TxMD NEWS

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Low Titer Group O Whole Blood – Implications for Practice

What is Low Titer Group O Whole Blood (LTOWB)?

Low Titer Group O Whole Blood (LTOWB) is a unit of whole blood (WB) containing red cells, cold stored platelets and plasma collected from a single Group O donor. 'Low titer' indicates the donor has a "low" level of ABO antibodies (anti-A, anti-B) at the time of blood donation. Currently, LTOWB units supplied by Versiti are non-leukocyte-reduced with an expiration of 21 days. Nationwide, LTOWB may or may not be leukocyte-reduced depending on the manufacturing process at the local blood supplier.

Criteria for LTOWB donation include an adult who meets standard donor eligibility; is Group O (usually RhD positive); not taking aspirin, platelet-inhibiting drugs or other anticoagulants; is reduced risk for transfusion-related acute lung injury (TRALI); and after testing, ABO antibodies are less than the blood center's designated titer threshold. Titration is a semi-quantitative method to determine the relative amount of antibody present. Titer levels are not standardized, and depending on the blood center, a "low titer" can range from less than 50 to less than 256 and still be considered safe for transfusion. About 60-70% of Group O donors will test as "low titer". However due to variations in titer seen in the same individual, testing for anti-A and anti-B titers are performed at each donation.

At Versiti, WB units from Group O RhD positive donors with anti-A and anti-B titers of less than 256 are considered for further manufacturing into LTOWB.

Why use LTOWB in massively bleeding patients?

Over the past several years, a growing body of evidence has shown that massively bleeding patients benefit from early hemorrhage control and aggressive transfusion of all blood components. Early administration of any blood product improves survival.[1] Furthermore, key studies in trauma patients, including PROPPR and PROMMMT, concluded that early transfusion of higher plasma and platelet ratios resulted in improved control of bleeding.[2,3] LTOWB may more effectively and quickly deliver these higher ratios than the use of individual components, especially in the initial resuscitation efforts.

Per the Circular of Information for the Use of Human Blood and Blood Components, Whole Blood may be indicated in treatment of life-threatening hemorrhage when oxygen-carrying capacity, nonlabile coagulation factors, platelets, and volume expansion is needed.[4]

LTOWB offers several advantages:

- Rapid availability of a single product for balanced resuscitation of red cells, platelets and clotting factors,
- Ability to expedite treatment when there is massive bleeding,
- Simpler logistics for storage and transport (no need for refrigerated and room temperature environments).
- Ease of transfusing one product rather than 3 different blood components,
- Reduction in the number of donor exposures,
- Overall reduced amount of additive solution and anticoagulant transfused to patient, compared to cumulative total of 3 different blood components, thereby lessening potential for dilutional coagulopathy,
- Contains cold-stored platelets with potentially better hemostatic effect due to cold induced platelet activation, and
- Product is less acidotic compared to the cumulative effect of RBCs, platelets and plasma, which is critical in trauma/massively bleeding patients who are at risk for trauma-induced coagulopathy.

Is LTOWB safe to transfuse for massively bleeding patients of unknown blood type?

Based on the prevalence of RhD in the U.S. population, approximately 85% of individuals are predicted to be RhD-positive. To lessen the constraints already on the O RhD-negative RBC supply, most blood suppliers offer only RhD-positive LTOWB.

Use of O positive RBCs for acute traumatic bleeding and in massive transfusion protocols when the blood group is unknown is increasingly being adopted by hospitals and generally considered a safe practice. In the setting of hemorrhage and exposure to at least one unit of RhD-positive RBC, the risk of an RhD-negative, hospitalized patient developing an anti-D is estimated at 21-26%. The risk may even be lower in an RhD-negative trauma patient presenting to the emergency room due to the immunomodulatory effects of traumatic injury and massive transfusion.[5] The overall goal in treatment of any massively bleeding patient is the provision of blood products as rapidly as possible in order to improve survival.

Is there a risk for hemolytic transfusion reaction in patients receiving LTOWB?

The overall risk of hemolysis with LTOWB is quite low. Group O RBCs in LTOWB are considered the universal donor and can safely be given to anyone, even those of unknown blood type. The plasma in LTOWB contains naturally occurring anti-A and anti-B, though at a low titer (thus the name "Low Titer O Whole Blood"), and could be ABO-incompatible with the recipient's red cells. (Refer to Acceptable ABO/RhD Substitutions for Blood Products – Adults, Plasma Section.) Concern arises that anti-A and/or anti-B may lead to hemolysis of the recipient's own red cells if the recipient is not Group O. However, the concentration of these passive antibodies is further diluted with concurrent administration of other intravenous fluids. The body's other protective mechanisms include A and/or B antigen expression on the individual's tissues and presence of circulating A and/or B substance; both of which adsorb some of the passive antibody and thus help to prevent hemolysis.[5]

The safety and efficacy of LTOWB has been described in multiple studies. A systematic review of 5 studies showed that use of LTOWB in hemorrhaging trauma patient was not associated with an increase in transfusion reactions.[6] In two independent single center retrospective studies, initial resuscitation of up to 4 units of LTOWB to non-group O adult trauma patients was not associated with laboratory or clinical evidence of hemolysis.[7,8] Likewise, in two large retrospective studies of group A plasma use for trauma patients, no differences in mortality were observed between those who received ABO-identical or compatible plasma versus those who received ABO-incompatible plasma.[9,10]

Can LTOWB be given to massively bleeding females of childbearing potential?

Transfusion of LTOWB is a viable option for females of childbearing potential in massive bleeding episodes. The controversy arises on whether these units should be O RhD-negative or O RhD-positive. For a female of childbearing potential (age less than 50) and unknown blood type who requires an emergent transfusion, the preference is to provide Group O, RhD-negative RBCs. This practice is based on the potential future risk, albeit low, for RhD alloimmunization and Hemolytic Disease of Fetus and Newborn (HDFN) if the woman is RhD-negative, develops anti-D due to exposure of RhD-positive RBCs, and then later was to become pregnant with a RhD-positive fetus. The immediate benefit of a life-saving transfusion should be balanced against an uncertain risk of a future pregnancy that may (or may not) be affected with HDFN. Several models have shown that when RhD-negative females were transfused with RhD-positive RBCs there is a low risk of HDFN, approximately 3%.[11-13]

From surveys on the willingness to accept an urgent transfusion that could potentially affect a future pregnancy, the majority of respondents, which included medical professionals and the general public, would accept the transfusion despite the future risk.[14] Hospitals will need to consider protocols for young female trauma patients and the development of processes to monitor RhD-negative women who may receive emergency release O RhD-positive RBCs or LTOWB.

Implications for Practice:

LTOWB can provide a more balanced resuscitation for bleeding patients. The safety of LTOWB appears equivalent to individual component therapy with no increased risk of hemolysis or transfusion reactions. Production

of Group O RhD-positive LTOWB best meets the growing demand without impacting the limited number of O negative donors.

When deciding on whether LTOWB should be part of an institution's suite of blood products for trauma patients, several factors need to be considered. Development of policies for its appropriate use, including for childbearing potential females, maximum number of LTOWB units a patient can receive, preference on number of units for stock and location (lab versus emergency department), and monitoring any associated adverse effects are essential.

While administration of LTOWB should follow the same blood administration policies as for other blood components, education of the product's safety and beneficial use can ease the acceptance of this product for trauma victims. Thus, a multidisciplinary approach is best for determining the practical considerations and logistics for implementation.

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