Blood transfusion in critical care

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Abstract

Blood transfusion is frequent in critical care. Transfusion raises the mass of transfused blood components and is lifesaving in acute hemorrhage. In massive transfusion (>10 units of red blood cells), early attempts to restore coagulation function appear helpful. Transfusion in non-bleeding patients is largely prophylactic, is seldom evidence-based, and may be deleterious. In hemodynamically stable critical care patients, level I evidence suggests that a hemoglobin of >7 g/dL and platelet counts of >10,000/ μ L are well tolerated.

Introduction and context

The need for critical care is expanding as society ages. Patients in intensive care units (ICUs) are highly transfused, with one-third of ICU patients transfused and 50% of mechanically ventilated patients receiving at least one transfusion [1]. The prevalence of transfusion is lower in injured patients, with 9% of trauma patients transfused and 2% massively transfused.

Transfusion is safer than ever, with the fraction of transfused units contaminated with HIV, hepatitis B or C, syphilis, West Nile virus, or Chagas disease agents at all-time lows. Transfusion is still complicated by acute and delayed reactions and by immunosuppressive effects and association with lung injury.

By raising the mass of transfused blood components, transfusion can increase oxygen-carrying capacity, provide substrate for clot formation, and replace plasma functions as well. Both observational and randomized clinical trials have sought to balance these benefits against the pro-inflammatory and immunosuppressive effects of allogenic transfusion. Transfusion in the absence of clear need is best avoided as it is wasteful and potentially dangerous.

There is class I evidence that supports a conservative transfusion strategy in the critically ill patient. The Transfusion Requirements in Critical Care (TRICC) study [2] randomly assigned 838 hemodynamically stable ICU patients whose hemoglobin (Hb) reached 9 g/dL either to receive transfusions to support them above an Hb of 10 g/dL or to be transfused only when their Hb went below 7 g/dL. Outcomes were equivalent or better with reduced transfusions, even in patients with cardiovascular disease. For patients with acute coronary ischemia, no randomized trial to guide the transfusion threshold exists. On the basis of animal and observational studies, patients with acute coronary syndromes should be transfused at a threshold Hb of between 8 and 11 g/dL [3]. There appears to be no benefit (in fact, there is possible harm) in transfusing at thresholds higher than these. It is not known whether there is a cerebral equivalent to acute coronary ischemia, but transfusion above other body requirements generally is not beneficial in brain injury. Investigators have explored using packed red blood cell (RBC) transfusion in multi-modality trials to increase oxygen delivery in septic shock. Although two of these studies reported improved survival (while many have not), this was likely due to other therapies in the intervention. Multiple well-performed studies

have failed to find improvements in oxygen consumption or end-organ perfusion in septic patients after transfusion.

As is the case for packed RBCs, there is compelling evidence that supports a conservative platelet transfusion strategy. Data from nine randomized clinical trials in acute leukemia and bone marrow transplant patients show that a threshold of 10,000 platelets/ μ L is associated with no more bleeding than higher transfusion triggers [4]. Prior studies have addressed the platelet count necessary for bedside procedures. Invasive procedures can be performed at platelet counts of 40,000/ μ L, according to American Society of Clinical Oncology guidelines [5]. Largely on the basis of consensus, the American Society of Anesthesiologists recommends platelet counts of 50,000/ μ L for general surgery and 100,000/ μ L for neurosurgery. Good operative technique is the best protection against excessive bleeding.

Fewer data to guide fresh frozen plasma administration exist, although it can be inferred that current usage may be greater than necessary. Non-bleeding patients on warfarin with international normalized ratios (INRs) of as high as 8 can be treated by simply holding the warfarin. Invasive bedside and operative procedures, with the possible exception of neurosurgery, are generally safe with prothrombin time (PT) and activated partial thromboplastin time (PTT) ratios of up to 1.5 times normal, and plasma and fresh frozen plasma transfusion should not be given without clinical evidence of coagulopathy.

The pathophysiology of the trauma patient differs markedly from that of the non-hemorrhagic patient. About a quarter of severely injured trauma patients arrive at the trauma center coagulopathic as measured by a prolonged PT. Even those who are normal but actively bleeding will become coagulopathic after the transfusion of 6 units of RBCs in the absence of additional plasma. Treating the coagulopathy of these patients early appears to improve their outcome. Thus, patients who are severely injured, actively bleeding, and likely to be massively transfused appear to benefit from the early administration of RBCs, plasma, and platelets in a 1:1:1 unit ratio [6]. This should be continued until the rate of bleeding slows to the point at which continued correction can be based on laboratory measurements. Several recent expert panels have suggested that platelet counts of 100,000/ μ L are an appropriate goal in severely injured polytrauma patients. Even with 1:1:1 replacement, it may be difficult to achieve an Hb of >9 , a platelet count of $>90,000/\mu$ L, and an INR of <1.5 during massive transfusion given that components become diluted

during the collection process and suffer loss of potency during storage and reinfusion.

Recent advances

Our understanding of the acute coagulopathy of trauma has been expanded by a comparison of admission coagulation studies with outcome in 35,000 trauma patients [7]. As injury severity increased, abnormalities of the PT, PTT, fibrinogen concentration, and platelet count all became more frequent, and elevations of any of these indices were associated with increased mortality in a stepwise manner. Our understanding of the risks and benefits of aggressive plasma resuscitation in trauma has been aided by a review of a large prospective study of inflammatory mediators in trauma patients, which showed that the greater use of plasma was associated with a higher rate of lung injury but lower overall mortality.

Results of the largest randomized trial in transfusion, the Platelet Dose (PlaDo) trial, have been presented at international meetings. PlaDo also found that a more liberal prophylactic platelet replacement strategy was not associated with improved outcomes, including reductions in bleeding risk. Additionally, this study validated the use of a 10,000/ μ L transfusion trigger as safe. Although PlaDo found that bleeding among thrombocytopenic patients is common, only one hemorrhage-related death occurred among the 1,278 patients in this study.

Recent observational studies have found that transfusion is associated with the development of acute lung injury and can also increase the risk of death from it [8]. These studies have led to a call to expand the definition of transfusion-related acute lung injury [9] and have reinforced the need for a conservative transfusion strategy in non-hemorrhagic patients.

Implications for clinical practice

Evidence for a general approach of avoiding transfusion as much as possible in patients who are not bleeding and that of treating massive hemorrhage to abolish coagulopathy have both been strengthened. Neither approach is as dangerous as its alternative. Clinicians should continue a conservative packed RBC transfusion strategy, transfusing 1 unit at a threshold of 7 g/dL in non-hemorrhagic patients. For patients with coronary syndromes, the target Hb is likely higher. The PlaDo study upends the historic assumption that the bleeding risk increases as platelet counts decline in oncology patients. Given that unnecessary platelet transfusion carries with it the risk of alloimmunization, transfusion reactions, and additional cost, it is increasingly difficult for clinicians

to justify using transfusion triggers of $>10,000/\mu\text{L}$ in non-bleeding patients.

Abbreviations

Hb, hemoglobin; ICU, intensive care unit; INR, international normalized ratio; PlaDo, Platelet Dose; PT, prothrombin time; PTT, partial thromboplastin time; RBC, red blood cell; TRICC, Transfusion Requirements in Critical Care.

Competing interests

The authors declare that they have no competing interests.

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