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Red blood cell transfusion in neurosurgical patients

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Abstract

Purpose of review—Anemia is common in neurosurgical patients, and is associated with secondary brain injury. Although recent studies in critically ill patients have shifted practice toward more restrictive red blood cell (RBC) transfusion strategies, the evidence for restrictive versus liberal transfusion strategies in neurosurgical patients has been controversial. In this article, we review recent studies that highlight issues in RBC transfusion in neurosurgical patients.

Recent findings—Recent observational, retrospective studies in patients with traumatic brain injury, subarachnoid hemorrhage, and intracranial hemorrhage have demonstrated that prolonged anemia and RBC transfusions were associated with worsened outcomes. Anemia in patients with ischemic stroke was associated with increased ICU length of stay and longer mechanical ventilation requirements, but mortality and functional outcomes did not improve with RBC transfusion. In elective craniotomy, perioperative anemia was associated with increased hospital length of stay but no difference in 30-day morbidity or mortality.

Summary—There is a lack of definitive evidence to guide RBC transfusion practices in neurosurgical patients. Large randomized control trials are needed to better assess when and how aggressively to transfuse RBCs in neurosurgical patients.

Keywords

neurosurgery; red blood cell; subarachnoid hemorrhage; transfusion; traumatic brain injury

INTRODUCTION

Anemia is common among patients in the ICU. Up to half of ICU patients are transfused with red blood cells (RBCs) during their hospital stay [1]. Patients with traumatic brain injury (TBI), subarachnoid hemorrhage (SAH), intracranial hemorrhage (lCH), and acute ischemic stroke admitted to the Neurosurgical Intensive Care Unit (NICU) commonly develop anemia and require RBC transfusion. A recent large-scale study examined 38 000 neurosurgical cases from the National Surgical Quality Improvement Program database, and reported that the need for preoperative transfusion with more than 4 units of RBCs is

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Conflicts of interest

There are no conflicts of interest.

significantly associated with complications in neurosurgery [2]. It remains unclear whether anemia is a marker of disease severity, or an independent predictor of worsened outcomes. What is clear, however, is that RBC transfusion in neurosurgical patients deserves special attention and considerations.

The brain is especially vulnerable to decreased perfusion and hypoxia, and brain oxygenation is highly dependent on adequate cerebral blood flow. The risks associated with both transfusion and anemia should be carefully weighed when deciding when, and how aggressively to transfuse RBCs in neurosurgical patients. However, transfusion goals in neurosurgical patients are controversial and vary depending on the type of neurological injury or surgery [3]. Furthermore, RBC transfusion strategies for neurosurgical patients vary greatly among clinicians [4,5].

There has been a considerable debate about the optimal hemoglobin (Hb) trigger for transfusion in neurosurgical patients, and both anemia and RBC transfusion appear to negatively impact clinical outcomes. There are, therefore, convincing arguments for using both liberal and restrictive transfusion guidelines [4]. In recent years, several articles have emphasized the risks associated with RBC transfusion in hospitalized patients. A recent meta-analysis reported that a restrictive RBC transfusion strategy was associated with a reduced risk of healthcare-associated infections as compared with a more liberal transfusion strategy [6▪]. Similarly, another meta-analysis and systematic review concluded that restrictive RBC transfusion criteria, in which a Hb trigger of less than 7 g/dl was used, were associated with a significant reduction in cardiac events, rebleeding, bacterial infections, and mortality [7▪]. In the absence of cardiac disease, many authors have cited these studies as a reason to use more restrictive transfusion protocols in critically ill patients. In this article, we will discuss some recent articles that have highlighted the important issues in RBC transfusion in neurosurgical patients.

TRAUMATIC BRAIN INJURY

Anemia is common in patients with severe TBI, and can result in decreased cerebral oxygen delivery and secondary brain injury [4]. Acute traumatic coagulopathy (ATC) is an acquired coagulation disorder that has been described in the context of isolated TBI, and coagulopathy increases the possibility that a patient will require an RBC transfusion. In a recent systematic review and meta-analysis, Epstein *et al.* [8▪▪] reported that ATC was uniformly associated with worse outcomes and high mortality that ranged from 17 to 86%. ATC was also associated with transfusion rates of 41%, as well as longer ICU stays, decreased ventilator-free days, and multiple organ failure.

The threshold for RBC transfusion in patients with TBI is controversial, and the optimal transfusion trigger is unknown [9]. In a recent retrospective review of 635 patients with isolated, severe TBI (Glasgow Coma Scale 3–8), the association between Hb levels and mortality was assessed [10]. In the 38% of patients who received RBC transfusion during their hospitalization, 5-day mean Hb levels less than 10 g/dl were associated with a two-fold increase in mortality. However, another large retrospective review of TBI patients found that RBC transfusion when the Hb level was greater than 10 was associated with worse

outcomes [11▪]. This emphasizes the importance of implementing guidelines to prevent and treat sustained anemia in TBI.

Very less is known regarding optimal RBC transfusion practices in pediatric patients with TBI. A recent retrospective study reviewed outcomes in 1607 pediatric patients with TBI, of which 178 received RBC transfusion [9]. The authors demonstrated that RBC transfusions in these patients were associated with poor outcomes and increased mortality. They, therefore, suggested that a transfusion trigger of 8.0 g/dl be considered in children with TBI.

SUBARACHNOID HEMORRHAGE

Anemia is common in patients with SAH, and may be caused by hemodilution, occult hemorrhage, drug effects, surgical blood loss, and aneurysm rupture and rebleeding [12▪]. As with TBI, both anemia and RBC transfusion in SAH have been associated with increased mortality. Historically, the threshold for RBC transfusion in patients with SAH was on the basis of expert opinion, and there is a lack of clinical guidelines to guide RBC transfusions in these patients.

A recent retrospective study examined 318 patients with SAH, of which 23% received RBC transfusion [12▪]. The study demonstrated that patients who received RBC transfusion had a three-fold increase in mortality as compared with patients who were not transfused. The authors suggest that anemia might have a ‘protective’ effect by increasing cerebral blood flow, decreasing blood viscosity, and inducing cerebral vasodilation by upregulating nitric oxide production. Another recent retrospective study demonstrated that RBC transfusion in patients with SAH was associated with a dose-dependent increased risk of thrombotic events and venous thromboembolism [13▪].

Although other studies have demonstrated a strong association between anemia and poor outcomes, it is difficult to establish causal relationships in these retrospective studies [14]. Currently, the threshold to transfuse RBCs in patients with SAH is still debated and varies among practitioners. These studies highlight the need for large, prospective RCTs that address which patients might benefit from more restrictive or liberal transfusion strategies.

INTRACRANIAL HEMORRHAGE

Very few studies have examined the impact of anemia on clinical outcomes in patients with ICH. A recent observational study retrospectively examined 435 patients with spontaneous ICH, and demonstrated that the presence of anemia (defined as Hb <12 mg/dl for women and <13mg/dl for men) resulted in a seven-fold increase in the risk of a poor outcome [1]. Even in minor-volume ICH, anemia was a strong predictor of unfavorable functional outcome. Another retrospective study demonstrated that low nadir Hb, not admission Hb, can be used to predict poor functional outcomes in patients with ICH [15].

Despite this fact, a recent retrospective study failed to demonstrate an improvement in outcomes with RBC transfusion in patients with ICH [16]. Outcomes in patients with ICH who receive RBC transfusion have been contradictory. In one study, RBC transfusion was associated with a trend toward worse outcomes compared with patients who were not

transfused [16]. In another study, however, RBC transfusion was not an independent predictor of poor outcomes [15].

A retrospective study analyzed various factors associated with an increased risk of developing acute respiratory distress syndrome after ICH [17]. They found that RBC transfusion was a modifiable risk factor associated with increased risk of acute respiratory distress syndrome. The authors did not examine the indication or Hb level at the time of transfusion, so the relative necessity of the transfusions could not be ascertained. Large, prospective trials are needed to further examine the risks of anemia and RBC transfusion in patients with ICH.

CEREBRAL ISCHEMIA

Patients in the neurological ICU frequently present with ischemic stroke, and these patients often require endovascular or decompressive surgery during their hospital stay. These patients generally have a poor prognosis, and prevention of secondary brain injury is vital [18]. To date, there have been no RCTs or large-scale studies that have investigated the role of anemia RBC transfusion strategies in NICU patients with ischemic stroke.

A recent observational, retrospective study examined the effects of anemia and RBC transfusion in 109 patients admitted to the NICU with ischemic stroke [18]. Nearly every patient in their cohort developed anemia, defined as Hb less than 12 g/dl in women and 13 g/dl in men. About one-third of patients were transfused RBCs, at the discretion of the attending physician, during their hospital stay. They found that decreasing Hb and hematocrit (Hct) were associated with increased NICU length of stay and longer mechanical ventilation requirements. There were no differences in mortality or functional outcomes, and patients who were administered RBC transfusions did not experience any benefits. Their limited data suggest that anemia should probably be avoided in patients with cerebral ischemia, but until larger prospective studies are done, no specific transfusion strategies for these patients can be recommended at this time.

ELECTIVE CRANIAL SURGERY

There have been no RCTs to date that have examined whether patients undergoing elective craniotomy benefit from either aggressive or restrictive perioperative RBC transfusion criteria. Alan *et al.* [19▪] recently published the first largescale study examining the effect of perioperative anemia on outcomes in patients undergoing elective cranial surgery. Using the National Surgical Quality Improvement Program database, they identified more than 6500 patients who underwent elective craniotomy for brain tumor, developed perioperative anemia, but were not transfused. Anemia was defined as mild (Hct 30–38%), moderate (Hct 26–30%), and severe (Hct <26%). The study found that perioperative anemia, irrespective of severity, was associated with increased hospital length of stay but not increased 30-day morbidity or mortality.

OTHER CONSIDERATIONS

Currently, there are few alternatives to RBC transfusion for anemic patients. Although RBCs are being transfused less frequently in recent years because of adverse patient outcomes and their associated costs, the use of alternatives to RBCs that is currently under investigation will likely also be driven by patient costs and clinical outcomes [20]. Autologous blood procurement, erythropoiesis-stimulating agents, and hemostatic agents have shown some promise in preventing sustained anemia in neurosurgical patients, but larger RCTs are needed to evaluate their efficacy. For patients undergoing neurosurgical procedures, there is limited evidence that blood conservation methods, such as acute normovolemic hemodilution, may be safe [21].

AGE OF STORED BLOOD

Many have questioned whether RBC age alters RBC function, thereby possibly increasing morbidity and mortality in neurosurgical patients [14]. It has been argued that progressively decreasing levels of 2–3 diphosphoglycerate in older blood may impair oxygen unloading and the release of vasodilators. However, patients transfused with older blood have not consistently demonstrated worse outcomes compared with transfusion of younger blood. A recent systematic review concluded that the quality of evidence is too poor to implement changes in current transfusion practices [22▪▪].

CONCLUSION

Anemia and RBC transfusion in neurosurgical patients are common. The brain is especially sensitive to hypoperfusion and hypoxia, and anemia may be associated with an increased risk of secondary brain injury. However, the inherent risks associated with RBC transfusion should not be underestimated. Although anemia is associated with a poor outcome, especially in the presence of cerebral ischemia, RBC transfusion is also associated with a worsened outcome. Currently, there is no level 1 evidence by which definitive RBC transfusion guidelines for neurosurgical patients can be recommended. Large RCTs are needed to better understand the balance between the risks associated with anemia and RBC transfusion in neurosurgical patients. Although some authors have recently advocated for a more liberal transfusion trigger (Hb of 9 g/dl) in patients with TBI, SAH, and acute ischemic stroke, there are also studies that suggest that a restrictive transfusion trigger (Hb of 7–8 g/dl) does not worsen outcome and may be of benefit to some patients. RBC transfusion decisions should be guided by risk and benefit analysis should be determined for each patient.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

▪ of special interest

▪▪ of outstanding interest

1. Kuramatsu JB, Gerner ST, Lucking H, et al. Anemia is an independent prognostic factor in intracerebral hemorrhage: an observational cohort study. Crit Care. 2013; 17:R148. [Epub ahead of print]. [PubMed: 23880122]
2. Rolston JD, Han SJ, Lau CY, et al. Frequency and predictors of complications in neurological surgery: national trends from 2006 to 2011. J Neurosurg. 2014; 120:736–745. [PubMed: 24266542]
3. Chang TR, Naval NS, Carhuapoma JR. Controversies in neurosciences critical care. Anesthesiol Clin. 2012; 30:369–383. [PubMed: 22901615]
4. LeRoux P. Haemoglobin management in acute brain injury. Curr Opin Crit Care. 2013; 19:83–91. [PubMed: 23385374]
5. Desjardins P, Turgeon AF, Tremblay MH, et al. Hemoglobin levels and transfusions in neurocritically ill patients: a systematic review of comparative studies. Crit Care. 2012; 16:R54. [PubMed: 22471943]
6. Rohde JM, Dimcheff DE, Blumberg N, et al. Healthcare-associated infection after red blood cell transfusion: a systematic review and meta-analysis. JAMA. 2014; 311:1317–1326. [PubMed: 24691607] Systematic review and meta-analysis demonstrated that RBC transfusion was associated with an increased risk of healthcare-associated infection.
7. Salpeter SR, Buckley JS, Chatterjee S. Impact of more restrictive blood transfusion strategies on clinical outcomes: a meta-analysis and systematic review. Am J Med. 2014; 127:124–131. e3. [PubMed: 24331453] Systematic review and meta-analysis demonstrated the many benefits of restrictive RBC transfusion strategies on outcomes.
8. Epstein DS, Mitra B, O'Reilly G, et al. Acute traumatic coagulopathy in the setting of isolated traumatic brain injury: a systematic review and meta-analysis. Injury. 2014; 45:819–824. [PubMed: 24529718] Systematic review and meta-analysis demonstrated the effect of acute traumatic coagulopathy on clinical outcomes.
9. Acker SN, Partrick DA, Ross JT, et al. Blood component transfusion increases the risk of death in children with traumatic brain injury. J Trauma Acute Care Surg. 2014; 76:1082–1088. [PubMed: 24662875]
10. DeCuypere M, Phillips G, Muhlbauer MS. Anemia and associated hospital mortality after severe traumatic brain injury. Surg Forum Abstracts. 2013; 217:S69.
11. Elterman J, Brasel K, Brown S, et al. Transfusion of red blood cells in patients with a prehospital Glasgow Coma Scale score of 8 or less and no evidence of shock is associated with worse outcomes. J Trauma Acute Care Surg. 2013; 75:8–14. Discussion. [PubMed: 23778432] Large, retrospective study demonstrated that RBC transfusion when Hb more than 10 g/dl was associated with worse outcomes.
12. Festic E, Rabinstein AA, Freeman WD, et al. Blood transfusion is an important predictor of hospital mortality among patients with aneurysmal subarachnoid hemorrhage. Neurocrit Care. 2013; 18:209–215. [PubMed: 22965325] Retrospective study demonstrated that RBC transfusion was independently associated with increased mortality compared with patients who were not transfused.
13. Kumar MA, Boland TA, Baiou M, et al. Red blood cell transfusion increases the risk of thrombotic events in patients with subarachnoid hemorrhage. Neurocrit Care. 2014; 20:84–90. [PubMed: 23423719] Retrospective, observational cohort study demonstrated an increased risk of thrombotic events and venous thromboembolism with RBC transfusion in patients with SAH.
14. Rosenberg NF, Koht A, Naidech AM. Anemia and transfusion after aneurysmal subarachnoid hemorrhage. J Neurosurg Anesthesiol. 2013; 25:66–74. [PubMed: 23047622]
15. Chang TR, Boehme AK, Aysenne A, et al. Nadir hemoglobin is associated with poor outcome from intracerebral hemorrhage. Springerplus. 2013; 2:379. [PubMed: 24010037]
16. Mohamed W, Reddy S, Sivakumar S, et al. Blood transfusion does not improve outcomes in patients with spontaneous intracerebral hemorrhage. Neurology. 2014; 82 (Suppl) 143:P7.
17. Elmer J, Hou P, Wilcox SR, et al. Acute respiratory distress syndrome after spontaneous intracerebral hemorrhage_. Crit Care Med. 2013; 41:1992–2001. [PubMed: 23760151]
18. Kellert L, Schrader F, Ringleb P, et al. The impact of low hemoglobin levels and transfusion on critical care patients with severe ischemic stroke: STroke: RelevAnt Impact of HemoGlobin,

Hematocrit and Transfusion (STRAIGHT)– an observational study. J Crit Care. 2014; 29:236–240. [PubMed: 24332995]

19. Alan N, Seicean A, Seicean S, et al. Impact of preoperative anemia on outcomes in patients undergoing elective cranial surgery. J Neurosurg. 2014; 120:764–772. [PubMed: 24286148] Large, retrospective study demonstrated that anemia was associated with prolonged hospitalization after elective cranial surgery but not an increased risk for adverse outcomes.
20. Spahn DR, Goodnough LT. Alternatives to blood transfusion. Lancet. 2013; 381:1855–1865. [PubMed: 23706802]
21. Oppitz PP, Stefani MA. Acute normovolemic hemodilution is safe in neurosurgery. World Neurosurg. 2013; 79:719–724. [PubMed: 22381828]
22. Lelubre C, Vincent JL. Relationship between red cell storage duration and outcomes in adults receiving red cell transfusions: a systematic review. Criti Care. 2013; 17:R66. [Epub ahead of print]. Systematic review demonstrated that no definitive studies supported that transfusion with fresh RBCs improved outcomes over transfusion with older RBCs.

KEY POINTS

- The brain is highly dependent on adequate cerebral blood flow, and anemia may worsen secondary brain injury.
- Although the risks associated with RBC transfusion may warrant restrictive transfusion strategies in many critically ill patients, the optimal Hb trigger to transfuse neurosurgical patients is unknown.
- In patients with TBI, SAH, and ICH, both prolonged anemia and RBC transfusion were associated with worsened outcomes.
- Although few alternatives to RBC transfusion have been demonstrated to be effective in improving outcomes in neurosurgical patients, some evidence suggests that normovolemic hemodilution may be safe.
- Although anemia is associated with a poor outcome, especially in the presence of cerebral ischemia, RBC transfusion is also associated with a worsened outcome.
- Large randomized controlled trials (RCTs) are needed of which neurosurgical patients may benefit from more restrictive or liberal transfusion strategies.