

Surgical Innovation

Whole-Blood Resuscitation of Injured Patients

Innovating from the Past

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What Is the Innovation?

Whole-blood (WB) transfusion for the treatment of hemorrhagic shock and coagulopathy after injury has a long history in military medicine. Within the last century, whole blood was replaced in civilian trauma by component products and an overreliance on crystalloid resuscitation. The era of hemostatic resuscitation emphasizes a balanced transfusion strategy, with ratios of plasma and platelets to packed red blood cells (RBC) that attempt to mimic or reconstitute the composition of whole blood. Within the past decade, the pendulum has swung back to WB, although in an innovative and modified form: cold-stored low-titer anti-A and anti-B group O whole blood (LTOWB).

Historical limitations to WB use in trauma resuscitation included concerns regarding the efficacy of cold-stored platelets, the potential for hemolysis, the AABB (formerly the American Association of Blood Banks) requirement that WB be administered in an ABO identical manner to the recipient, and, to a lesser extent, the lack of a platelet-sparing WB leukoreduction filter. However, with multiple in vitro and in vivo studies beginning to address these issues,¹⁻³ an AABB policy change permitting the transfusion of LTOWB in an ABO incompatible manner, and technological advances, such as the use of cold-stored WB in acute trauma resuscitation, has been facilitated. The LTOWB innovation resulted in a resurgence of WB use in trauma and a rapidly evolving change in the paradigm of hemostatic trauma resuscitation.

The LTOWB is procured from US Food and Drug Administration-licensed blood centers. Units can be stored for up to 21 days between 1 °C and 6 °C. Standard transmissible disease tests are performed prior to issuing each unit. Some hospitals produce an RBC unit from an unused LTOWB unit to help offset the cost of maintaining these bespoke units.

What Are the Key Advantages Over Existing Approaches?

The LTOWB confers biologic advantages over conventional component therapy including higher hematocrit levels, greater platelet count and factor concentrations, and less additive solution compared with an equivalent volume of reconstituted WB (Table). An additional advantage to LTOWB relates to the cold storage of platelets in the WB unit. Whereas platelets are typically stored at room temperature (20-24 °C) under agitation to maximize their circulating life span, cold-stored platelets (1-6 °C) have better performance in in vitro coagulation testing compared with room-temperature platelets.¹ Not only does this potentially confer superior hemostatic function in the setting of acute bleeding, but cold storage also permits a greater than 7-day storage time and facilitates the use of a platelet-containing blood product in prehospital settings and other locations where an inventory of conventional room-temperature platelets would not be routinely maintained.⁴ Lastly, patients receiving LTOWB require fewer transfusions⁵; recipients are

therefore exposed to fewer donors compared with recipients of conventional components.

How Will This Affect Clinical Care?

Trauma-induced coagulopathy (TIC) is a well-described entity that is associated with increased morbidity and mortality in severely injured trauma patients. Trauma-induced coagulopathy is evident soon after injury and can be mitigated by early and aggressive hemostatic resuscitation, in particular with plasma. The LTOWB is safe, feasible, and efficient; incorporation of LTOWB in both hospital and prehospital protocols facilitates rapid and balanced hemostatic resuscitation, which has been shown to decrease morbidity and mortality after injury. Further resuscitation then may be tailored to the patient using point-of-care testing, such as viscoelastic assays, which permit real-time targeted component transfusion.

Is There Evidence Supporting the Benefits of the Innovation?

In a single-center comparison⁵ of LTOWB vs component therapy in adult trauma patients, LTOWB was associated with a 53% reduction in post-emergency department blood product transfusion and 2-fold increase in likelihood of 28-day survival compared with component therapy after controlling for age, injury severity, and prehospital physiology.⁵ The LTOWB transfusion is a logistically easier alternative to component therapy, as evidenced by the significantly faster time to transfusion of at least 1 unit of RBCs, plasma, and platelets among pediatric trauma patients who received LTOWB vs conventional components (median, 5 minutes vs 303 minutes, respectively).⁶ In both adults and children, most patient outcomes are not significantly different between LTOWB and component groups (mortality, functional disability, intensive care unit and ventilator days, hospital length of stay, and transfusion reactions).⁵⁻⁷ Data from large clinical trials comparing LTOWB with component products are lacking; further study is required to validate the indications and benefits for different trauma patient groups.

Table. Composition of Whole Blood Compared With "Reconstituted" Whole Blood Using Component Products

Variable	Whole blood	Components
	1 Unit whole blood	1 Unit red blood cells; 1 unit plasma; 1 pack platelets; 1 unit Cryoprecipitate
Product volume, mL	570	675
Hematocrit, %	38-50	29
Platelet count	150 000-400 000	88 000
Factor activity, %	100	65
Fibrinogen, mg	1000	750

SI conversion factor: To convert hematocrit to proportion of 1.0, multiply by 0.01.

What Are the Barriers to Implementing This Innovation More Broadly?

Availability of LTOWB is inconsistent across civilian trauma centers. While there are biologic and logistical advantages to LTOWB transfusion, the stocking and reprocessing of LTOWB can be a labor- and time-intensive task for blood bankers. **Product waste** is a **concern** because the **donors who are qualified to donate LTOWB are very limited** in number; however, **waste is minimized** with use of **leukoreduced WB**, which **facilitates recycling** of **LTOWB units to RBC units**.

There are **theoretical concerns** regarding the **safety** of group **O WB** administered to **non-group O** recipients because **hemolysis** might occur owing to the **anti-A and anti-B** that are **naturally occurring in all-group O WB units**. However, studies in both adult and pediatric trauma patients^{6,7} demonstrate an excellent safety profile and no increased risk of hemolysis among the non-group O recipients compared with the group O recipients of WB who are not susceptible to hemolysis following LTOWB transfusion (I. Harrold, J. S. Seheult, A. Alarcon, et al, unpublished data, 2019).^{6,7}

Concerns regarding the transfusion of Rh(D)-positive LTOWB to Rh(D)-negative women of childbearing potential are sometimes raised as a barrier to the transfusion of Rh(D)-positive LTOWB in emergencies. Two strategies to assuage these concerns are (1) use of Rh(D)-negative LTOWB, which is a very scarce resource, and (2) recognizing that the risk of demise of a future fetus as a result of alloimmunization after receiving Rh(D)-positive LTOWB in a bleeding emergency (0.3%) is small compared with the lifesaving benefits of early blood product resuscitation.

In What Time Frame Will This Innovation Likely Be Applied Routinely?

Low-titer anti-A and anti-B group O whole-blood transfusion is already considered the standard of care in at least 70 high-volume civilian trauma centers across the United States. Research comparing LTOWB with existing ratio-driven empirical transfusion algorithms will serve to increase acceptance and implementation of LTOWB protocols. Ongoing trials are also investigating the expansion of LTOWB in the prehospital setting whereby hemostatic resuscitation is initiated as close to the time of injury as possible.

ARTICLE INFORMATION

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Section Editor: Justin B. Dimick, MD, MPH.

Published Online: May 13, 2020.
doi:10.1001/jamasurg.2020.0811

Conflict of Interest Disclosures: Dr Neal reported grants from National Institute of General Medical Sciences during the conduct of the study, grants and personal fees from Janssen Pharmaceuticals and Haeomentsics, other support from Haima Therapeutics, personal fees from CSL Behring, and grants from Noveome and Instrument Laboratories

outside the submitted work. No other disclosures were reported.

Submissions: Authors should contact Justin B. Dimick, MD, MPH, at jdimick@med.umich.edu if they wish to submit Surgical Innovation papers.

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