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Mitigating the risk of low-titer group O-positive whole blood resuscitation in females of childbearing potential: toward a systems-based approach

Elizabeth P Crowe,[1] Steven M Frank ,[2] Matthew J Levy[3]

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[1]Pathology, Division of Transfusion Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA
[2]Anesthesiology and Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA
[3]Emergency Medicine and Surgery, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Correspondence to
Dr Elizabeth P Crowe; ecrowe3@jhmi.edu

The use of low-titer group O-positive whole blood (LTO+WB) in critically injured females of childbearing potential (FCPs) remains the subject of institutional hesitation. The Shock Whole Blood and Assessment of TBI (SWAT) secondary analysis study by Brito *et al*[1] in this issue of *TSCAO* revealed that only 26.2% of women under age 50 years received LTOWB. These findings highlight the complexities surrounding a potential disparity in life-saving care, the ongoing uncertainty surrounding a treatment with potential for harm, and the need for standardized protocols. In comparison, men and women over age 50 years were more than twice as likely to receive LTO+WB.

The central concern surrounding LTO+WB stems from the predominantly RhD-positive donor pool, creating an inherent risk of RhD alloimmunization in RhD-negative recipients. When FCPs receive LTO+WB, this poses a potential risk of hemolytic disease of the fetus and newborn for future pregnancies. When contextualized, this outcome is infrequent on a population level[2]; however, it can be extremely consequential for individual patients. Despite accumulating observational evidence supporting improved survival in trauma and the practical advantages of providing complete transfusion support more rapidly,[3 4] neither LTOWB research nor research on legacy component therapies has consistently accounted for the specific needs and risks for FCPs. Nonetheless, this demographic remains under-represented in both trauma patient populations and as LTOWB recipients. Furthermore, the only two completed randomized controlled trials (RCTs) have been pilot studies focused on feasibility and were not powered to assess important clinical outcomes.[5 6] Larger RCTs with LTOWB are underway (NCT05638581, NCT04684719, NCT06070350) with results eagerly awaited. Until then, this controversy is likely to continue.

RCTs take time, and some postulate these RCTs may not be able to fully answer this question. While ethicists, scientists, and scholars contextualize the impacts of LTO+WB for FCPs, trauma resuscitation teams will continue to face the real decision of whether to administer this treatment. Varied practices reflect an ongoing struggle to balance immediate life-saving interventions against potential reproductive risks. We propose three pragmatic principles: (1) maintain appropriate caution in protocol development, to include indications for use during only the most critical moribund situations; (2) prioritize education and post-exposure workflows that include patient-centered, multidisciplinary systems of care for RhD-negative FCPs who receive LTO+WB; and (3) remain ready to adapt protocols as new evidence emerges.

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ORCID iD
Steven M Frank http://orcid.org/0000-0003-3533-3190

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