Review Article

Blood transfusion practices in cardiac anaesthesia

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ABSTRACT

The primary reasons for blood transfusion in cardiac surgery are to correct anaemia and to improve tissue oxygen delivery. However, there is a considerable debate regarding the actual transfusion trigger at which the benefits of transfusion overweight the risk. The association between extreme haemodilution, transfusion and adverse outcome after cardio pulmonary bypass (CPB) is not clear and the current available literature is not sufficient to provide a strong recommendation regarding the safe haematocrit range during CPB. There is no quality evidence to support use of fresh red blood cell except during massive transfusion or exchange transfusion in neonate. Overall concern regarding the safety of allogeneic blood transfusion resulted in the search for autologous blood transfusion and perioperative blood salvage. The aim of this review is to provide cardiac surgery specific clinically useful guidelines pertaining to transfusion triggers, optimal haemodilution during CPB, autologous blood transfusion and role of perioperative blood salvage based on available evidence.

Key words: Blood transfusion, cardiac surgery, cardiopulmonary bypass

INTRODUCTION

Cardiovascular surgery is often accompanied by a dual threat for perioperative bleeding problems and attendant complications of blood and blood products transfusion. The threat can be either due to inadequate surgical haemostasis or coagulation abnormality as a result of cardiopulmonary bypass (CPB) leading to unacceptable microvascular bleeding. Although blood transfusion can be lifesaving, recent evidence suggests its negative outcome in terms of increased morbidity and mortality, prolonged hospital stay and decrease in long-term quality of life.[1,2] Introduction of beating heart surgeries has shifted the focus towards the use of antifibrinolytics, blood components and hypotensive anaesthesia with the use of thoracic epidural technique as a mean of blood conservation strategy. However, many centres in India still do cardiac surgeries using a conventional CPB with limited resources and there is a considerable variation in blood transfusion practice in different medical centres in India. One report from Western India indicates over-transfusion in more than 50% of cases,[3] whereas a South Indian study reveals appropriate blood transfusion in 90% of patients from their study cohort,[4] which implies differences in perioperative practice patterns as well as possible inappropriate use and therefore, current transfusion practices may require re-evaluation.

RED BLOOD CELL TRANSFUSION

Cardiac surgery patients consume a significant number of red blood cell (RBC) transfusion in proportion to other surgeries in the operating room, but there is little quality evidence to suggest the optimal haemoglobin (Hb) concentrations for transfusion in the perioperative setting in patients having cardiac surgery. The most common causes of excessive bleeding in cardiac surgical patients have been related to the interaction of blood components with the artificial surfaces of the CPB pump circuitry resulting in derangements in platelet function, impairment of coagulation cascades and excessive fibrinolysis. The predictors for bleeding complications after cardiac surgery are well analysed and includes older age, female gender, comorbidities, small body size, low pre-operative haematocrit (Hct), pre-operative antiplatelet or anti-thrombotic medication, redo and

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complex procedures, emergency operations, and on-pump surgery (in contrast to off-pump surgery). Further contribution to perioperative bleeding problems in cardiac surgery comes from need to use high dose anticoagulant like heparin during CPB, induction of hypothermia and use of large amount asanguinous crystalloid fluid as prime and pre-operative anticoagulant/antiplatelet therapy.

There is a paradigm shift in transfusion of RBC based on single Hb transfusion trigger to transfusion based on meeting the oxygen demand at tissue level and Hb based transfusion at best serves as a guide in case of insufficient or unreliable information on patients global or regional tissue oxygenation status.[5] The determination of an appropriate transfusion trigger during cardiac surgery need to address the level of Hb/Hct at which RBC transfusion should be commenced in the perioperative setting and also during CPB. But, unfortunately, the evidences are not conclusive at present.

PERIOPERATIVE TRANSFUSION TRIGGER

Murphy *et al*.,[6] found no benefit from transfusion for Hcts as low as 21% (Hb, 7 g/dl), and the risk of death within 30 days following surgery was almost 6 times greater for patients who received blood. There are several studies comparing restrictive transfusion (to maintain a Hb ≥ 7.0-9.0 g/dl) to liberal RBC transfusion strategy (10-12 g/dl) during cardiac surgery and most of the randomised clinical trials support a restrictive transfusion strategy in adult patients undergoing cardiac surgery because of a beneficial risk benefit ratio of not doing any harm and a clear economic benefit of using less blood. Bracey *et al*., prospectively divided patients into two transfusion trigger groups after coronary artery bypass grafting (CABG) surgery to receive RBC transfusion if Hb < 8 g/dl (restrictive transfusion) or < 9 g/dl (liberal transfusion) and reported that reducing the Hb trigger to 8 g/dl did not adversely affect patient outcome and resulted in lower costs.[7] Similarly, the transfusion requirement after cardiac surgery trial evaluated two different transfusion trigger with a predefined non-inferiority margin of −8% among patients undergoing elective cardiac surgery and opined that a restrictive transfusion strategy targeting a Hct of 24% is as safe as a liberal strategy targeting a Hct of 30%, with respect to a composite end point of 30 days mortality and inpatient clinical complications.[8] However, in paediatric patients with cyanotic heart disease a transfusion threshold of 9 g/dl is more appropriate.[9]

Many cardiac centres from India favour fast tracking and aim for early discharge of the patient from the hospital but the current evidence do not address issues like exercise tolerance and functional recovery aspect while adopting a liberal or restrictive transfusion strategy. The decision to transfuse when the Hb is between 7 and 10 g/dl is entirely the subjective perception of the physician based on risk benefit analysis as determined by the patient's clinical condition and clinical setting. Further studies are warranted to guide the cut-off level for perioperative anaemia tolerance in patients with pre-existing comorbidity. Again the evidence is not strong enough to transfuse additional RBC to patients having a Hb > 10 g/dl but are at risk of critical non-cardiac end organ ischemia of central nervous system or gut.[10] However, there is a consensus that RBC transfusion is lifesaving at a Hb below 6 g/dl and a transfusion trigger of 7 g/dl are reasonable for the perioperative setting. Patients are having Hb level more than 10 g/dl should not be transfused because there is a risk related to transfusion without favourable improvement in oxygen transportation [Table 1].

TRANSFUSION TRIGGER DURING CARDIOPULMONARY BYPASS

Haemodilutional anaemia is an inevitable consequence of CPB using asanguinous prime of circuits with conventional priming volumes. The beneficial effects of haemodilution during CPB is often negated by excessive haemodilution, which may compromise oxygen delivery at the tissue level and contribute to hypotension during CPB, induce ischaemic organ injury, and necessitate transfusion of allogeneic blood. Retrograde autologous priming (RAP) during CPB is an effective technique to limit haemodilution and can be achieved by using patients own blood to replace the crystalloid prime in CPB circuits. Two large meta-analyses demonstrated a significant reduction in number of allogeneic blood transfusions in adults with RAP, but failed to prove any clinical benefit because of reduced transfusion.[11,12]

A determination of optimal Hct on CPB requires an assessment of the risks and benefits of both haemodilutional anaemia and RBC transfusion. The optimal safe Hct level during CPB is yet to be decided. Early studies have suggested a safe Hct level somewhere

Table 1: Transfusion triggers/practices during cardiac surgery

Clinical condition	Transfusion trigger	Suggested practice guidelines	Comments
Pre-operative period	Hb<6 g/dl	Transfusion of RBC life saving	Transfusion is unlikely to improve oxygen transport when the Hb >10 g/dl and is not recommended
During CPB with moderate hypothermia		Transfusion of RBC reasonable	Indications for RBC transfusion if, Hb>6 g/dl are guided by patient-related factors**, the clinical setting† and laboratory or clinical data‡
Without the risk for decreased cerebral oxygen delivery*	Hb≤6 g/dl		
With risk for critical end-organ ischemia/injury	Hb<7 g/dl		
Post-operative period	Hb≤7 g/dl	Transfusion of RBC indicated	RBC transfusion may be needed in patients with critical non-cardiac end-organ ischemia# whose Hb levels are as high as 10 g/dL
Acute normovolemic hemodilution or IABD		Could be used as a part of multimodal blood conservation strategy	Usual contraindications for IABD are unstable patients, especially with evolving myocardial infarction, unstable angina, cardiogenic shock, pre-operative anaemia, sepsis or known bacteremia and low ejection fraction (<30%)
Residual pump blood		Salvage through centrifugation and re-infusion back to the patient	Some form of pump salvage and reinfusion at the end of CPB is reasonable

*History of cerebrovascular attack, diabetes, cerebrovascular disease, carotid stenosis; **Age (elderly), severity of illness, cardiac function, or risk for critical end-organ ischemia; †Massive (≥30% of blood volume) or active blood loss; ‡Mixed venous oxygen saturation (reduction of mixed venous O_2 saturation to below 50%; peripheral mixed venous PO_2 to below 32 mmHg or central venous O_2 saturation to below 60%), electrocardiogram (newly occurring ST segment elevation or depression, onset of arrhythmias), or echocardiographic evidence (newly occurring localised altered contractility of the myocardium) of myocardial ischemia; #Central nervous system and gut. RBC – Red blood cell; Hb – Haemoglobin; CPB – Cardiopulmonary bypass; IABD – Intraoperative autologous blood donation

between 14% and 19% during CPB.[13,14] An analysis in Jehovah Witness patients undergoing cardiac surgery suggests that haemodilution to a Hb of 5.0 g/dl can be tolerated with minimal morbidity.[15] Whereas, recent studies have found an increased association of renal failure with a Hct below 21-24%.[16,17] Karkouti *et al.*,[16] in an observational study of more than 9000 patients undergoing cardiac surgery with CPB has found that an independent, nonlinear relationship exists between the degree of haemodilution during CPB and patient needing dialysis support as a result of renal failure. They reported that the risk of developing post-operative renal failure is 2.34 times odds for a severe haemodilution (nadir Hct < 21%) compared to moderate haemodilution (nadir Hct 21-25%). Apart from renal failure, neurocognitive dysfunction has also been interrelated to degree of haemodilution during CPB. Mathew *et al.*,[18] observed increased cognitive decline in elderly patients managed on CPB with Hct 15-18% compared to Hct > 27%. A recent study by Ranucci *et al.*,[19] studied patients who had undergone isolated coronary operations without receiving blood transfusions during their hospital stay and concluded that low values of pre-operative Hct were not associated with an increased morbidity, provided that the lowest Hct on CPB was maintained above 28%.

Combining all these prospective, retrospective and observational studies, a transfusion trigger during CPB is reduced to 6 g/dl with moderate hypothermia except in patients with history of cerebrovascular accidents, cerebrovascular disease, diabetes mellitus, and carotid stenosis and in these group of patients with a risk of decreased cerebral oxygen delivery or end-organ ischaemia/injury it is not unreasonable to keep the Hb level at ≥ 7 g/dl [Table 1]. In the setting of Hb values exceeding 6 g/dl while on CPB, the patient's clinical situation should be considered as the most important component of the decision making process. Indications for transfusion of RBC in this setting are multifactorial and should be guided by patient-related factors such as age, acuity of illness, end-organ ischaemia, cardiac function, the clinical setting of active blood loss and laboratory or clinical data (Hct, electrocardiogram or echocardiographic evidence of myocardial ischaemia and mixed venous saturation).

There is a common concern regarding the age of transfused RBC. Few studies suggested a negative impact of old RBC transfusion,[20] whereas others failed to find any association between the age of stored blood and adverse outcome.[21] Transfusion-associated microchimerism (TA-MC) is a condition described in trauma victims who receive multiple units of bank blood with relatively short storage time. The pathophysiology behind this TA-MC is the altered immunity following trauma, which predispose to a transient tolerance to allogeneic cells enabling low-level engraftment, thus manifesting as TA-MC. Considering the fact that cardiac surgery

is an iatrogenic trauma and the post-CPB period is associated with immune perturbation the existence of a TA-MC cannot be ruled out. A Dutch study concluded a two-fold increase in mortality rate after fresh RBC transfusion compared to old RBC and suggested that the tendency to demand for fresh blood during cardiac surgery actually could harm a certain patient population. They speculated that increased MC is responsible for adverse outcome after fresh RBC transfusion.[22] Further study on MC after fresh blood transfusion in cardiac surgery may reveal important information regarding potential clinical consequences of TA-MC as well as basic haematologic and immunologic processes.

ALTERNATIVE TO HOMOLOGOUS TRANSFUSION PRACTICES

Developing and guiding practice of autologous transfusion either with a pre-operative autologous blood donation, intraoperative autologous blood donation (IABD), or transfusing the CPB salvaged or surgical site shed blood (with or without a cell saver technique) is particularly important in a developing country like India with limited resources, variable quality of blood banking and surgical expertise with exponential growth of cardiac surgical centres.

PRE-OPERATIVE AUTOLOGOUS BLOOD DONATION

Most of the studies concluded that both pre-operative and intraoperative autologous donation significantly reduces allogeneic blood requirement in cardiac surgery. However, pre-operative autologous donation in cardiac surgical setup is limited by factors like timing of procedure, withdrawal amounts, safety, crossover of unused blood, preparation and storage and cost-effectiveness. The updated guidelines from the society of thoracic surgeons and society of cardiovascular anaesthesiologists have come out with improved level of evidence for use of human recombinant erythropoietin (EPO) or EPO with iron to increase red cell mass in patients with pre-operative anaemia, at risk of post-operative anaemia and in case of Jehovah's Witness.[23] However, a very strong recommendation could not be made with the absence of large scale safety studies for use of these agents in cardiac surgical patients, and the task force suggested a balanced risk benefit ratio considering a potential risk of thrombotic cardiovascular events, especially in patients posted for coronary revascularization with unstable symptoms. Hence in a cardiac surgical setup many centres rely on intra-operative autologous donation techniques with acute normovolemic haemodilution (ANH).

INTRAOPERATIVE AUTOLOGOUS BLOOD DONATION

In the IABD-ANH technique, the collected autologous blood is transfused first followed by the allogeneic blood to maintain the optimal Hct. To maintain circulating volume, crystalloids or colloids were replaced for the withdrawn blood in a ratio of 1:1. In contrast to pre-operative donation, IABD is performed in the operating room, immediately prior to CPB. The benefits include: Preservation of stored blood from haemolysis due to bypass; decrease in blood loss via lap pads, discard suction and field drapes; and provision for fresh autologous RBCs, platelets, and coagulation factors after bypass. Intraoperatively autologous blood can be collected either prior to heparinisation from antecubital vein or via a central venous catheter which is routinely placed for cardiac surgery or after heparinisation via the venous line at the commencement of bypass, the arterial monitoring line, or off the arterial cannula. Around 30% of patients total blood volume can be slowly drained into anti-coagulated blood bags intra-operatively in selected cohort of patients. The usual contraindications for IABD are unstable patients, especially with evolving myocardial infarction, unstable angina, cardiogenic shock, pre-operative anaemia, sepsis or known bacteraemia and low ejection fraction (<30%) [Table 1].

PERIOPERATIVE BLOOD SALVAGE

Autotransfusion of blood collected through a cardiotomy suction or the salvaged CPB blood either directly or through a cell saver have been practiced in many adult cardiac centres. Both controlled and uncontrolled cardiotomy suction result in some degree of platelet activation without reaching a statistical significance but once uncontrolled suction exceeds beyond 3 h the risk of late post-operative bleeding (beyond 18 h) increases and may require additional blood unit transfusion. The quality of evidence to support a cell saver technique over direct transfusion during CPB is either very poor or yield conflicting results.[24,25] A meta-analysis,[25] suggested that the use of a cell saver reduces exposure to allogeneic blood products or RBC transfusion for patients undergoing cardiac surgery. However, the cell saver may be beneficial only when it is used for

shed blood and/or residual blood or during the entire operative period and processing cardiotomy suction blood with a cell saver only during CPB has no significant effect on blood conservation and increases fresh frozen plasma transfusion. The cell saver is very expensive, and the disposable kits used are also expensive.

Many cardiac surgical teams favour reinfusion of residual pump blood to the patient at the end of CPB as a part of blood conservation strategy but there is considerable debate regarding whether to transfuse the residual pump blood directly or to subject this blood to further processing (centrifugation or ultrafiltration) before transfusing back to the patient. Studies comparing centrifugation, ultrafiltration or direct transfusion did not reveal any difference in terms of blood product usage, total chest tube drainage, or discharge Hct values.[26] A study comparing centrifugation to that of ultrafiltration concluded that both the methods were equally effective in achieving haemo-concentration during extracorporeal circulation and while salvaging the diluted residual CPB blood.[27] However, they suggested use of haemofiltration over centrifugation to avoid loss of plasma fraction during the process of centrifugation.[25] However, few other studies found significantly less allogeneic red cell use in the centrifugation group compared with the direct infusion group.[28,29] Despite limitations of the current body of literature (small sample size, only CABG patients), all studies have showed superiority of the pump salvage strategy compared with no salvage of residual blood [Table 1]. However, direct transfusion of shed mediastinal blood from post-operative chest tube drainage is not recommended; but reinfusion of washed shed mediastinal blood can be adopted as a part of multimodal blood conservation program.[23]

SUMMARY

The general consensus among the cardiac anaesthesiologists is that it is reasonable to transfuse red cell if the Hb is below 7 g/dl and not reasonable when the Hb > 10 g/dl. But the decision to transfuse when the Hb is between 7 and 10 g/dl is entirely the subjective perception of the physician based on risk benefit analysis. The safe Hct during CPB is still undefined and probably more sophisticated method to measure the tissue oxygen delivery status is needed to further guide the optimal degree of haemodilution during CPB. The introduction of the concept of MC may reduce the demand for fresh blood transfusion in the coming days. In a country like India it may be prudent to use a restrictive transfusion therapy in combination with an intraoperative blood salvage method to minimise the need for allogeneic blood transfusion and its associated risk in a safe and cost effective manner.

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