Blood Conservative Strategies during Surgery

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Abstract

Objectives : Perioperative blood conservation . Methods : Different methods mentioned in the article are Autologus blood transfusion , perioperative blood salvage , Acute normovolaemic haemodilution , Acute hypervolaemic haemodilution . Drugs like Tranexemic acid , Desmopressin , Aprotinin , Lysine analogues ,Erythropoetin and hypotensive anaesthesia . Conclusion : We can avoid unnecessary blood transfusion during perioperative period by following the above mentioned methods after evaluating benefits against the risk of the patients .

Keywords — *Blood conservation,autologous blood transfusion*

I. INTRODUCTION

We must remember that BLOOD IS A TISSUE, we should not waste or misuse it. Secondly we also know that tissue transplantation, is not without risks, especially the potential hazards of blood transfusion. Hence, blood has to be conserved. Anaesthesiologists play an important role in blood conservation.

II. METHODS OF BLOOD CONSERVATION [1]

- Meticulous surgical haemostasis.
- Proper pre-operative evaluation and correction of pre-existing anaemia.
- Acceptance of lower transfusion triggers even in critically -ill patients.7-8g/dl hb,23-25%hct in patients without co-morbidities.
- Employing techniques such as induced hypotension and appropriate positioning.
- Pharmacologic agents like desmopressin, anti-fibrinolytics to reduce blood loss.
- rFVIIa
- erythropoetin
- fibrin glues
- preoperative therapeutic embolisation of vascular tumours
- Last but not the least **AUTOLOGOUS BLOOD TRANSFUSION**[2]

a. -Preoperative autologous blood donation [PABD]
b. -intra & postoperative blood salvage
c. -Acute Normovolaemic hemodilution.
d. –acute hypervolaemic hemodilution.

III. BLOODLESS MEDICINE

it is a team approach that reduces blood loss and employs the best available alternatives to allogeneic Transfusion therapy while focusing on the provision of the best possible medical care to all patients.

Definition:

Autologous blood transfusion is the collection, storage &re-infusion of patient's own blood. Allogeneic blood, on the other hand is collected from someone other than the patient.

IV. CONTRA-INDICATIONS TO PARTICIPATION IN AUTOLOGOUS BLOOD DONATION PROGRAMME

1. Evidence of infection and risk of bacteraemia
2. Scheduled surgery to correct aortic stenosis.
3. Unstable angina
4. Active seizure disorder
5. Myocardial infarction and Cerebrovascular accidents within 6 months of donation
6. Patients with significant cardiac or pulmonary disease
7. High grade left main coronary artery disease
8. Cyanotic heart disease
9. Uncontrolled hypertension.

IV. PENNSYLVANIA HOSPITAL ADULT TRANSFUSION GUIDELINES

A. Red blood cells

1. Blood loss >30% of blood volume (>1500 ml), severity evidenced by:
a. tachycardia;
b. reduced systolic and/or diastolic pressures.
2. Hb <7 g/dL with symptoms of anemia.
3. Hb <8 g/dL in high-risk patients (either of following):
a. cardiovascular disease;
b. chronic pulmonary disease.
4. Peri-operative blood loss, with:
a. Hb <6 g/dL; or
b. Hb 6-10g/dL and risk of complications due to inadequate oxygenation
(judgment of surgeon or anesthesiologist).
5. Sickle cell disease with acute chest syndrome or other special circumstances.

B. Platelets

1. Prophylaxis: <10,000/mm3.
2. Active bleeding: <50,000/mm3.
3. Perioperative:
a. <50,000/mm3 - major invasive procedure;

b. <100,000/mm3 - CNS or eye surgery;
c. <100,000 /mm3 - post-cardiopulmonary bypass with bleeding or pre-op
aspirin effect;
d. <20,000/mm3 - bedside invasive procedure.

V. BENEFITS OF AUTOLOGOUS BLOOD TRANSFUSION [3,4]

TO THE DONOR PATIENT-Serological compatibility.
No risk of infections-hepatitis, HIV, CMV, malaria.
Avoid allo-immunisation-no resultant compatibility problem with future transfusions or pregnancy.
minor transfusion reaction decreases from incompatible WBCs
Potential benefit of Haemodilution on blood flow& decreased incidence of postop.thrombosis.
Acceptable alternative to Homologous blood transfusion [HBT] to certain religious sects who otherwise refuse transfusions [Jehovah's Witness].

TO TRANSFUSION CENTRES [5]
Ready availability of blood for patients for whom it is difficult to obtain homologous blood.
Blood supply in remote/ isolated areas & down base in community.

SURGICAL PROCEDURES [6]
1. coronary artery bypass
2. major vascular surgery
3. primary & revision hip replacement
4. total knee replacement
5. major spine surgery
6. selected neurosurgical procedures [AV malformations]
7. hepatic resection
8. major urosurgical procedures

[1] TECHNIQUE [7]-The decision to collect blood preoperatively should be based on a discussion between doctor &patient regarding procedure's risks & benefits, after which the patient can be referred to a blood collection facility where patient is evaluated for eligibility of autologous donation.
[2] Patients can donate blood as frequently as every 3 days, although once a week is more than enough. Oral iron supplementation with ferrous sulphate or gluconate 325 mg t.d.s is given. The optimal donation period begins 4-6 weeks before surgery &the last donation should not be collected later than 72 hrs before surgery for restoration of blood volume.[8]
[3] Recombinant erythropoietin in a total dose of 1000 units /kg during the three week period of PABD can also be given however the FDA does not approve its use in autologous donation.

HANDLING & STORAGE [6]Autologous blood component therapy requires a special handling & segregated processing & storage than allogeneic units. It increases personnel time for collecting blood from a patient with complex medical diseases as opposed to healthy donors.

Blood is mixed with CPDA-1 as preservative. ADSOL or nutricel can be added to increase the shelf life to 42 days. If surgery is delayed beyond 42 days, blood can be frozen.

Predonated units are conspicuously labeled as autologous & patient donor's identification number & tag are attached. ABO-Rh grouping is confirmed.

Blood is also tested for anti-HIV, HBsAg, HBC & syphilis. If found positive, the FDA recommends that it should be discarded [9]. However donor may be transfused with these units if permitted by the hospital facility.

RELEASE OF UNUSED BLOOD OR CROSSOVER is a controversial issue. Ideally autologous blood should be discarded because donors often do not meet the health criteria required for allogeneic blood donation. Hence it would be less safe than voluntary donors. Secondly by the time it is released it has a very short shelf-life [6].

2. PERIOPERATIVE BLOOD SALVAGE[10]

Perioperative blood salvage is the collection & re-infusion of blood during & immediately after surgery. It is either -intra-operative or peri operative

V. INTRA-OPERATIVE BLOOD SALVAGE

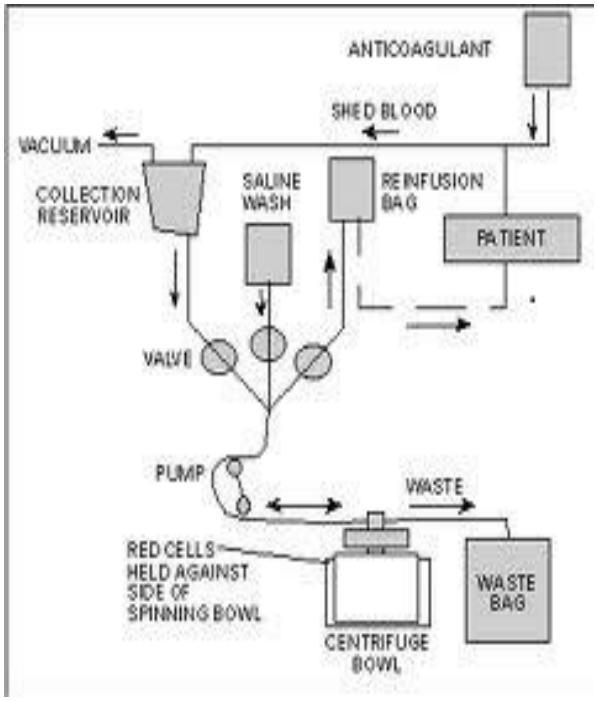
The amount of RBCs recovered during surgery varies with the procedure & may be 50% of the blood lost. This may be of significant benefit, especially when combined with other autologous transfusions.

Technique

Blood salvaged intra-operatively can be transfused directly after collection or preserved.(Figure 1) Washed blood has the theoretical advantage of reducing infusion of free hemoglobin, tissue debris etc. Small amounts <2 lts can be transfused without processing. [20]

Semi-continuous flow centrifugation devices

this disposable equipment consists of an anti-coagulation & aspiration assembly, a reservoir with filter, a centrifuge bowl, a waste bag & tubing.
Suction systems that collect blood without washing are also available. These machines are relatively inexpensive & technically easy to use.



VI. CHARACTERISTICS OF PROCESSED BLOOD

a. Haematocrit—50-60%
b. RBCs—oxygen carrying capacity & survival – superior
c. Ph—alkaline [4]
d. Na+/k+ levels are normal
e. Plasma hemoglobin, tissue necrosis factor, & plasma elastase –increased [5]
f. Coagulation proteins, antithrombin3 are removed during wash cycle

Catecholamine are not removed during washing

A. Complications

1. air & fat embolism
2. pulmonary dysfunction due to infusion of debris
3. coagulopathy
4. renal dysfunction
5. sepsis
6. dissemination of malignant cells

B. Postoperative blood recovery

Collected from mediastinal & joint drains without washing as it is defibrinogenated & does not require anticoagulant.

1. Cardiac surgery—blood within the mediastinum undergoes coagulation & fibrinolysis &no anticoagulation is required before ABT. Fibrin degradation products are detected in unwashed blood—misdiagnosis of DIC & unnecessary treatment. Serum creatine kinase, serum glutamic oxaloacetic acid &lactic dehydrogenase enzymes are also elevated—false diagnosis of MI.
2. Orthopedic surgeries—recovered blood contains complement activators. It also contains high levels of cytokines [tumor necrosis factor-α, interleukin-1α, interleukin 6, and interleukin 8, bone fragments, fat & other debris, including methylmethacrylate have also been isolated.
3. Traumatic hemothorax-blood that collects in the thoracic cavity following blunt & penetrating trauma can be collected & transfused using chest drainage devices that have been adopted for blood salvage.

C. *Acute normovolaemic haemodilution [11] [anh]*

Definitions:

Acute Normovolaemic Haemodilution—is the removal of blood with the simultaneous infusion of solution/s to maintain intravascular volume prior to surgical blood loss.

or

Removal of blood from the surgical patient immediately before or after induction of anesthesia, replacement with asanguinous fluid and later with withdrawn blood.

Acute limited or moderate normovolemic haemodilution---when haematocrit is reduced to approximately 28%.

Acute extreme haemodilution ---when haematocrit is reduced <20%.

Augmented acute normovolaemic haemodilution---administration of oxygen carrying RBC substitute in addition to other asanguinous fluid.

Advantages:

1. Reduces need for allogeneic blood.
2. Avoids potential complications of blood transfusion.
3. No clerical error.
4. No biochemical alterations.
5. Room temperature so platelet function preserved.
6. No hypothermia.
7. Improvement in tissue perfusion due to decreased viscosity.
8. Patients with cardiovascular & neurologic disorders can undergo this if monitored.
9. Can be used in sepsis & malignancy.
10. Blood withdrawn is reinfused hence iatrogenic anaemia or blood wastage does not occur.

VII. PATIENT SELECTION

For any patient with an adequate Hb who is expected to lose >25% of expected blood volume, Hb>11g/dl or Hct>25%.can be applied for adults as well as children.

TECHNIQUE: The amount of blood withdrawn depends on the patient's expected blood volume [EBV], pre-op Hct [Ho] &the lowest Hct [Hf] desired

$$V=EBV\ [(Ho)-(Hf)]/Havg$$

E.g.---EBV=5lt,Ho=45%, Hf=30%, Havg=37.5%

V=5(45-30)/37.5=2000ml

Haemodilution is done in the operating room or induction room with or without anaesthesia. Crystalloid [3:1] is infused as blood is withdrawn.

Blood is withdrawn from a large peripheral or central vein or radial artery. Blood is collected in blood bags containing CPD anticoagulant. Autologous blood- collection kits are also available.

Patient is monitored for haemodynamic stability &chest is auscultated for rales. Each unit is labelled with the patient's name &hospital number & time of blood collection. It is kept in the same operating room at room temperature, unless more than 8hrs will elapse before transfusion. Then blood is refrigerated to be used within 24hrs or discarded. The units are reinfused in the reverse order of collection so that the first unit which has highest hct is and most clotting factors is administered last.

A. Physiologic effects-

1. Decrease in arterial O2 content
2. Increase in cardiac output
3. Decreased viscosity-increased venous return, decreased peripheral resistance & reduced afterload
4. Increased myocardial contractility
5. Increased sympathetic stimulation in anaesthetized patient's heart rate may not increase, but stroke volume increases.

B. Complications

1. Myocardial ischaemia & cerebral hypoxia
2. Coagulopathy related to dilution of clotting factors & increased bleeding
3. Peripheral oedema-common with crystalloids
4. Pulmonary oedema

VIII. ACUTE HYPERVOLAEMIC HAEMODILUTION [AHH][12]

AHH involves rapid infusion of cell-free substitutes without withdrawal of blood, the purpose being dilution of blood & reduction in hct & thereby decreasing red cell loss in shed blood. The volume expansion increases maximum tolerable blood loss for set acceptable hemoglobin.

Compared to ANH it is easier, less time consuming &does not require extra personnel. A study was done in LTMC, Mumbai using 3.5% polygeline for this purpose.

15ml/kg of the diluent gives approximately21% expansion of circulating volume. This reduces the hb, hct &RBCs by 23-25%.

Maximum benefit of this procedure is seen in patients with blood loss of 500-1500ml.

A. Blood substitutes

Blood substitutes are solutions that can be used in resuscitation emergencies or during surgery when rapid intravascular volume expansion is needed in view of acquired red cell losses. The three main types of products in development are primarily based on cell-free hemoglobin solutions called hemoglobin-based oxygen carrying solutions (HBOCs) or perfluorocarbon emulsions. None of the agents are currently approved for clinical use, but are in different stages of clinical development.

B. Desmopressin

Desmopressin acetate (1-deamino-8-D-arginine vasopressin- DDAVP), is a synthetic analogue of vasopressin decreased vasopressor activity. Desmopressin therapy causes a two to twenty fold increase in plasma levels of factor VIII, and stimulates vascular endothelium to release the larger multimers of von Willebrand factor (vWF)

C. Lysine analogs

Epsilon-aminocaproic acid (EACA, Amicar) and its analogue, tranexamic acid (TA) are derivatives of the amino acid lysine and have been reported in clinical studies of cardiac surgical patients. Both of these drugs inhibit the proteolytic activity of plasmin and the conversion of plasminogen to plasmin by plasminogen activators. Plasmin cleaves fibrinogen and a series of other proteins involved in coagulation.

D. Tranexamic acid [13, 14]

Tranexamic acid is a synthetic derivative of the amino acid lysine that exerts its antifibrinolytic effect through the reversible blockade of lysine binding sites on plasminogen molecules. Dose- 10mg/kg body weight to a maximum of 30mg/kg.

E. Aprotinin [15]

Aprotinin is a serine protease inhibitor isolated from bovine lung that produces antifibrinolytic effects, inhibits contact activation, reduces platelet dysfunction and attenuates the inflammatory response to CPB.

F. Recombinant factor viia[16]

Recombinant RECOMBINANT FACTOR VIIa factor VIIa (rFVIIa) has been shown to induce hemostasis in hemophilia patients with inhibitors against factor VIII or factor IX independent of factor VIII/factor IX.

Dose-a nonweight dosage strategy in which a4.8mg vial administered to an adult patient weighing50-100kg represents a dose of100mcg/kg-50mcg/kg.

G. Fibrin sealants.[17]

Surgical hemostatic agents derived from human plasma that reproduce the final steps in the coagulation pathway and form a stable fibrin clot. Used in broad range of surgical procedures to assist hemostasis, including cardiovascular, hepatic, and splenic surgery, gastrointestinal hemorrhage, skin grafting, and dental extractions in anticoagulated patients.

H. Fibrin glue-

Derived from a source of fibrinogen and fXIII,in which fibrinogen is mixed with a solution of thrombin and applied to surgical field. Potential hazards of allogeinic transfusion.

I. Erythropoietin [18,19]

Erythropoietin, a glycoprotein hormone, is synthesized predominantly in the kidney and secreted by renal cortical interstitial cells in response to tissue hypoxia. Erythropoietin is the main regulator of the production of red blood cells.

J. Hypotensive anaesthesia-

Wherever possible, regional anesthesia can be employed. Combined spinal and epidural anaesthesia using clonidine or dexmedetomedine has been widely accepted for hip and knee arthroplasties, urologic and other hip surgeries.

Table 1: Summary of clinical recommendations and evidence base for blood conservation strategies to reduce the need for blood transfusions in critically ill patients

Strategy	Mechanism of action	Potential benefits and advantages	Evidence base
To reduce acute blood loss			
Antifibrinolytic agents			
Tranexamic acid or epsilon aminocaproic acid	Improved hemostasis	• Reduced risk of recurrent bleeding and death associated with gastrointestinal bleeding†	Meta-analysis
		• Reduced risk of perioperative bleeding and need for reoperation in cardiac surgery patients	Meta-analysis
		• Under investigation for use in trauma patients	
Aprotinin	Improved hemostasis	• Reduced risk of perioperative bleeding and need for reoperation in cardiac surgery patients	Meta-analysis
Desmopressin	Improved hemostasis from increased factor VIII and von Willebrand levels	• Reduced risk of bleeding in patients with congenital coagulation defects (platelet dysfunction, von Willebrand's disease, mild hemophilia A) and those with renal failure	Observational studies
Recombinant activated factor VII	Improved hemostasis	• Possible benefit in selected cases refractory to standard surgical and medical treatment†	Case reports; expert opinion
Artificial oxygen carriers (modified hemoglobin substitutes, perfluorocarbons)	Increased oxygen transport without blood transfusion; increased ability to perform acute normovolemic hemodilution	• Possible reduction in need for transfusion†	RCT
		• Prolonged shelf-life	
		• Products can be stored at room temperature	
		• No risk of disease transmission	
		• No immunologic effects	
Postoperative blood recovery techniques (cell salvage)	Return of blood collected in surgical drains	• Reduced need for perioperative blood transfusion in orthopedic surgery but not in cardiac surgery	Meta-analysis
To prevent subacute anemia			
Reducing blood loss associated with diagnostic testing		• Increase in hemoglobin level	RCT
Closed blood sampling techniques	Reduction of iatrogenic blood loss from diagnostic testing	• Elimination of "discard" blood loss before testing in patients with in-dwelling central catheters	RCT
		• Reduced risk of bacterial contamination of catheter hubs and blood-stream infections	Expert opinion
Small-volume sample tubes	Reduction of iatrogenic blood loss from diagnostic testing	• Reduced blood loss	RCT
Point-of-care microanalysis	Reduction of iatrogenic blood loss from diagnostic testing	• Short turnaround time for test results	Expert opinion
		• Reduced personnel time	
Erythropoietin	Increased production of red blood cells in bone marrow	• Increase in hemoglobin level and possible reduced need for transfusion	RCT; meta-analysis
		• Possible reduction in mortality among trauma patients†	RCT subgroup analysis
Restrictive red blood cell transfusion trigger*	Raised hemoglobin threshold for red blood cell transfusion	• Reduced need for blood transfusion without increase in morbidity or mortality in most critically ill patients	RCT

Note: RCT = randomized controlled trial.
*For example, a change in hemoblogin threshold for transfusion of 70 g/L.
†Further results from recent phase III randomized controlled trials are required to determine benefits and harms.

Table 2: Potential risks and disadvantages associated with blood conservation strategies

Strategy	Potential risks and disadvantages
Antifibrinolytic agents	• Thrombosis
	• Possible increased risk of death with use of aprotinin
Desmopressin	• Thrombosis
Recombinant activated factor VII	• Thrombosis
	• No benefit with routine use in cases of trauma or massive bleeding
Artificial oxygen carriers (modified hemoglobin substitutes, perfluorocarbons)	• Short half-life
	• Interference with laboratory measures with use of hemoglobin substitutes
	• Vasoreactivity with use of hemoglobin substitutes
	• Use of 100% oxygen to provide effective oxygenation with use of perfluorocarbons may cause lung injury
Postoperative blood recovery techniques (cell salvage)	• Limited applicability to most critical care patients
	• Reduced quality of reinfused blood (hemolyzed, diluted, cytokines [e.g., interleukins])
Reduction of blood loss associated with diagnostic testing	
Closed blood sampling techniques	• Retrograde arterial embolization
Small-volume sample tubes	• Potential for insufficient volume for diagnostic testing
Point-of-care microanalysis	• Variable accuracy and precision (need for ongoing quality assurance and calibration)
Erythropoietin	• Thrombosis
Restrictive blood transfusion trigger	• Possible risk of death among patients with active cardiac disease

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