Review Article

Indications for blood and blood product transfusion

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ABSTRACT

Transfusion of blood products carries certain inherent risks and hence it should be undertaken only if it improves patient outcome. A review of the literature was carried out to find the indications and effects of transfusion on morbidity and mortality of patients. There is high-quality evidence showing that restrictive blood transfusion with a transfusion trigger of haemoglobin of 7-8 g/dl or the presence of symptoms of anaemia is safe and not associated with increased mortality compared with liberal transfusion. Thus, restrictive strategy is strongly recommended in surgical and critically ill-patients. There is moderate evidence for the use of plasma and platelet transfusion in patients receiving massive blood transfusion. There is not enough evidence to support the use of plasma, platelets and cryoprecipitate in any other clinical setting. Retrospective studies show improved survival after high plasma and platelet to red blood cell ratio of 1:1:1, but this has not been confirmed in randomised trials.

Key words: Blood, blood products, plasma, platelets, red blood cells, transfusion, transfusion trigger

BLOOD TRANSFUSION

Blood transfusion has been widely used and overused in medical practice since early 20th century to treat anaemia and haemorrhage. The efficacy of transfusion in improving patient outcomes is unsupported by scientific evidence, and its benefits have been mostly taken for granted. Excessive use of transfusion continues despite limited availability of blood on the one hand and high cost and serious risks associated with transfusion on the other.

In this review, the quality of evidence (QoE) and strength of recommendation (SoR) are given for each recommendation. Wherever available, effect estimates are accompanied by their 95% confidence intervals (CI) in brackets, thus: (Estimate [95% CI]).

Reasons for blood transfusion

Transfused red blood cells (RBCs) provide three beneficial effects: Circulatory (volume-related), rheological (viscosity-related) and oxygen carriage.[1] Blood transfusion is currently not recommended for volume expansion alone, except in cases of severe haemorrhage. Similarly, transfusion is required to increase viscosity only in cases of severe haemodilution. High viscosity in itself may impede circulation. Transfused blood also does not immediately increase oxygen delivery or utilisation at the tissue level.[2] Therefore, clinical situations where blood transfusion is beneficial to the patient and improves outcome are limited. The decision to administer blood should be taken after weighing the risks and benefits of blood transfusion against those of anaemia. A brief summary of indications of blood transfusion is given in Table 1.

Transfusion triggers

Transfusion trigger is defined as that value of haemoglobin (Hb) below which RBC transfusion is indicated. Transfusion target is the Hb one aims to achieve after RBC transfusion. Traditionally, the rule of "10/30" was followed for RBC transfusion, according to which a Hb level of 10 g/dl or a haematocrit of 30% was recommended in surgical patients. Over the years, the trigger for transfusion has become more conservative or restrictive. In addition, the decision to transfuse RBCs is based not only on the laboratory values, but also on the objective evaluation of the patient's clinical condition and her ability to compensate for the blood loss. Therefore, the patient's age, co-morbidities, severity of illness, and the rate

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Table 1: Summary of clinical indications of blood transfusion

Clinical condition	Transfusion trigger	Reference
Acute anaemia		
Surgical haemorrhage	Hb≤8 gm/dl or presence of symptoms	[12]
Traumatic haemorrhage	Haemorrhagic shock, inadequate oxygen delivery	[11]
Non-surgical/non-trauma haemorrhage	Hb<7 gm/dl or presence of symptoms	[6]
Critical illness	Hb<7 gm/dl or presence of symptoms	[11]
Early sepsis with inadequate oxygen delivery	Hb<9 gm/dl (weak evidence)	[14]
Septic shock, Late sepsis	Hb<7 gm/dl	[8,14]
Acute coronary syndrome with ischaemia	Hb 8-9 gm/dl (weak evidence)	[14]
Chronic anaemia		
Chronic blood loss (hepatic disorders, bleeding disorders)	No clear-cut transfusion triggers have been defined. Decision to transfuse is individualized based on symptoms and functional impairment	[1]
Decreased erythropoiesis (malignancies, chemotherapy, other drugs suppressing bone marrow, renal disorders, nutritional deficiencies)		

Symptoms of anaemia include symptoms of myocardial ischaemia, and orthostatic hypotension or tachycardia unresponsive to fluids

and amount of haemorrhage are taken into account before transfusion.

Scientific evidence

A number of clinical trials in the last few decades have found the restrictive transfusion strategy to be as safe as the conventional (or liberal) strategy. A Cochrane meta-analysis published in 2012 which included 6264 patients in 19 such trials in the settings of surgery (including cardiac surgery), critical care, trauma and acute haemorrhage found that the use of restrictive transfusion strategy (Hb: 7-9 g/dl) led to 39% fewer patients receiving transfusion (risk ratio [RR]: 0.61 [0.52-0.72]) and a decrease in the total number of transfusions (mean decrease 1.19 [1.85-0.53]) compared to liberal strategy (Hb: 9-12 g/dl).[3] The two strategies produced similar 30-day mortality rates (RR: 0.85 [0.70-1.03]). There was a lower in-hospital mortality with the restrictive strategy (RR: 0.77 [0.62-0.95]). Two RCTs[4,5] had adequate power to assess mortality and were major contributors to this meta-analysis. Other outcomes such as rate of adverse events, length of hospital stay and functional recovery were not affected by restrictive transfusion, even in older patients with a history of or risk factors for cardiovascular disease.

In patients with acute severe upper gastrointestinal haemorrhage, restrictive transfusion strategy (trigger Hb < 7 g/dl, target Hb: 7-9 g/dl) resulted in lower 45-day all-cause mortality (5% vs. 9%, $P = 0.02$) than liberal strategy (trigger Hb < 9 g/dl, target Hb: 9-11 g/dl).[6] Incidence of further bleeding and other serious adverse effects was also reduced. However, the results of this single-centre trial with strict protocol adherence may not be generalizable. A multicentric pragmatic cluster-randomised feasibility trial reflecting real world settings in patients with upper gastrointestinal haemorrhage is currently under way in the UK (TRIGGER trial).[7]

In a multicentric RCT (Transfusion Requirements in Septic Shock (TRISS) trial) in 1000 patients with septic shock in 32 ICUs there was no difference in the 90-day mortality (RR 0.94 [0.78-1.09]), the number of patients with ischaemic events (0.90 [0.58-1.39]) or in the use of life support in patients receiving leukoreduced RBCs at a transfusion trigger of 7 or 9 gm/dl.[8]

In 200 patients with traumatic brain injury, the rate of favourable neurological outcome (difference 0.1 [-0.06 to 0.25]; $P = 0.28$) was similar in patients receiving blood at a transfusion trigger 7 or 10 gm/dl. However, the lower transfusion trigger was associated with a lower incidence of thromboembolic events (Odds ratio 0.32 [0.12 to 0.79]; $P = 0.009$].[9]

Guidelines for transfusion

Guidelines for the use of blood transfusion have been published by many scientific societies. Some of the recent ones are from the American Society of Anesthesiologists,[10] the Society of Critical Care Medicine,[11] the American Association of Blood Banks (AABB),[12] the American College of Physicians[13] and the British Committee for Standards in Haematology.[14] Most recommend the use of restrictive transfusion strategy. However, high-quality evidence is available for very few clinical settings. A summary of these guidelines is as follows:

Post-operative patients

- In haemodynamically stable post-operative surgical patients, the trigger for transfusion is Hb ≤ 8 g/dl or presence of symptoms of

inadequate oxygen delivery (chest pain of cardiac origin, orthostatic hypotension or tachycardia unresponsive to fluid resuscitation, or congestive heart failure).[12] QoE: High; SoR: Strong.

Patients in the intensive care unit

- In critically ill normovolaemic patients transfusion is considered at a Hb level of ≤7 mg/dl with a target of 7-9 g/dl, unless specific co-morbidities or acute illness-related factors modify clinical decision-making.[12,14] QoE: Moderate to High; SoR: Strong
- During the early resuscitative phase of severe sepsis if there is evidence of inadequate oxygen delivery to the tissues (central venous oxygen saturation <70%, mixed venous oxygen saturation <65% or lactate concentration >4 mmol/L), blood transfusion is considered to achieve a target Hb of 9-10 g/dl.[14] There is only one single-centre trial in which the effect of a complex intervention (of which Hb target was one of the many components) on mortality was studied.[15] QoE: Low; SoR: Weak
- In the later phases of severe sepsis, the guidelines are similar to those for other critically ill patients with target Hb of 7-9 g/dl.[14] QoE: Moderate; SoR: Strong
- Blood transfusion should not be used to assist weaning from mechanical ventilation if the Hb is >7 g/dl.[14] QoE: Very low; SoR: Weak.

Patients with cardiac disease

- In haemodynamically stable patients with cardiovascular disease transfusion is considered for Hb ≤ 8 g/dl, or the presence of symptoms of inadequate oxygen delivery. The overall mortality is not affected by the use of restrictive transfusion in these patients, but the evidence for the risk of perioperative myocardial infarction is not clear due to heterogeneity and inadequate power of the studies.[12] QoE: Moderate; SoR: Weak
- In critically ill patients with stable angina, Hb should be maintained >7 g/dl. Transfusion to a Hb of >10 g/dl has uncertain benefit.[14] QoE: Moderate; SoR: Weak
- In patients suffering from acute coronary syndrome, the Hb should be maintained at >8-9 g/dl.[14] QoE: Low; SoR: Weak
- Restrictive transfusion strategy (trigger Hb: 7-8 g/dl) is recommended for patients with coronary artery disease.[13] QoE: Low; SoR: Weak.

Patients with neurotrauma or neurological diseases

- In patients with traumatic brain injury, the target Hb should be 7-9 g/dl; and in those with additional evidence of cerebral ischaemia the target Hb should be >9 g/dl.[14] QoE: Low; SoR: Weak
- In patients with subarachnoid haemorrhage the target Hb should be 8-10 g/dl.[14] QoE: Low; SoR: Weak
- In patients with an acute ischaemic stroke the Hb should be maintained above 9 g/dl.[14] QoE: Low; SoR: Weak.

High-quality evidence from adequately powered randomised controlled trials with measurement of appropriate patient outcomes is needed in different patient populations so that optimum transfusion triggers can be defined. Lower thresholds such as Hb of 6 g/dl also need to be explored. There is a paucity of data from India on the use restrictive transfusion strategy, and this gap needs to be filled.

BLOOD PRODUCT TRANSFUSION

Transfusion of blood products carries risks similar to those of RBC transfusion. In fact, some of the risks such as acute lung injury occur more often with transfusion of plasma.[16] Use of plasma, platelets and cryoprecipitate is discussed here.

Reasons for transfusion

Plasma is conventionally prescribed to replace coagulation factors in patients receiving massive transfusion (>one blood volume or 70 ml/kg in 24 h or >50% of blood volume in 3 h), for urgent reversal of the effect of warfarin, in known coagulation factor deficiency, and in cases of thrombotic thrombocytopaenic purpura.[17,18] The decision to transfuse is based on both presence of bleeding and abnormal laboratory values of prothrombin time (>1.5), international normalized ratio (>2) and partial thromboplastin time (>2 times). Plasma should not be used to replace intravascular volume.

Platelet transfusion is usually required in a bleeding patient below a platelet count of 50×10^9/L but rarely above 100×10^9/L. If the values fall between these two, transfusion is considered in case of platelet dysfunction (e.g., clopidogrel therapy), on-going bleeding and surgeries in confined spaces such as eye and brain.[10]

Cryoprecipitate is used to increase fibrinogen levels in patients with dysfibrinogenaemia and

hypofibrinogenaemia (fibrinogen <80-100 mg/dl), microvascular bleeding in patients receiving massive transfusion when fibrinogen cannot be measured and congenital fibrinogen deficiency.[10,17]

Scientific evidence and guidelines

Similar to blood transfusion, there is limited scientific evidence to support transfusion practices of blood components. A large proportion of components transfused is inappropriate. The AABB practice guidelines suggest that plasma be transfused to trauma patients who receive massive blood transfusion (MBT) (QoE: Moderate).[19] The guidelines also suggest that plasma be transfused in case of warfarin-related intracranial haemorrhage (QoE: Low). Plasma transfusion is not recommended for any other clinical situation.

A high ratio of plasma and platelets to RBC (1:1:1) during MBT has been shown to improve survival in a number of recent studies.[20-22] However, these studies are retrospective with a high degree of bias, especially survival bias. The AABB guidelines do not recommend for or against a plasma: RBC ratio of 1:3 or greater in trauma patients during massive transfusion due to low QoE.[19] The Canadian National Advisory Committee on Blood and Blood Products also does not recommend high plasma and platelet to blood ratio during MBT.[23]

It has been suggested that the use of point-of-care haemostasis assays such as thromboelastogaphy and rotational thromboelastometry provide better guidance to blood component therapy during MBT. However, a meta-analysis has shown that the use of these techniques in patients receiving MBT does not decrease the mortality, morbidity, or the use of platelets and FFP.[24] QoE: Moderate.

As for RBC transfusion, prospective randomised trials are needed to define the indications where the use of plasma, platelets and fibrinogen improves patient outcomes. It also needs to be evaluated if the use of high plasma/platelet to blood ratio and employment of point-of-care monitoring of coagulation improve outcomes.

SUMMARY

Blood and its components are life-saving drugs with inherent risks. Therefore, they should be used optimally and prudently to maximise patient outcomes. Current evidence shows that restrictive transfusion of blood is safe in stable post-operative and normovolaemic critically ill-patients with the trigger for transfusion being Hb of 7-8 g/dl or symptoms of anaemia. The transfusion trigger for patients with acute coronary syndrome is not known. There is recent evidence that in both septic shock and head injury, a lower transfusion trigger of 7 g/dl is better. There is not enough scientific evidence to guide the use of plasma, platelets and cryoprecipitate. Prospective randomised studies are required to determine the thresholds for transfusion of these products.

REFERENCES

1. Shander A, Gross I, Hill S, Javidroozi M, Sledge S, College of American Pathologists, *et al*. A new perspective on best transfusion practices. Blood Transfus 2013;11:193-202.
2. Fernandes CJ Jr, Akamine N, De Marco FV, De Souza JA, Lagudis S, Knobel E. Red blood cell transfusion does not increase oxygen consumption in critically ill septic patients. Crit Care 2001;5:362-7.
3. Carson JL, Carless PA, Hébert PC. Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion. Cochrane Database Syst Rev 2012;4:CD002042.
4. Hébert PC, Wells G, Blajchman MA, Marshall J, Martin C, Pagliarello G, *et al*. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion requirements in critical care investigators, Canadian critical care trials group. N Engl J Med 1999;340:409-17.
5. Carson JL, Terrin ML, Noveck H, Sanders DW, Chaitman BR, Rhoads GG, *et al*. Liberal or restrictive transfusion in high-risk patients after hip surgery. N Engl J Med 2011;365:2453-62.
6. Villanueva C, Colomo A, Bosch A, Concepción M, Hernandez-Gea V, Aracil C, *et al*. Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med 2013;368:11-21.
7. Kahan BC, Jairath V, Murphy MF, Doré CJ. Update on the transfusion in gastrointestinal bleeding (TRIGGER) trial: Statistical analysis plan for a cluster-randomised feasibility trial. Trials 2013;14:206.
8. Holst LB, Haase N, Wetterslev J, Wernerman J, Guttormsen AB, Karlsson S, *et al*. Lower versus higher hemoglobin threshold for transfusion in septic shock. http://www.nejm.org/doi/full/10.1056/NEJMoa1406617 accessed on 2/10/2014.
9. Robertson CS, Hannay HJ, Yamal J-M, Gopinath S, Goodman JC, Tilley BC, *et al*. Effect of erythropoietin and transfusion threshold on neurological recovery after traumatic brain injury. A randomized clinical trial. J Am Med Assoc 2014;312:36-47.
10. American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. Practice guidelines for perioperative blood transfusion and adjuvant therapies: An updated report by the American Society of Anesthesiologists Task Force on perioperative blood transfusion and adjuvant therapies. Anesthesiology 2006;105:198-208.
11. Napolitano LM, Kurek S, Luchette FA, Corwin HL, Barie PS, Tisherman SA, *et al*. Clinical practice guideline: Red blood cell transfusion in adult trauma and critical care. Crit Care Med 2009;37:3124-57.
12. Carson JL, Grossman BJ, Kleinman S, Tinmouth AT, Marques MB, Fung MK, *et al*. Red blood cell transfusion: A clinical practice guideline from the AABB. Ann Intern Med 2012;157:49-58.

13. Qaseem A, Humphrey LL, Fitterman N, Starkey M, Shekelle P, Clinical Guidelines Committee of the American College of Physicians. Treatment of anemia in patients with heart disease: A clinical practice guideline from the American College of Physicians. Ann Intern Med 2013;159:770-9.
14. Retter A, Wyncoll D, Pearse R, Carson D, McKechnie S, Stanworth S, *et al*. Guidelines on the management of anaemia and red cell transfusion in adult critically ill patients. Br J Haematol 2013;160:445-64.
15. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, *et al*. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001;345:1368-77.
16. Dara SI, Rana R, Afessa B, Moore SB, Gajic O. Fresh frozen plasma transfusion in critically ill medical patients with coagulopathy. Crit Care Med 2005;33:2667-71.
17. O'Shaughnessy DF, Atterbury C, Bolton Maggs P, Murphy M, Thomas D, Yates S, *et al*. Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. Br J Haematol 2004;126:11-28.
18. Murad MH, Stubbs JR, Gandhi MJ, Wang AT, Paul A, Erwin PJ, *et al*. The effect of plasma transfusion on morbidity and mortality: A systematic review and meta-analysis. Transfusion 2010;50:1370-83.
19. Roback JD, Caldwell S, Carson J, Davenport R, Drew MJ, Eder A, *et al*. Evidence-based practice guidelines for plasma transfusion. Transfusion 2010;50:1227-39.
20. Holcomb JB, Wade CE, Michalek JE, Chisholm GB, Zarzabal LA, Schreiber MA, *et al*. Increased plasma and platelet to red blood cell ratios improves outcome in 466 massively transfused civilian trauma patients. Ann Surg 2008;248:447-58.
21. Johansson PI, Stensballe J. Hemostatic resuscitation for massive bleeding: The paradigm of plasma and platelets – A review of the current literature. Transfusion 2010;50:701-10.
22. Lustenberger T, Frischknecht A, Brüesch M, Keel MJ. Blood component ratios in massively transfused, blunt trauma patients – A time-dependent covariate analysis. J Trauma 2011;71:1144-50.
23. Dzik WH, Blajchman MA, Fergusson D, Hameed M, Henry B, Kirkpatrick AW, *et al*. Clinical review: Canadian National Advisory Committee on Blood and Blood Products – Massive Transfusion Consensus Conference 2011: Report of the panel. Crit Care 2011;15:242.
24. Afshari A, Wikkelsø A, Brok J, Møller AM, Wetterslev J. Thrombelastography (TEG) or thromboelastometry (ROTEM) to monitor haemotherapy versus usual care in patients with massive transfusion. Cochrane Database Syst Rev 2011:CD007871.

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Announcement

Conference Calendar Details

Name of the conference: 62nd Annual National Conference of the Indian Society of Anaesthesiologists, ISACON 2014
Date: 25th to 29th December 2014
Venue: Velammal Medical College "Velammal Village", Madurai – Tuticorin, Ring Road, Annupanadi, Madurai – 625009, Tamil Nadu, India
Organising Secretary: Prof. Dr. S C Ganesh Prabhu, ISACON 2014, Institute of Anaesthesiology, Government Rajaji Hospital, Panagal Road, Madurai – 625 020, Tamil Nadu, India
Contact: +91 93448 17143, 94434 96835
E-mail: isaconmadurai2014@gmail.com
Website: www.isacon2014.com

Name of the conference: National CME ISAJAC 2014 & BJSAC 2014 - EAST ZONE CONFERENCE
Date: 7th to 9th November 2014
Venue: DSA City Branch – Dhanbad, Jharkand
Organising Secretary: Dr. Dinesh Kumar Singh
E-mail: dksdhn@gmail.com
Website: www.isajac2014.in

Name of the conference: RSAPCON 2014 - 24th Annual Conference of Research Society of Anaesthesiology Clinical Pharmacology
Date: 14th to 16th November 2014
Venue: Department of Anaesthesiology & Pain Management HIMS, HIHT University, Swami Ram Nagar, Jolly Grant, Dehradun, Uttarakhand - 248140
Organising Secretary: Dr. J P Sharma
Contact: +91 94117 18466
E-mail: info@rsacpcon2014.com

Name of the conference: ICA CON - 2014
Date: 21st to 23rd November 2014
Venue: Narayana Hrudayala Hospitals #258/A, Bommasandra Industrial Area Anekal Tk, Bangalore, Karantaka
Organising Secretary: Dr. Muralidhar Kanchi
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