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Recommendations for transfusion in ABO-incompatible hematopoietic stem cell transplantation

Diarmaid O'Donghaile, MB BCh, **Walter Kelley, DO**, **Harvey G. Klein, MD**, and **Willy A. Flegel, MD**
Department of Transfusion Medicine, Clinical Center, National Institutes of Health, Bethesda, MD

Daniel-Johnson and Schwartz[1] addressed blood product selection for ABO-incompatible hematopoietic stem cell transplantation (HSCT). They provided a clear guide to the selection of red blood cell (RBC) products and illustrate the complexity of platelet product selection. Hemolysis due to major ABO incompatibility dictates a limited choice of RBC products, while platelet product selection is less restricted. Platelets may be chosen in an order of ABO preference, with less favorable choices potentially interacting with donor or recipient or both. Isoagglutinins of donor origin, like anti-A and anti-B antibodies, may target engrafting erythroid precursors, while those of recipient type bind to the transfused platelets known to bear variable amounts of ABO blood group antigens.

There are no evidence based guidelines for platelet product selection in the setting of ABO incompatible HSCT, because good data to direct our practice are lacking. Any institution's policies reflect its understanding and application of the basic principles of ABO compatibility. However, it seems to be wise to consider the patient's original ABO phenotype even after a complete HSC engraftment. We propose an alternative guide to platelet and plasma product selection (Table 1) which accounts for both the diverse expression of the ABO blood groups in the body and the complexity of ABO-incompatible HSCT.

The ABO blood antigens are not limited to hematopoietic cells alone, but are present on many tissues, including the kidney and endothelia, are soluble in body fluids and are bound to certain plasma proteins. For example, von Willebrand Factor (VWF), which is synthesized and stored in endothelial cells, is coated with carbohydrate structures that carry A and B antigens. In HSCT, while patient's RBC switch to donor blood group, most tissues continue to express the patient's blood group antigens for life.[2] Even HSC donor derived RBCs of blood group O may adsorb structures, like glycosphingolipids, from plasma, and these RBCs often become weakly positive for A and B antigens.

In minor incompatible HSCT after full engraftment, by forward and reverse typing, non hematopoietic stem cell derived tissues can be continuously exposed to minor ABO incompatibility, which is an unavoidable problem. This is due to the production of donor type isoagglutinins, often at low titers; advantageously, most transplanted patients do not develop strong isoagglutinins, active at 37 °C. It is unknown if donor lymphocytes develop tolerance or isoagglutinins are absorbed from plasma onto endothelium rendering them undetectable or both. The clinical effects of HSC donor type isoagglutinins are also largely unknown; whether it may lead to reduced concentrations of plasma proteins, like VWF,

Address for correspondence: Willy A. Flegel MD, Laboratory Services Section, Department of Transfusion Medicine, Clinical Center, National Institutes of Health; Bethesda MD 20892 Phone: (301) 594-7401, FAX: (301) 496-9990 bill.flegel@nih.gov.

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generate immune complexes, or damage endothelia, is yet to be demonstrated. What we can avoid is the transfusion of minor incompatible plasma.

Based on physiological considerations, we propose an alternative model of support, which is the preferred practice at the NIH Clinical Center (Table 1), and avoids any unnecessary exposure to isoagglutinins:

Firstly, a complete switch to transfusion of the donor blood group in Phase III, as recently recommended,[1] unnecessarily exposes the recipient to isoagglutinins. Therefore transfusion for life with plasma compatible with both donor and recipient would clearly be preferable (Table 1). A platelet product may contain more isoagglutinins than a plasma unit, as long as most platelet products produced from whole blood or collected by apheresis remain untested for high-titer ABO antibodies. Hence, we also recommend transfusion of platelets in Phase III should follow an ABO preference identical to Phase II.

Secondly, in our view, protecting the engraftment process during Phase II takes priority. While we agree that platelets of blood group AB are the first choice for many patients, they are often unavailable, and the second choices are frequently transfused. In difference to the recent recommendation,[1] we favor the blood group of the donor as second choice followed by the blood group of the recipient and blood group O for platelet transfusions in Phase II (Table 1). However, we see no need to wash RBC units or to restrict the use of RBC units from donors with high-titer ABO antibodies.

Finally, two additional options to mitigate or avoid potential adverse effects may be considered. There is a move to exclude donors with high-titer ABO antibodies from use in platelet production, particularly, by plateletpheresis.[3] We wash or volume-reduce platelet products only if they harbor high-titer ABO antibodies and must be transfused in the setting of minor ABO incompatibility. Also platelet transfusion choices may be expanded by subgrouping the A antigen. Platelets from blood group A2 donors do not express A antigen.[4] Hence, they are fully blood group O compatible with the further advantage of lacking anti-A antibodies. Blood banks that have the capability may increase their inventory by A2 subgrouping. Such platelets have the advantages of lacking susceptibility to recipient isoagglutinins and of post transfusion corrected count increments that are improved over blood group A1 platelets.[5]

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Table 1

RBC, platelet and plasma transfusion support for patients undergoing ABO-incompatible HSCT

ABO incompatibility			Phase I	Phase II (post HSC infusion)*					Phase III (complete HSC engraftment)†				
					Platelet		Plasma			Platelet		Plasma	
	Recipient	Donor	All products	RBC	First choice	Second choices‡	First choice	Second choice	RBC	First choice	Second choices‡	First choice	Second choice
Major	O	A	Recipient	O	A	AB, B, O	A	AB	Donor	A	AB, B, O	A	AB
	O	B	Recipient	O	B	AB, A, O	B	AB	Donor	B	AB, A, O	B	AB
	O	AB	Recipient	O	AB	A, B, O	AB	-§	Donor	AB	A, B, O	AB	-
	A	AB	Recipient	A	AB	A, B, O	AB	-	Donor	AB	A, B, O	AB	-
	B	AB	Recipient	B	AB	B, A, O	AB	-	Donor	AB	B, A, O	AB	-
Minor	A	O	Recipient	O	A	AB, B, O	A	AB	Donor	A¶	AB, B, O	A	AB
	B	O	Recipient	O	B	AB, A, O	B	AB	Donor	B¶	AB, A, O	B	AB
	AB	O	Recipient	O	AB	A, B, O	AB	-	Donor	AB¶	A, B, O	AB	-
	AB	A	Recipient	A	AB	A, B, O	AB	-	Donor	AB¶	A, B, O	AB	-
	AB	B	Recipient	B	AB	B, A, O	AB	-	Donor	AB¶	B, A, O	AB	-
Major and Minor	A	B	Recipient	O	AB	B, A, O	AB	-	Donor	AB¶	B, A, O	AB	-
	B	A	Recipient	O	AB	A, B, O	AB	-	Donor	AB¶	A, B, O	AB	-

*The transition from Phase I (before HSCT) to Phase II should occur no later than the infusion of the HSC product, but can be defined by institutional guidelines to occur earlier. Day 14 before HSCT is often chosen, like at the initiation of induction chemotherapy.

†The transition from Phase II to Phase III is marked by complete engraftment as defined by the recipient's peripheral blood typing as donor in both forward and reverse blood group typing. Institutional guidelines may define a delayed transition, like 1 year or later after HSCT; patients with successful engraftment may soon become transfusion-independent, while continuing transfusion need may indicate a clinically relevant engraftment issue.

‡in order of preference

§-, not applicable

¶For practical reasons, institutional guidelines often may define the use of donor type platelets as first choice.