Sangre completa del grupo 0 negativo para la resucitación hemostática

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RESUMEN

El empleo de sangre completa en pacientes pediátricos y adultos mejora la supervivencia, particularmente en casos de hemorragia de origen traumático. Mientras que la evidencia científica actual avala su perfil de seguridad, la ausencia de estudios aleatorizados genera la necesidad de continuar investigando sobre este tema. Es esencial asentar el conocimiento de las líneas de tratamiento actuales basados en la terapia con hemocomponentes, aunque se carezca de datos sólidos para fundamentar su empleo.

En ausencia de los resultados definitivos de los estudios aleatorizados, análisis comparativos han demostrado la no superioridad del tratamiento con hemocomponentes y sugieren los beneficios potenciales de la sangre completa en la supervivencia a corto plazo de los pacientes y en la reducción del empleo de productos sanguíneos.

PALABRAS CLAVE: Sangre completa, Resucitación hemostática.

Low titer group o whole blood for hemostatic resucitation

SUMMARY

The utilization of whole blood in both pediatric and adult populations with life-threatening traumatic hemorrhage may improve survival. While existing evidence suggests it is also safe, the absence of randomized controlled trials (RCTs) underscores the imperative for further research in this domain in addition to other etiologies of hemorrhagic shock. It is essential to acknowledge that the current standard of care, reliant on component-based approaches, lacks robust RCT data to substantiate its efficacy and safety.

KEYWORDS: Whole blood, Hemostatic resuscitation.

INTRODUCTION

John Holcomb coined the concept "damage control resuscitation" twenty years ago, describing a bundle of care aimed at improving survival for patients with traumatic hemorrhage. Traditionally resuscitative efforts consisted of starting with crystalloid solutions, subsequently transitioning to blood products guided by laboratory parameters. Consequently, contemporary damage control resuscitation emphasizes hemostatic resuscitation with a blood-centric therapeutic approach and avoidance of crystalloids to manage life-threatening bleeding[1].

Members of the 31st Combat Support Hospital deployed to Baghdad from 2004 to 2005, published a retrospective analysis, reporting an independent association between the use of warm fresh whole blood with 28-day survival rates compared to casualties receiving only component therapy. Despite limitations of retrospective studies, these findings served as a catalyst for renewed interest surrounding resuscitative practices dating back to the World War I[2].

The gravity of mortality associated with traumatic, life-threatening bleeding in adults cannot be overstated, with 28-day mortality rates typically ranging from 20 % to 24 %. The swift onset of mortality, often within 4-6 hours following injury, underscores the urgent imperative for efficacious intervention strategies. Mortality rates in pediatric cohorts exhibit significantly higher mortality rates ranging from 37 % to 50 %. We need an effort to devise and implement tailored therapeutic strategies that account for the unique physiological responses and clinical exigencies characterizing both adult and pediatric populations. Only through such comprehensive endeavors can we hope to effectuate meaningful reductions in mortality rates and enhance the prospects of survival among trauma patients across diverse age cohorts[3-5].

Hemostatic resuscitation can be implemented by two different approaches: the 1:1:1 ratio of blood components, or the utilization of low titer group O whole blood (LTOWB). In addition, goal-directed hemostatic resuscitation can be implemented with the use of viscoelastic testing which can utilize both whole blood and component therapy.

The PROPPER trial was a study that evaluated different ratios of blood products. While 30-day mortality was not different between the high and low ratio groups there was a significant reduction in death from hemorrhage at 24 hours. In a secondary analysis, the PROPPER trial reported that time to initial transfusion matters, indicating that for every one minute in delay to the first blood product there is a 5 % increase risk of mortality[3,6].

Historically, there has been skepticism about the functional viability of platelets stored under cold conditions. This is held

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Table 1. *Advantages and risks of LTOWB.*

Advantages of LTOWB	Risks of LTOWB
More potent product Higher Hb, plasma, platelets per volume	Incompatible plasma/immune complexes? Theoretical risk
Cold platelets – improved hemostasis (RCT data)	Waste? Reduced/eliminated if used in non-trauma massive bleeding
Increased storage duration of platelet product	Ease of over-resuscitation
Less risk of ABO incompatible transfusion reactions than ABO compatible components	
Less bacterial contamination risk	
Logistical advantages Quicker transfusion of balanced product One product vs four products	
Independent association with improved Survival	

with the fact that cold-stored platelets do not persist for prolonged periods within the circulatory system. However, since the 1960s we know that cold-stored platelets exhibit better hemostatic activity. A recent manuscript demonstrates that cold temperatures enhanced hemostatic function of whole blood persists for at least 21 days[7].

The group in Pittsburgh led by Dr. Leeper recently published a metanalysis specifically focused on publications that exclusively investigated LTOWB, comprising nearly 60 000 patients in 24 studies. Both 24 hour and 28 day/in hospital mortality were associated with improved survival in both children and adults[8].

In one study from St. Louis whole blood was both independently associated with improved 24 hour and 28 day survival and also reduced total amount of blood used in the whole blood group compared to the component only group. This suggests that whole blood may be a useful blood management or conservation tool to use for patients with life-threatening bleeding. There was a reduction of a median of two liters less of blood used in the whole blood group compared to components[9].

In pediatric populations when whole blood is used compared to components there is an independent association with improved outcomes, takin into account the faster resolution of shock, faster resolution of coagulopathy and better platelet aggregation[5,10,11].

Regarding obstetric bleeding, the group in San Antonio and Utah used whole blood for postpartum hemorrhage in a small prospective observational study of 34 women, sixteen of them that received whole blood and eighteen received components. A relative reduction of 40 % was reported for those transfused whole blood which equated to approximately two liters less of blood products. In San Antonio they have developed a prehospital program that shares whole blood with the trauma center and as a result they have reported less than 1 % waste of whole blood[12].

In 2017, the THOR Network lobbied The American Association of Blood Banks to change their 31st standards to allow LTOWB to be a permitted product for patients with severe bleeding. Starting from two centers (Pittsburgh and the Mayo Clinic), now there are 302 centers only six years later in the US using low titer group O whole blood (Yazer *et al.,* 2018). LTOWB is also used for civilians in Norway, Brazil, Czech Republic and Israel and there are plans to start soon in Spain, Italy and Australia.

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There are at least three definitive randomized controlled trials ongoing evaluating LTOWB. TOWAR (Phase III) in prehospital population, using 30-day mortality, TROOP (Phase III) in hospitalized population and MATIC-2 (Phase III) in pediatric population comparing not only whole blood to components but also comparing tranexamic acid to placebo.

The main obstacles for initiating whole blood transfusion are: the lack of randomized control trials results, and constraints with Type O donors within the blood supply chain. Blood collectors are limited in their capacity to procure whole blood due to the necessity of diverting a significant portion of collected blood for component extraction. This dual demand complicates concurrently producing whole blood units, showing the need of innovative strategies of recruiting donors. The availability of RhD-negative blood, particularly concerning its implications for maternal and fetal health is another barrier. The scarcity of RhD-negative blood complicates transfusion protocols for women of childbearing age, even though there are many reports suggesting the potential survival benefit outweighs the potential risk of hemolytic disease of the newborn[14].

CONCLUSIONS

In summary, the utilization of whole blood in both pediatric and adult populations may improve survival outcomes in traumatic hemorrhage. While existing evidence suggests its safety profile, the absence of randomized controlled trials (RCTs) underscores the imperative for further research in this domain. It is essential to acknowledge that the current standard of care, reliant on component-based approaches, lacks robust RCT data to substantiate its efficacy.

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