBCs) mediated by autoantibodies directed against autologous RBCs. AIHA can be classified into different types including warm AIHA, cold agglutinin syndrome, paroxysmal cold hemoglobinuria, mixed-type AIHA, and drug-induced immune hemolytic anemia.

Some patients with AIHA may require blood transfusion, according to the severity of anemia and their clinical status. It is generally thought that when the incompatibility is due to the presence of an autoantibody alone, the survival of transfused RBCs is similar to that of a patient's RBCs. However, classical pretransfusion hemagglutination assays are often difficult to interpret for patients with AIHA because of the interference

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AT A GLANCE COMMENTARY

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Background

Patients with autoimmune hemolytic anemia (AIHA) are at high risk to develop a hemolytic transfusion reaction due to an alloantibody. The rate of alloimmunization in these patients is often higher than in other multitransfused patients and, because of autoantibodies, traditional compatibility tests can be challenging or impossible. We, thus, started to determine blood group genotype of patients with AIHA and we report its application and feasibility.

Translational Significance

In our experience, RBC genotyping techniques for patients with AIHA allow selecting antigen-matched units without laborious, costly, lengthy, and sample consuming adsorption procedures. This application is particularly useful for pediatric patients with small blood samples.

by autoantibodies that can be panreactive. It is essential to exclude these autoantibodies because they can also mask the detection of alloantibodies that can lead to a harmful immuno-hemolytic reaction.

Additionally, the rate of alloimmunization is higher in patients with warm AIHA than in other multitransfused patients.[1] In fact, several studies report that 12% to 40% of patients with warm AIHA have significant alloantibodies.[2-8] The risk of underlying alloantibodies has prompted transfusion laboratories to provide specialized compatibility testing procedures that allow for the detection of alloantibodies in patients with masking autoantibodies. A variety of methods have been described for the selection of RBCs for patients with autoantibodies. Selecting RBCs for transfusion by providing "least incompatible units" or by testing a patient's diluted serum against a panel of RBCs to detect a more strongly reacting alloantibody are deemed to be unacceptable procedures.[1] For patients with warm AIHA, the most effective compatibility testing rely on autoadsorption techniques that consist in incubating patient's RBCs at 37°C with his or her own serum to remove the autoantibody and to allow detection of clinically significant alloantibodies. In this technique, some of the antibody is also eluted from the patient RBCs thanks to a treatment with proteolytic enzyme. A less labor-intensive alternative involves an autoadsorption using polyethylene glycol, which negates the need for an additional enzymatic step.[1,9,10] This technique, although less labor-intensive, might, however, not be feasible in patients with severe anemia, as the large volume of autologous blood required for autoadsorption procedure is not always available. Moreover, if the patient has already received transfusions in the past, the validity of an autoadsorption is questionable because of the mixture of the patient and donor RBCs.[11] The most suitable procedure will then consist in adsorption using allogeneic RBCs of different known phenotypes that allows removing the autoantibody from the patient's serum.

In general, adsorption procedures are heavy, lengthy, and sample-consuming. A strong collaboration between the clinician and the blood bank staff is, therefore, essential to evaluate the need and the urgency of the transfusion and to guide the selection of appropriate compatibility test procedures in a way that will provide RBC units as safely and timely as possible.

Depending on the urgency of the transfusion need, the results may not be available prior to the transfusion of the first RBC unit but remain useful for further transfusions. For these reasons, the determination of the most complete phenotype (including RH1, RH2, RH3, RH4, RH5, KEL1, FY1, FY2, JK1, JK2, MNS1, MNS2, MNS3, and MNS4 antigens) coupled with the delivery of prophylactic antigen-matched donor blood has been proposed as an alternative method to the adsorption techniques[12] for patients with warm AIHA. This approach is only applicable when the patient does not have a strongly positive direct antiglobulin test (DAT) or has not been transfused.[12] In cases of patients with recent transfusions or strongly positive DATs, there are no effective serologic alternatives to adsorption procedures.

Although hemagglutination remains the gold standard method in immunohematology reference laboratories, molecular immunohematology is increasingly used as a valuable method to provide appropriate transfusion support, to reduce the risk of transfusion reactions, and to prevent alloimmunization in multitransfused patients such as those with sickle cell disease patients or thalassemia.[13,14] Blood group genotyping is also used to detect variants when hemagglutination tests show a weak or altered antigen expression, especially in a context of pregnancy or previous transfusion.[15,16]

Therefore, we have considered the option to apply blood group genotyping using a high-throughput deoxyribonucleic acid (DNA) assay rather than extended RBC phenotyping to manage the transfusion support of patients with AIHA who have a high risk of alloimmunization and are likely to be multitransfused.