REVIEW ARTICLE

BLOOD CONSERVATION TECHNIQUES IN SURGICAL PATIENTS: A REVIEW ARTICLE

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ABSTRACT: SUMMARY: Anemia is a recognized complication of major trauma, surgery, and critical illness. Both anemia and its correction in the form of blood transfusion are associated with increased morbidity and mortality. American society of anesthesiologist's guidelines needs to be followed whenever blood transfusion is contemplated in surgical patients. Perioperative blood transfusion is associated with various complications in addition to increased cost to the patients. Principal blood conservation strategy which should start pre-operatively includes diagnosing and correction of anemia, restrictive blood transfusion, use of newer pharmacological agents, meticulous less invasive surgical techniques, proper patient positioning, autologous blood transfusion and use of blood substitutes. In critically ill patients as transfusion trigger is less compared to healthy subjects, blood wastage during diagnostic tests should be minimized. There need to urgent re-evaluation of our current practice of liberal blood transfusion. A well formulated pre-operative plan integrating various techniques of blood conservation will help in reducing the need for allergenic blood transfusion, which may contribute to improved overall outcome of the surgical patients.

KEYWORDS: Anaemia, blood conservation, transfusion trigger, blood substitutes.

INTRODUCTION: Anemia is a recognized complication of major trauma, surgery, and critical illness. It is associated with increased morbidity and mortality.¹ American society of anesthesiologist² gave the following evidence based guidelines for blood transfusion in perioperative and postpartum settings:

1. Transfusion is rarely indicated when the hemoglobin concentration is greater than 10 g/dl and is almost always indicated when it is less than 6 g/dl, especially when anemia is acute.
2. The determination of whether intermediate hemoglobin concentration (6–10 g/dl) justify or require RBC transfusion should be based on the patient's risk for complications of inadequate oxygenation.
3. The use of single hemoglobin trigger for all patients and other approaches that fail to consider all important physiological and surgical factors affecting oxygenation are not recommended.
4. The indications for transfusion of autologous RBCs may be more liberal than allogeneic RBCs because of lower (but still significant) risks associated with the former.
5. When appropriate preoperative autologous blood donation, intraoperative and postoperative blood recovery, acute normovolemic hemodilution and measures to decrease blood loss (deliberate hypotension and pharmacological agents) may be beneficial.

Perioperative blood transfusion is associated with greater postoperative complications (Table 1), including nosocomial infections, immune-suppression, transfusion-related acute lung injury, decreased health-related quality of life, and reduced early and long-term survival.³

REVIEW ARTICLE

I. Infectious Risks of Blood Transfusion (all products)	
Transfusion-Transmitted infection	Residual Risk Per Transfused Component
HIV	1 in 1,467,000
Hepatitis C	1 in 1,149,000
Hepatitis B	1 in 282,000
West Nile Virus	Uncommon
Cytomegalovirus	50-85% of donors are carriers.
Bacterial Infection	1 in 2-3,000 (mostly platelets)
Parasitic Diseases: Babesiosis, Malaria	Relatively uncommon
II. Non-infectious Risks of Blood Transfusion	
Reaction	Incidence
Acute hemolytic transfusion reaction (AHTR):	1:76,000
Overall ABO incompatibility	1:40,000
Fatal ABO incompatibility	1:1.8x10 ⁶
Febrile non-HTR	0.1-1.0%
Allergic (urticarial) reactions	1-3%
Anaphylactoid/anaphylactic	1:20,000-50,000
Transfusion-related acute lung injury (TRALI)	~1:10,000
Other rare reactions: delayed HTR, Transfusion-associated graft-versus-host disease	
Table 1: Adverse Effects of Transfusion ⁴	

Potential complications of allogenic transfusion that can be eliminated or minimized when autologous blood is administered include acute and delayed hemolytic reactions, alloimmunization, allergic and febrile reactions, and transfusion-transmitted infectious diseases.⁵ In addition, the financial burden is significant on the health care system.

It includes the cost of blood collection, processing and storage. In smaller setups where 50 units are processed per week, the cost of blood is as high as Rs/- 1825 per unit in comparison to a place where 5000 units are processed in a week costing Rs/- 339 per unit.⁶ Hence, initiatives to treat anemia and optimize patient blood management using blood conservation strategies may improve patient outcomes along with overall safety of anesthesia and surgery for patients with anemia.^{7,8}

REVIEW ARTICLE

Fig. 1: Strategies of blood conservation during perioperative period

BLOOD CONSERVATION STRATEGIES: Blood conservation techniques are essential to decrease the development of anemia and need for blood transfusion. Various strategies that could be adopted in the perioperative period as illustrated (Figure 1).

PREOPERATIVE CORRECTION OF ANEMIA: There is a high prevalence of moderate anemia found in patients awaiting elective surgery. It ranges from 30% in cardiovascular⁹ and critically ill patients,¹⁰ to 76% in patients with advanced colon cancer.¹¹ Careful assessment of the patient for identification of factors that may increase the need for blood transfusion such as anaemia, coagulopathies, malignancy, renal failure, cardiac/vascular diseases, nature of surgery etc; helps in early detection and treatment of anemia in the preoperative period. Further, when the haemoglobin (Hb) is less than 10g/dl, the cause of anaemia is investigated and treated. (Figure 2).

IRON AND VITAMIN THERAPY: The preferred route of iron supplementation is oral. The patient needs to be given at least 200 mg of elemental iron a day (e.g. ferrous sulfate 325-mg tablets, which contain about 65 mg of elemental iron, 3 times daily). Intravenous supplementation can be given in more severe cases to raise Hb levels by approximately 1-2 g/dL per three weeks of treatment. Anemia due to cobalamine (vitamin B₁₂) and folate deficiency also responds to replacement within approximately 10 days, but replacements might have to be used intravenously. The recommended doses are folic acid 1 mg/d and Vitamin B₁₂ is 1000 microgram/d IM for 5 days, followed by similar doses per week until normal haematocrit (Hct) is reached.

RED BLOOD CELL GROWTH FACTOR THERAPY: Erythropoietin is a 34 kDa glycoprotein which is secreted from interstitial fibroblasts in the kidney. Apart from augmenting erythropoiesis by action on CFU-E cells (precursors of reticulocytes), it also induces angiogenesis, smooth muscle proliferation, increases iron absorption from gut and cause systemic vasoconstriction. Erythropoietic

REVIEW ARTICLE

agents together with iron replacement have a response rate of 75%–100%. Epoietin alfa has been used at 200 U/kg bodyweight twice per week or 150 U/kg bodyweight three times per week. Darbepoetin alfa is used at 0.9 g/kg body weight once per week. EPA is started at least 4 weeks preoperatively.

The adverse effects of erythropoietin are hypertension, stroke, venous thromboembolism, tumor recurrence, altered graft function, myocardial infarction and death.¹²

COAGULATION PROFILE: Anticoagulant and anti-platelet medications that may be interfering with the coagulation process should be checked. Long-term anticoagulation with warfarin is often indicated in patients with a history of venous thromboembolism, mechanical heart valves, and atrial fibrillation. Anti-platelet therapy with aspirin and thienopyridine derivatives (e.g. clopidogrel) for varying durations are required in patients with bare metal or drug eluting coronary stents. These patients may present for elective or emergency surgical procedures. Continued use of medications is associated with protection against thromboembolism (and associated morbidity and mortality) at the cost of increased risk of surgical bleeding. Perioperative management involves balancing the risks of surgical bleeding and thromboembolism.

Minor surgical procedures can be carried out without interruption of pre-operative anticoagulants, while major surgeries are associated with significant blood loss if these drugs are continued. It is critical to assess whether planned surgical procedure necessitates interruption of antithrombotic/anti-platelet therapy and, if so, whether the patient will need 'bridge' therapy (LMWH) to minimize the risk of thromboembolism during the time the antithrombotic effect is sub-therapeutic. It may also be necessary to postpone elective surgeries in patients where a suitable 'Bridge' has not been identified and in whom antithrombotic therapy is critical; premature discontinuation of dual anti-platelet therapy with a intention to minimize surgical bleeding in patients with coronary stents has been associated with stent thrombosis, myocardial infarction and death.^{13,14} When such patients are encountered in clinical practice, ASRA practice advisory-2010 has to be followed.¹⁵

RESTRICTIVE BLOOD TRANSFUSION/TRANSFUSION TRIGGER¹⁶: Various trials, including a large randomized controlled trial in 25 Canadian intensive care units the TRICC (transfusion requirements in critical care) trial, demonstrated that a restrictive transfusion strategy with goal Hb levels of more than 7 g/dL was not associated with higher 30-day mortality compared to a liberal transfusion strategy with goal Hb levels of more than 10 g/dL. But morbidity increased with each gram decrement postoperatively when the Hb concentration was less than 7 g/L. With this background, published guidelines generally agree that transfusion is not beneficial when the Hb > 10 g/dL, but might be beneficial when the Hb < 6–7 g/dL. In patients with cardiovascular disease, perioperative myocardial ischemic episodes are related to Hct concentrations less than 28%. Thus the transfusion trigger should be different (Hb ≤ 8 g/dl) for elderly and patients with major systemic illness.

A newer concept of "physiologic" transfusion triggers of O₂ extraction ratio to guide red cell transfusion has emerged. "Transfusion triggers" based on absolute Hb or Hct levels are considered almost an obsolete concept. O₂ER > 50% is generally considered a sign of impending exhaustion of the compensatory mechanisms (dysoxia) and impending decrease of VO₂ (O₂ uptake). This threshold might be used to consider the transfusion of RBC. O₂ER is derived entity using the formula $O_2ER = (SaO_2 - SvO_2)/SaO_2$.

REVIEW ARTICLE

REDUCED INTRA-OPERATIVE BLOOD LOSS: Pharmacological agents: These drugs reduce blood loss and decrease the likelihood of blood transfusion:

- 1. Antifibrinolytic drugs (EACA, Tranexamic acid, Aprotinin):** These drugs act by inhibiting the breakdown of blood clots. Epsilon amino caproic acid (dosage: 100-150mg/kg followed by 25 mg/kg/hour) and tranexemic acid (dosage: 10 mg/kg followed by 1 mg/kg/hour) are lysine analogues. They inhibit plasminogen by binding to lysine binding sites on plasminogen molecule. They also cause sparing of platelet function by inhibiting the deleterious effects of plasmin on platelets. Tranexemic acid is 10 times more potent than EACA. Aprotinin (no longer available in clinical practice) also limits the action of plasmin but by binding to serine protease. Studies have shown that perioperative use of antifibrinolytics reduce the need for blood transfusion.
- 2. Desmopressin (DDAVP):** It is a synthetic analogue of Arginine Vasopressin. It induces the release of stored factor VIII and von Willebrand factor from endothelial cells. It is effective in controlling the bleeding in patients with mild haemophilia A, von Willebrand's disease and in haemophilia carriers. It is also effective in controlling and preventing bleeding in patients who have congenital platelet disorders or platelet dysfunctions due to renal disease. Dosage- 0.3µg/kg IV, s/c or intra nasal. It increases the levels of factor VIII and von Willebrand's factor by 3-5 folds.

Figure 2

REVIEW ARTICLE

Figure 2: Algorithm for preoperative investigation and correction of anemia. (Reproduced with permission from National Blood Authority Australia, Patient blood management guidelines: Module 2 – Perioperative, Available at www.nba.gov.au/guidelines/module2/index.html).

3. **Recombinant factor VIIA (rFVIIA):**¹⁷ It is a vitamin K dependant glycoprotein. It binds to tissue factor and activates of factor X on the platelets surface. This helps in the formation of prothrombin complex thrombin formation. FDA has approved its use for the treatment of severe bleeding in haemophilics with factor inhibitors, patients with factor VII deficiency, patients with congenital platelet dysfunction and also in traumatic/surgical haemorrhage not responding to other routine treatments. It is also effective to control the bleeding in patients with liver disease, GI bleeding and in patients receiving massive blood transfusion. Dosage: 90 µg/kg I.V. for hemophiliacs and 15-180 µg/kg I.V. for severe intractable bleeding.

SURGICAL TECHNIQUES: Careful planning and preference minimally invasive surgical procedure by an experienced surgical team is ideal for reducing the surgical blood loss. Numerous techniques and advanced instruments could help in efficient control of bleeding. A few are enlisted below:

- **Minimally invasive surgery:** Minimally invasive surgeries such as laparoscopic/robotic technique may result in less blood loss from incisional bleeding and overall surgery. Usal and colleagues¹⁸ have shown that preoperative blood type and screening are not necessary in patients undergoing laparoscopic cholecystectomy; they found transfusion rates were 0.46% (laparoscopic) versus 5.47% (open), demonstrating that need for red blood cell transfusion is decreased by the laparoscopic approach. Various studies have shown that blood loss was minimal with laparoscopic splenectomy compared with open splenectomy.^{19, 20, 21} With use of hemlocks, fibrin glue, advanced laparoscopes, and meticulous technique in carefully selected patients; it is possible to minimize blood loss.
- **Endovascular procedures:** Endovascular procedures like vascular embolization and intravascular stenting have revolutionized the treatment of aneurysms, arterio-venous malformations and atheromas. Vascular embolization is done in the feeding arteries of highly vascular tumors, varicosities or arterio-venous malformations with thrombogenic particulate material like foam, or glue or alcohol to decrease blood loss during surgery. The ability of endovascular alternatives to reduce blood loss compared to standard, open vascular surgical operations is still uncertain. Although some authors have reported less blood loss with endovascular techniques, others have reported similar amounts or more. This may be due to learning curves that have prolonged endovascular procedures allowing more blood loss.
- **Tourniquet:** It is useful for upper and lower limb surgeries as it cuts of the arterial and venous circulation to the limbs. A maximum of up to 3 hours duration and tourniquet pressure not exceeding 250 mmHg for upper limb and 300 mmHg for lower limb is considered safe. Ta-Wei Tai et al ²² have found that use of tourniquet in knee replacement surgery, is associated with smaller decreases in Hb and Hct.
- **Adrenaline infiltration:** Many studies^{23, 24, 25} have shown that use of dilute adrenaline in strengths between 1:200,000 to 1:500,000 are associated with reduced intra-operative blood loss, less reduction in post-operative Hb and less transfusion rates without complications. It is especially useful for scalp, facial and ENT surgeries.

REVIEW ARTICLE

- **Haemostasis:** Use of electro cautery, laser, CUSA (ultrasonic scalpel), vascular clips, vessel sealants, harmonic scalpel is associated with effective haemostasis, reduced micro and macro vascular bleeding.
- **Gamma knife surgery:** This technique uses doses of radiation to kill cancer cells and shrink tumors, delivered precisely to avoid damaging healthy brain tissue. It is proved useful in arterio-venous malformation and associated with lesser blood loss compared to conventional approach.
- **Local use of fibrin sealants and glues:** Fibrin glue is made up of fibrinogen and thrombin that are applied to the tissue sites to glue them together and reduce blood loss. Fibrin sealant mimics the final stage in the coagulation cascade. Fibrin sealant has been used in vascular, cardiac and liver surgery and in situations where even small amounts of bleeding can be problematic (e.g. middle ear surgery). Everts PA et al ²⁶ have shown that peri-operatively applied platelet gel and fibrin sealant may reduce the incidence of allogeneic blood transfusions and complications associated with total knee arthroplasty.
- **Others:** Topical haemostatic drugs used to achieve haemostasis include bone wax, ostene, acrylates, ferric subsulfate solution, gelatin (gelfoam, gelfilm), microfibrillar collagen, poly-n-acetyl glucosamine, kaolinite, pro QR powder, thrombin etc.

CONTROLLED HYPOTENSION²⁷: Studies have demonstrated a 2-4 fold reduction in intraoperative blood loss if mean arterial pressure is maintained between 50 to 60 mmHg in young and healthy individuals. It also facilitates better surgical exposure and outcome. This can be achieved using either general or regional anesthesia. During general anaesthesia, inhalation agents, propofol, dexmedetomidine, direct vasodilators, Ca⁺² channel blockers, beta blockers and various other drugs are used to produce controlled hypotension. Use of regional anaesthesia reduces the need for blood transfusion in peri-operative period by 50%. It has an added advantage of lowered incidence of deep venous thrombosis and pulmonary embolism. But the use of controlled hypotension is restricted in patients with major systemic illness as the vital organ perfusion is dependent on maintaining adequate blood pressure.

IMPORTANCE OF POSITIONING: Coordinated optimal intra-operative patient positioning with good surgical access, associated with minimal physiological disturbances and reduced blood loss is key to blood conservation and to reduce the need for blood transfusion. Numerous studies carried out to assess effect of patient posture on blood loss demonstrated that lateral, reverse Trendelenburg or an appropriate prone positioning reduced the blood loss.^{28,29,30} Surgical site (both during and after the procedure) should be maintained above the level of the heart to reduce the mean capillary pressure and to facilitate venous drainage. In case of neurosurgical procedures, excessive neck flexion is associated with compression of major neck veins their by increasing venous pressure with increased blood loss. In contrast, sitting or head raised position leads to negative pressure in the venous sinuses causing life threatening venous embolism.

AUTOLOGOUS BLOOD TRANSFUSION³¹: In an effort to minimize reliance on blood transfusion, various techniques and devices are being used in the past few decades. But not all patients are suitable for autologous blood transfusion (Table 2). There are three techniques of autologous blood transfusion:

REVIEW ARTICLE

- a) Preoperative autologous donation:** A patient donates one to five units of blood, once a week (or as often as every 72 hrs); in advance (starting 28 days prior to surgery) of a planned surgical procedure that has a high likelihood of blood loss. The donor should have Hb>11g/dl and can donate up to 10.5ml/kg during each donation. During this month long procedure, patient receives iron, vitamin supplements and sometimes erythropoietin. Blood is stored at 2-8 degrees for up to 35 days and is physically separated from homologous or cross matched blood. If the storage period likely to exceed the limit, the oldest unit can be re transfused (leap-frogging), but the donations can continue. Donor units do not need to undergo any infectious disease testing. Studies³² show that patients who donate autologous blood preoperatively are less likely to receive allogeneic blood but more likely to undergo any transfusion with autologous and/or allogeneic blood. This is due both to a lower Hct in patients donating blood preoperatively and a more liberal transfusion policy associated with autologous blood donation. The risk of infection from bacterial contamination of blood products, clerical errors, volume overload and wastage of unused blood are problems that still exist with this procedure. In addition, preoperative autologous blood donation, processing and storage are considerably more expensive than allogeneic blood transfusion.

Contraindications
1. Evidence of infection and risk of bacteremia
2. Scheduled surgery to correct aortic stenosis
3. Unstable angina, High-grade left main coronary artery disease
4. Active seizure disorder
5. Myocardial infarction or cerebrovascular accident within 6 months of donation
6. Patients with significant cardiac or pulmonary disease who have not yet been cleared for surgery by their treating physician
7. Cyanotic heart disease
8. Uncontrolled hypertension
Table 2: Contraindications to participation in autologous blood donation programs

- b) Acute normovolemic hemo dilution:** This was first used as a substitute for allogeneic blood transfusion in 1970. It involves removing a portion of patient's blood (2 to 3 units) immediately prior to the surgery and simultaneous replacement with a crystalloid (1: 3 ratio) or colloid (1: 1 ratio) to maintain normovolemia. The blood should be collected in standard blood bags containing anticoagulant on a tilt-rocker with automatic cut off via volume sensors. This collected blood is stored at room temperature (for a maximum of 8 hrs) at the patient's side and given back after completion of surgery or when transfusion is needed. The rationale behind this method is that during surgery, patient loses diluted blood and later, the replacement will be with the blood of higher Hct. There is an added advantage of preserving haemostatic factors as there is little deterioration of platelets and coagulation factors. Numerous retrospective and prospective studies have concluded that acute normovolemic hemodilution reduced the need for allogenic blood transfusion in various major surgeries. The prerequisites for this technique is that patient's Hb should be >12gm%. This technique is advantageous as there is no risk of

REVIEW ARTICLE

ABO incompatibility. Testing and storage requirements along with the complications associated with them are absent.

- c) Intra and postoperative cell salvage:** In this method the shed blood during the surgery or postoperative period (from surgical field and drains) is collected in a closed suction device. It is then filtered and transferred into an anticoagulant containing reservoir. If the immediate replacement is required the unprocessed blood can be administered from this reservoir to the patient. But for haemodynamically stable patients this blood may be centrifugally washed to remove debris and contaminants (processing of blood) before reinfusion. It reduces the need for allogenic blood transfusion especially in patients undergoing high blood loss surgical procedures such as cardiothoracic, vascular and major orthopaedic surgeries. Salvaged blood provides not only red blood cells, but more importantly, plasma proteins including clotting factors and platelets. The oxygen-transport properties and survival of recovered RBCs are equivalent to those of stored allogenic RBCs. Cell washing devices can provide the equivalent of 12 units of banked blood per hour to a massively bleeding patient. Decreased risk of blood borne infections and transfusion reactions are the advantages. It is safe in patients with rare blood groups with multiple antibodies. Requirement of costly setup, staff training and risk of bacterial contamination are the main disadvantages

BLOOD SUBSTITUTES: Blood substitutes (Also known as artificial blood or blood surrogates) are the substance used as alternatives to autologous blood transfusion which performs some of functions of blood notably oxygen transport and haemostasis. There are several advantages of these products (Table 3).

Advantages
1. Useful for rapid resuscitation in trauma and hemorrhagic shock
2. Can be used in Jehovah's Witnesses.
3. Can be stored for much longer (1-3 years) at room temperature.
4. Allow for immediate full capacity oxygen transport
5. Devoid of transmission of HIV /AIDS
6. Synthetic oxygen carriers by increasing the effectiveness treatments like photodynamic therapy and chemotherapy may also show potential for cancer therapy. ³³
Table 3: The possible advantages of blood substitutes over human blood

RED CELL SUBSTITUTES: Oxygen-carrying substitutes (artificial Hb/ oxygen therapeutics)- Currently oxygen carrying substitutes can be classified as Hb-based oxygen carriers (HbOC) and perfluorocarbon-based oxygen carriers (PFBOC).^{34,35}

- Hb-based oxygen carriers:** These substitutes use Hb from human, animal or recombinant technology sources.³⁶
 - Human source – from stored blood which has reached its expiry date. On an average 1 unit of Hb solution can be obtained from 2 units of discarded blood.
 - Bovine source - Forty units of Hb solution can be obtained per slaughtered cow.

REVIEW ARTICLE

- Recombinant technology- obtained by inserting the gene for human Hb into bacteria and then isolating the Hb. One unit of Hb solution can be produced from 750 L of Escherichia coli culture.

Hb obtained from any of the above sources needs purification and modification in its chemical structure before transfusion.³⁷ Due to the presence of residual red cell stroma in the products, use of un-processed Hb is shown to cause renal failure, intravascular coagulopathy, and vasoconstriction.

Free Hb breaks down into dimer and monomer which freely diffuse into the renal tubules and the sub-endothelium leading to renal toxicity. To decrease this toxicity artificial Hb needs to be modified so as to maintain its tetrameric structure. Surface-modified Hb, cross-linked Hb and polymerized Hb are some of the modified variety. Polymerized Hb is the only artificial Hb to date that has not triggered significant vasoconstriction after infusion. Its plasma half-life varies from 18–24 hrs and shelf life is about 12-18 months. It is marketed as Hemosol, Hemopure, and OxyVita etc.

RECOMBINANT HB: Fear of animal pathogen transmission with use of artificial Hb derived from animals lead to development of recombinant Hb with specific conformational and functional characteristics that render them suitable for application in different clinical situations. In contrast to chemically altered haemoglobin, recombinant Hb represents homogeneous and stable polymer. Studies in mice have shown that recombinant Hb retains physiologically relevant oxygen and haeme affinity, stability toward denaturation and oxidation, and effective oxygen delivery as indicated by reduced cerebral ischemic damage.³⁸

ENCAPSULATED HB: It is a form of oxygen carrier in which Hb is packed inside an artificial neohemocyte ("new blood cell"). Liposome-encapsulated Hb (LEH) has been found to be an effective oxygen carrier, without vasoconstriction³⁹. However adverse immune interactions occur with the liposome. This product is still in experimental stage.

2. Perfluorocarbon-based Substitutes: PFCs are synthetic hydrocarbons with halide substitutions and are about 1/40th the size of a red blood cell. These solutions have the capacity to dissolve up to 50 times more oxygen than plasma. They do not mix well with blood and must be emulsified with lipids or oils. This liquid is then mixed with antibiotics, vitamins, nutrients and salts, producing a mixture that contains about 80 different components, and performs many of the vital functions of natural blood. Their small size can enable PFC particles to traverse capillaries through which no RBCs are flowing. In theory this can benefit damaged, blood-starved tissue, which conventional red cells cannot reach.⁴⁰

All these products are still in the experimental stage and require clinical validation. Adverse reactions associated with Hb-based products include elevations in blood pressure, gastrointestinal dysmotility, and mild temporary increases in pancreatic enzymes. Hb-based blood substitutes may increase the odds of deaths and heart attacks.⁴¹ Though advantageous over Hb-based products (Table 4), risk of oxygen toxicity exists with prolonged administration PFC's. They are short acting, expensive, can interfere with laboratory testing.

REVIEW ARTICLE

Advantages of Perfluorocarbon-based substitutes
<ul style="list-style-type: none"> • Efficient oxygen delivery and carbon dioxide removal
<ul style="list-style-type: none"> • More oxygen carriage relative to Hb size
<ul style="list-style-type: none"> • Large amount can be manufactured to meet the demand.
<ul style="list-style-type: none"> • Heat-sterilization possible.
Table 4: Advantages of Perfluorocarbon-based substitutes over Hb-based products

PLATELET SUBSTITUTES: Ideally, a platelet substitute would have the following properties: effective hemostasis with a significant duration of action, no associated thrombogenicity, no immunogenicity, and sterility, long shelf life with simple storage requirements, and easy preparation and administration.³⁹ Different forms of platelet substitute are now under developmental stage including infusible platelet membranes (IPM), thrombospheres, and lyophilized human platelets.

FUTURE OF BLOOD SUBSTITUTES³⁹: Lot of clinical studies is underway to find physiologically acceptable alternative to blood. As of now there are no FDA approved blood substitutes for clinical use. Potential techniques in this research of blood substitutes include stem cell technique, dendrimers, biodegradable micelles, respirocyte, placental umbilical cord blood, hemerythrin etc.

BLOOD CONSERVATION STRATEGIES IN CRITICALLY ILL PATIENTS: In addition to above mentioned strategies, one has to pay attention to reducing blood loss associated with diagnostic testing. This is an important cause of blood loss in critically ill patients as their transfusion trigger is high in comparison to healthy subjects. Indwelling central venous and arterial catheters contribute to increased iatrogenic blood loss due to ease of sampling and need of discarding the first few ml of blood infusate mixture obtained during the collection of blood sample from the line. Studies from 1980s reported a mean blood loss per patient per day of 377 ml in cardiothoracic ICU, 240 ml in surgical ICU and 41.5 ml in medical ICU. Steps that can be taken to reduce this blood loss are:

1. Use of smaller volume (pediatric) blood collection tubes. It can reduce the blood volume used by up to 47%.
2. Elimination of discarding of blood while collecting blood from indwelling catheters. The use of three way stop cock and reinfusion of infusate- blood mixture after sampling reduces the blood loss by up to 50%.
3. Use of bedside testing (microanalysis), as these tests often require less than 0.5 ml blood.
4. Use of automated closed arterial systems also reduces the blood loss during diagnostic testing.
5. Use of bedside monitoring of SpO₂ and EtCO₂ instead of frequent blood tests.
6. Restricted blood sampling i.e. elimination of routine test orders, tests to be done only when specifically indicated and use of single blood sample for multiple lab tests.

SUMMARY: Blood transfusion is associated with increased mortality and morbidity necessitating re-evaluation of our current transfusion practices. A well laid out pre-operative plan, integrating various techniques of blood conservation during the peri-operative period will help in reducing and altogether eliminating the need for allogenic blood transfusion, which may contribute to improved overall outcome of the surgical patients.

REVIEW ARTICLE

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REVIEW ARTICLE

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REVIEW ARTICLE

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