Two-Unit Red Cell Transfusions in Stable Anemic Patients

Rajiv N. Thakkar, MD[1], Stanley J. Podlasek, MD[2], Leo C. Rotello, MD[1], Paul M. Ness, MD[2], Steven M. Frank, MD[3*]

[1]Department of Medicine, The Johns Hopkins Medical Institutions, Baltimore, Maryland; [2]Department of Pathology, Division of Transfusion Medicine, The Johns Hopkins Medical Institutions, Baltimore, Maryland; [3]Department of Anesthesiology and Critical Care Medicine and the Armstrong Institute for Patient Safety and Quality, The Johns Hopkins Medical Institutions, Baltimore, Maryland.

The "Things We Do for No Reason" (TWDFNR) series reviews practices which have become common parts of hospital care but which may provide little value to our patients. Practices reviewed in the TWDFNR series do not represent "black and white" conclusions or clinical practice standards, but are meant as a starting place for research and active discussions among hospitalists and patients. We invite you to be part of that discussion.

INTRODUCTION

Blood transfusion is not only the most common procedure performed in US hospitals but is also widely overused, according to The Joint Commission. Unnecessary transfusions can increase risks and costs, and now, multiple landmark trials support using restrictive transfusion strategies. This manuscript discusses the importance and potential impacts of giving single-unit red blood cell (RBC) transfusions in anemic patients who are not actively bleeding and are hemodynamically stable. The "thing we do for no reason" is giving 2-unit RBC transfusions when 1 unit would suffice. We call this the "Why give 2 when 1 will do?" campaign for RBC transfusion.

CASE PRESENTATION

A 74-year-old, 70-kg male with a known history of myelodysplastic syndrome is admitted for dizziness and shortness of breath. His hemoglobin (Hb) concentration is 6.2 g/dL (baseline Hb of 8 g/dL). The patient denies any hematuria, hematemesis, and melena. Physical examination is remarkable only for tachycardia—heart rate of 110. The admitting hospitalist ponders whether to order a 2-unit red blood cell (RBC) transfusion.

WHY YOU MIGHT THINK DOUBLE UNIT RED BLOOD CELL TRANSFUSIONS ARE HELPFUL

RBC transfusion is the most common procedure performed in US hospitals, with about 12 million RBC units given to patients in the United States each year.[1] Based on an opinion paper published in 1942 by Adams and Lundy[2] the "10/30 rule" set the standard that the ideal transfusion thresholds were an Hb of 10 g/dL or a hematocrit of 30%. Until human immunodeficiency virus (HIV) became a threat to the nation's blood supply in the early 1980s, few questioned the 10/30 rule. There is no doubt that blood transfusions can be lifesaving in the presence of active bleeding or hemorrhagic shock; in fact, many hospitals have blood donation campaigns reminding us to "give blood—save a life." To some, these messages may suggest that more blood is better. Prior to the 1990s, clinicians were taught that if the patient needed an RBC transfusion, 2 units was the optimal dose for adult patients. In fact, single-unit transfusions were strongly discouraged, and authorities on the risks of transfusion wrote that single-unit transfusions were acknowledged to be unnecessary.[3]

WHY THERE IS "NO REASON" TO ROUTINELY ORDER DOUBLE UNIT TRANSFUSIONS

According to a recent Joint Commission Overuse Summit, transfusion was identified as 1 of the top 5 overused medical procedures.[4] Blood transfusions can cause complications such as transfusion-related acute lung injury and transfusion-associated circulatory overload, the number 1 and 2 causes of transfusion-related deaths, respectively,[5] as well as other transfusion reactions (eg, allergic and hemolytic) and alloimmunization. Transfusion-related morbidity and mortality have been shown to be dose dependent,[6] suggesting that the lowest effective number of units should be transfused. Although, with modern-day testing, the risks of HIV and viral hepatitis are exceedingly low, emerging infectious diseases such as the Zika virus and Babesiosis represent new threats to the nation's blood supply, with potential transfusion-related transmission and severe consequences, especially for the immunosuppressed. As quality-improvement, patient safety, and cost-saving initiatives, many hospitals have implemented strategies to reduce unnecessary transfusions and decrease overall blood utilization.

In the past decade, clinicians have begun to realize that blood is like any other therapeutic agent; it is not without risk, it has a cost, and it should be given only when indicated and at the lowest effective dose. Guidelines and recommendations have shifted toward single-unit RBC transfusions in hemodynamically stable, nonbleeding patients.[7,8] The American Association of Blood Banks (AABB) supports single-unit transfusions for such patients.[9] Unfortunately, many clinicians are unaware of this recommendation.[10]

***Address for correspondence and reprint requests:** Steven M. Frank, MD, Zayed 6208, Johns Hopkins Hospital, 1800 Orleans St., Baltimore, MD 21287; Telephone: 410-955-8465, Fax: 410-955-0994; E-mail: sfrank3@jhmi.edu

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TABLE. Eight Prospective Randomized Trials Comparing Restrictive and Liberal Red Blood Cell Transfusion Strategies

Clinical Trial	Patient Population	Restrictive Strategy (Hb Trigger, Target)	Liberal Strategy (Hb Trigger, Target)	Reduction in Blood Utilization	Clinical Outcomes			
					Event	Restrictive (Incidence)	Liberal (Incidence)	*P* Value
Hebert et al., 1999[11] (n = 838)	Critically ill (adults)	7 to 8.5 g/dL	10 to 10.7 g/dL	54% fewer RBC units transfused	• 30-day mortality (all)	18.7%	23.3%	.11
					• 30-day mortality (age <55 years)	5.7%	13.0%	.02
					• 30-day mortality (APACHE II score ≤20)	8.7%	16.1%	.03
					• In-hospital mortality	22.2%	28.1%	.05
Lacroix et al., 2007[13] (n = 637)	Critically ill (pediatric)	7 to 9.4 g/dL	9.5 to 11.2 g/dL	47% fewer RBC units transfused	In-hospital Multiple-organ dysfunction syndrome	12%	12%	NS
Hajjar et al., 2010[12] (n = 502)	Cardiac surgery (adults)	8.0 to 9.1 g/dL	10 to 10.5 g/dL	58% fewer RBC units transfused	30-day composite all-cause mortality and severe morbidity	11%	10%	.85
Carson et al., 2011[14] (n = 2016)	Femur fracture (elderly adults)	8.0 to 9.5 g/dL	10.0 to 11.0 g/dL	65% fewer RBC units transfused	Composite endpoint	34.7%	35.2%	NS
					• 60-day mortality	28.1%	27.6%	NS
					• 60-day inability to walk	6.6%	7.6%	NS
Villanueva et al., 2013[15] (n = 921)	Gastrointestinal bleeding (adults)	7 to 9.2 g/dL	9 to 10.1 g/dL	59% fewer RBC units transfused	45-day all-cause mortality	5%	9%	.02
Robertson et al., 2014[17] (n = 200)	Traumatic brain injury	7 to 9.7 g/dL	10 to 11.4 g/dL	49% fewer RBC units transfused	• Favorable Glasgow Outcome Scale	42.5%	33.0%	.28
					• Thrombotic events	8.1%	21.8%	.009
Holst LB et al. 2014[16] (n = 998)	Septic shock (adults)	7 to 7.5 g/dL	9 to 9.5 g/dL	50% fewer RBC units transfused	90-day all-cause mortality	43.0%	45.0%	.44
Murphy GL et al., 2015[18] (n = 2007)	Cardiac surgery (adults)	7.5 to 9 g/dL	9.0 to 10 g/dL	40% fewer RBC units transfused	90-day serious infections or ischemic event	35.1%	33.0%	.30

NOTE: All studies employed single-unit RBC transfusion strategies except Robertson et al.[17] (unspecified strategy) and Lacroix et al.[13] (weight-based pediatric transfusions). Overall, no study showed an improved primary outcome using a liberal transfusion strategy. Villanueva et al.[15] showed a worse primary outcome (increased mortality) using a liberal transfusion strategy. Hebert et al.[11] showed a worse primary outcome in the 2 subgroups shown using a liberal strategy. Robertson et al.[17] showed a worse secondary outcome (thrombotic events) using a liberal strategy. Abbreviations: Hb, hemoglobin; NS, not significant; RBC, red blood cell.

This change in practice is evidence based and supported by 8 large, randomized trials that compared a restrictive to a liberal transfusion strategy, which are summarized in the Table.[11-18] These trials support (1) an Hb transfusion trigger of 7-8 g/dL and (2) transfusion of 1 RBC unit at a time, followed by reassessment of the Hb level and patient status. Five of the trials found no difference in the primary outcome[12-14,16,18] (meaning no benefit to giving more blood than is needed), and 3 of the trials showed worse outcomes with liberal transfusion[11,15,17] (or actual harm from giving extra blood). One issue to consider is that these clinical trials were focused on the Hb trigger (ie, defined as the Hb level at which clinicians start giving blood) but not on the Hb target (ie, the Hb level at which clinicians stop giving blood). The difference between the trigger and the target is determined by the dose of blood. In these trials, the standard strategy for transfusion was a single RBC unit followed by reassessment.

The above-mentioned studies support the concept that oftentimes less is more for transfusions, which includes giving the lowest effective amount of transfused blood. These trials have enrolled multiple patient populations, such as critically ill patients in the intensive care unit,[11,13] elderly orthopedic surgery patients,[14] cardiac surgery patients,[12] and patients with gastrointestinal hemorrhage,[15] traumatic brain injury,[17] and septicemia.[16] Outcomes in the trials included mortality, serious infections, thrombotic and ischemic events, neurologic deficits, multiple-organ dysfunction, and inability to ambulate (Table). The findings in these studies suggest that we increase risks and cost without improving outcomes only by giving more blood than is necessary. Since most of these trials were published in the last decade, some very recently, clinicians have not fully adopted these newer, restrictive transfusion strategies.[19]

ARE THERE REASONS TO ORDER 2-UNIT TRANSFUSIONS IN CERTAIN CIRCUMSTANCES?

Perhaps the most common indication for ordering multiunit RBC transfusions is active bleeding, as it is clear that whatever Hb threshold is chosen, transfusion should be given in sufficient amounts to stay ahead of the bleeding.[20] It is important to remember that we treat patients and their symptoms, not just their laboratory values. Good medical care adapts and/or modifies treatment protocols and guidelines according to the clinical situation. Intravascular volume is

also important to consider because what really matters for oxygen content and delivery is the total red cell mass (ie, the Hb concentration times the blood volume). If a patient is hypovolemic and/or actively bleeding, the Hb transfusion trigger, as well as the dose of blood, may need to be adjusted upward, creating clinical scenarios in which 2-unit RBC transfusions may be appropriate. Other clinical settings for which multiunit RBC transfusions may be indicated include patients with severe anemia, for whom both the pretransfusion Hb (the trigger) and the posttransfusion Hb (the target) should be considered. Patients with hemoglobinopathies (eg, sickle cell or thalassemia) sometimes require multiunit transfusions or even exchange transfusions to improve oxygen delivery. Other patients who may benefit from higher Hb levels achieved by multiunit transfusions include those with acute coronary syndromes; however, the ideal Hb transfusion threshold in this setting has yet to be determined.[21]

WHAT YOU SHOULD DO INSTEAD

For hemodynamically stable patients and in the absence of active bleeding, single-unit RBC transfusions, followed by reassessment, should be the standard for most patients. The reassessment should include measuring the posttransfusion Hb level and checking for improvement in vital sign abnormalities and signs or symptoms of anemia or end-organ ischemia. A recent publication on our hospital-wide campaign called "Why give 2 when 1 will do?" showed a significant (35%) reduction in 2-unit transfusion orders along with an 18% overall decrease in RBC utilization and substantial cost savings (≈$600,000 per year).[10] These findings demonstrate that there is a large opportunity to reduce transfusion overuse by encouraging single-unit transfusions.

RECOMMENDATIONS

- For nonbleeding, hemodynamically stable patients who require a transfusion, transfuse a single RBC unit and then reassess the Hb level before transfusing a second unit.
- The decision to transfuse RBCs should take into account the patient's overall condition, including their symptoms, intravascular volume, and the occurrence and rate of active bleeding, not just the Hb value alone.

CONCLUSIONS

In stable patients, a single unit of RBCs often is adequate to raise the Hb to an acceptable level and relieve the signs and symptoms of anemia. Additional units should be prescribed only after reassessment of the patient and the Hb level. For our patient with symptomatic anemia, it is reasonable to transfuse 1 RBC unit, and then measure the Hb level, and reassess his symptoms before giving additional RBC units.

Do you think this is a low-value practice? Is this truly a "Thing We Do for No Reason?" Share what you do in your practice and join in the conversation online by retweeting it on Twitter (#TWDFNR) and liking it on Facebook. We invite you to propose ideas for other "Things We Do for No Reason" topics by emailing TWDFNR@hospitalmedicine.org.

Acknowledgments

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