



Protecting patients with sickle cell disease from alloimmunization risk: benefits of genotyping

Red blood cell (RBC) transfusion is an important treatment for some patients with sickle cell disease (SCD), one of the most common blood disorders in the world. Transfusion can reduce morbidity and mortality in patients with SCD, but it comes with risks: if donor RBCs have antigens that are not found on the patient's RBCs, the patient's immune system attacks the donor's foreign RBC antigens through a process called alloimmunization. Alloimmunization puts SCD patients at risk of a haemolytic transfusion reaction (HTR), life-threatening hyperhaemolysis (rapid destruction of red blood cells) and other adverse outcomes. To minimize these risks, SCD patients are antigen matched to donors whose blood is typed for key RBC antigens through serology-based phenotyping. However, serological phenotyping is not foolproof; even when patients receive antigen-matched blood, alloimmunization rates can still reach 15% due to weak and partial antigen expression—this happens when mutations in one of the genes that code for a blood group antigen creates a variant of an RBC antigen. This study assessed whether genotyping could identify antigens not detected through serologic matching alone. By identifying differences in RBC antigen prediction and retrospectively evaluating alloimmunization-related outcomes, this study could help ensure safer transfusions for SCD patients.

IN BRIEF: Red cell antigen genotyping complements serological phenotyping and may prevent alloimmunization in sickle cell disease patients.

What did the researchers do?

The researchers conducted a retrospective cohort study on 106 SCD patients in a tertiary care centre in Canada. RBC antigen phenotyping and genotyping was performed by Canadian Blood Services' reference laboratories on consenting SCD patients. Patient demographic, clinical and transfusion-related data were obtained from a local transfusion registry. The primary outcome was the number and proportion of patients who had informative genotyping results. Informative was defined as: 1) the presence of a variant allele 2) discrepancy between the predicted antigen profiles from genotyping and serological phenotyping.

What did the researchers find?

Genotyping SCD patients provided clinically relevant transfusion information, such as variant alleles and rare predicted phenotypes, in addition to phenotyping. Ninety-six (91%) patients had a variant allele identified by genotyping. The majority of patients had a variant allele of the Duffy blood group system (FY*02N.01) and RH variant alleles were common. Fifteen (14.2%) of patients had a history of alloimmunisation, with 5 having HTR documented.

The primary findings of the study were:

1. Genotyping showed additional clinically relevant transfusion information compared to phenotyping alone in the majority of SCD patients.
2. Genotyping revealed variant alleles that would put some patients at risk of alloimmunization if RBC antigen matching was performed based on phenotyping results.
3. Using genotyping for providing prospectively matched blood for transfusion may provide an opportunity to prevent alloimmunization and HTRs, particularly if started before the first RBC transfusion.

How can you use this research?

This study showed a high frequency of variant alleles/polymorphisms in the SCD population. Genotyping can help prevent alloimmunization in SCD patients by identifying important changes to antigen matching profiles compared with serological phenotyping alone. Although identifying variant alleles could pose challenges in finding compatible blood for transfusion to SCD patients, large-scale genotyping of donors is feasible and has the potential to improve transfusion safety for this patient group, as well as decrease overall transfusion time and turnaround time (the time from when a physician orders a blood transfusion to the time when the patient starts receiving the transfusion). RBC antigen genotyping has already proven clinically successful for RHD alleles, and this research offers further support for a more widespread implementation of this practice.

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