Review Article

Perioperative neonatal and paediatric blood transfusion

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ABSTRACT

Paediatric patients undergoing surgical procedures commonly require some volume of blood or blood component replacement in the perioperative period. Paediatric patients undergoing major surgery associated with substantial blood loss should be evaluated pre-operatively. Pre-operative correction of anaemia may be done considering the age, plasma volume status, clinical status and comorbidities. Maximum allowable blood loss (MABL) for surgery must be calculated, and appropriate quantity of blood and blood components should be arranged. Intraoperative monitoring of blood loss should be done, and volume of transfusion should be calculated in a protocol based manner considering the volemia and the trigger threshold for transfusion for the patient and the MABL. Early haemostasis should be achieved by judicious administration of red blood cells, blood components and pharmacological agents.

Key words: Blood loss, blood transfusion, massive, neonatal, paediatric, perioperative

INTRODUCTION

Paediatric patients undergoing surgical procedures commonly require some volume of blood or blood component replacement in the perioperative period. Paediatric anaesthesiologists need to develop protocols and guidelines to manage the perioperative blood loss. Though the indications and complications of blood transfusion in paediatric patients are similar to adults, certain considerations merit attention since they simply are not miniature adults:[1-3]

PHYSIOLOGICAL AND HAEMATOLOGICAL DIFFERENCES FROM ADULTS

Children have higher metabolic rate, higher oxygen consumption and greater rates of cardiac output to circulating blood volume.[1,2] Neonatal oxygen flux does not increase by compensatory increase in cardiac output in the face of decreased oxygen carrying capacity. Neonatal haemoglobin (Hb) levels (normal range: 14-20 g/dl) are significantly influenced by timing of cord clamping. These levels stabilize by 2-3 months of age. If Hb levels are <9 g/dl in term infants and <7 g/dl in pre-term neonate, the same may require investigation of cause and management with pre-operative transfusion and adjuvant therapy.

Foetal haemoglobin (Hb F) makes up for up to 70% of total Hb in term infants as compared to 97% for pre-term neonates at birth.[3] Hb F has a higher affinity for oxygen with a consequent shift of oxygen Hb dissociation curve to the left implying decreased oxygen delivery to the tissues.

RED BLOOD CELL TRANSFUSION

Pre-operative evaluation and preparation

A complete blood count (CBC) must be done in infants <12 months of age to evaluate Hb levels, haematocrit (Hct) and the reticulocyte count. Tests to detect sickle cell disease must be performed in the population at risk viz., blacks of African origin. The sickle cell disease also occur in people of Mediterranean, Indian, Middle Eastern and South central American origin.[4] Tests to evaluate coagulation should be performed when major surgery is contemplated.

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While interpreting the CBC, consideration should be given to the age since the age related changes take place in these values[4,5] [Table 1].

Trigger threshold for blood transfusion will vary according to age, Hgb level and other factors as follows:

Infants of <4 months of age require red blood cells transfusion if

- Hgb < 12 g/dl in first 24 h of life
- Hct is<20% with symptoms of anaemia with low reticulocyte count
- Hct < 30% on oxygen therapy with FiO_2 > 35%/ continuous positive airway pressure or with clinical signs like apnoea, bradycardia, tachycardia and low weight gain
- Hct > 35% on oxygen in hood or on intermittent mandatory ventilation (IMV) with mean airway pressure (MAP) > 6 cm of H_2O
- Hct > 45% in presence of cyanotic congenital heart disease
- Blood losses > 10%.[6]

Infants of more than 4 months of age require red blood cells transfusion if

- Acute loss of >15% of estimated blood volume
- Hypovolemia not responsive to other treatment
- Post-operative anaemia (Hgb < 10 g/dl)
- Pre-operative Hgb < 12 g/dl in presence of severe cardiopulmonary disease
- Severe chronic anaemia with Hgb < 7 g/dl.

The volaemia must be estimated according to the age [Table 2].

The following formula of maximum allowable blood loss (MABL) is indicated as the volume of red packed cells to be transfused, in accordance with the desired haematocrit.

$$MABL = \frac{EBV \times (H0 - H1)}{H0}$$

(Where EBV is the estimated blood volume in ml; H0 is the original or starting haematocrit, H1 is the lowest acceptable/target haematocrit).

Communication with the blood bank should be done for confirmation of reservation of blood of required quantity of blood.

Intraoperative monitoring and management

Need for intraoperative transfusion will depend on the rapidity and amount of blood loss, assessment of patient's blood volume, pre-operative haematocrit, general medical condition including presence of cardiac/lung disease, nature of surgery and the risk:benefit ratio of transfusion in that situation. Adequate and appropriate replacement of blood losses is essential to reduce mortality and morbidity in paediatric surgical patient.

Intraoperative monitoring has to be carried out as mentioned in Table 3.

American Society of Anaesthesiologists (ASA) Task force on blood component therapy published practice guidelines in 1996.[10] These guidelines are for adult patients and can be applied to paediatric patients also with the possible exception of infants and toddlers and summarized as follows:[11]

- Transfusion is rarely indicated when Hgb concentration is >10 g/dl and almost always indicated when it is <6 g/dl, especially when the anaemia is acute

Table 1: Normal values for haemoglobin concentration and MCV in infancy and childhood[4]

Age	Haemoglobin (g/L)		Haematocrit		MCV (fL)	
	Mean	−2 SD	Mean	−2 SD	Mean	−2 SD
1-3 days	185	145	0.56	0.45	108	95
3-6 months	115	95	0.35	0.29	91	74
0.5-2 years	120	105	0.36	0.33	78	70
2-6 years	125	115	0.37	0.34	81	75
6-12 years	135	115	0.40	0.35	86	77

Adapted from nathan and orkin.[5] MCV – Mean corpuscular volume; SD – Standard deviation

Table 2: Estimated circulating blood volume (volemia) in accordance with the age of the patient[7]

Child age	Volemia
Pre-term newborn	90 ml/kg
Term newborn to 3 months	80-90 ml/kg
Over 3 months of age	70-80 ml/kg
Children over 2-year-old	70 ml/kg

Adapted from hawtrey R[8]

Table 3: Monitoring of the patients, according to expected blood loss

Expected blood loss	Monitoring/action required
<30% of circulating blood volume	Routine monitoring
30-50% of circulating blood volume	Additional urine output monitoring. Obtain 2 venous lines
50-100% of circulating blood volume	Central venous lines, arterial line, rapid transfusion equipments
Massive blood transfusion expected	Arterial blood gas, metabolic and coagulation monitoring,[9] prevent hypothermia

- Determination of whether intermediate Hgb (6 g-10 g/dl) require red blood cell (RBC) transfusion should be based on the patient's risk for complication of inadequate oxygenation
- Use of single 'Hgb Trigger' for all patients and other approaches that fail to consider all important physiological and surgical factors affecting the oxygenation are not recommended
- When appropriate, pre-operative autologous blood donation, intraoperative and post-operative blood recovery, acute normovolemic haemodilution and measures to decrease blood loss (deliberate hypotension and pharmacological agents) may be beneficial
- Indications for the transfusion of autologous blood may be more liberal than for the allogenic RBC because of the lower (but still significant risk) risk associated with the former.

In case of massive emergency transfusion, one should avoid transfusion of Rh + ve blood to Rh − ve patients, particularly in girls to avoid the risk of haemolytic disease in newborn in subsequent pregnancies after the first.

The volume of blood to be transfused must be estimated to achieve the target haematocrit.

Volume of blood to be transfused can be calculated using several methods.[7] These include:

Calculation of volume of blood to be transfused

- Estimated blood volume × (Ideal haematocrit − actual haematocrit)/haematocrit of the tranfusate blood.

Example: 1-year-old child and 10 kg of weight.

- Estimated blood volume = 10 × 75; Actual haematocrit: 20. Ideal haematocrit: 35
- Haematocrit of 1 unit of packed RBCs: 60-70
- Volume to transfuse: (10 × 75) × (35-20)/70
- 750 × 15/70
- 160. 71 ml of RBCs to transfused. An average of 1 ml/kg of packed RBCs increase the haematocrit by upto 1.5%.

The shed blood can be replaced with 3 times the volume by Lactated Ringer solution or with an equal volume of 5% albumin or hetastarch. Once the estimated blood loss reaches this target value, transfusion of RBCs should be initiated.[9]

BLOOD COMPONENT THERAPY

Platelets

Platelet concentrate has to be used when there is acute bleeding, or any invasive procedure is contemplated, with platelet count < 50,000/cubic meter.[12]

If the predicted blood loss is >40% of the circulating blood volume, it is helpful to supply platelets and clotting factors.

While using platelets, one should use ABO matched platelets as far as possible. Alternatively, plasma compatible with recipient's RBCs or units with low titres of anti-A or anti-B antibodies with plasma removed may be used.

The recommended dose is 1-2 units/10 kg or 10-15 ml/kg.[13]

Fresh frozen plama

Fresh frozen plasma (FFP) may be used in situations of coagulation factor deficiency as may be observed in cases of liver disease, Vitamin K deficiency, disseminated intravascular coagulation or dilutional coagulopathy in massive blood transfusion, von Willebrand's (VW) disease and haemophilia A.

The recommended dose of FFP is 1 unit/10 kg or 10-15 ml/kg. The FFP may alternate with equal volumes of packed RBCs.

The specific coagulation factors according to a deficiency must be used in preference over FFP where ever possible.[14] FFP should not be used as a plasma expander in hypoalbuminaemia or malnutrition.

Cryoprecipitate

It contains factor VIII (80 units), von Willebrand factor (VWF), factor XIII, fibrinogen (150-250 mg) And fibronectin. The recommended dose is 1 unit per 5-10 kg body weight. It is indicated when fibrinogen levels are <150 mg/dl with microvascular/active bleeding or massive blood transfusion. It is also indicated in fibrinogen deficiency due to dysfibrinogenaemia or afibrinogenaemia.[15]

METABOLIC CONSEQUENCES AND COMPLICATIONS OF MASSIVE BLOOD TRANSFUSION

The metabolic consequences of large blood transfusions also occur in adults but are more frequent in children due to the relationship between blood component

administered and their circulating blood volume. A unit of packed RBCs in an infant may be equal to its total circulating volume whereas it makes only approximately 10% of the blood volume in an adult.

Hypocalcaemia

Ionised calcium is essential for the successful initiation of the coagulation cascade.[16] The citrate present in stored blood is a chelating agent and therefore it chelates calcium and prevents clot formation, but produces hypocalcaemia. The degree of hypocalcaemia depends on the rate of transfusion and the state of liver function. This is more with administration of FFP since it exhibits a higher concentration of citrates per unit of volume.

Neonates are particularly vulnerable to deleterious effects of hypocalcaemia, on cardiac function since neonate's heart has reduced sarcoplasmic reticulum and is greatly dependent on ionised calcium (calcium flux) for normal contraction and relaxation of myocytes. This myocardial dysfunction may be further worsened by halogenated anaesthetics administered and can be prevented by limiting the rate of blood product infusion to below 1 ml/kg/min, administration of prophylactic calcium infusion and decreasing the concentration of halogenated inhalational agents.

Hypocalcaemia may be treated by administration of calcium fluoride 5-10 mg/kg IV or calcium gluconate 15-30 mg/kg. If the blood loss is continuous and prolonged infusion of calcium chloride at the rate of 10 mg/kg/h may be used.[17]

Hyperkalaemia

Transfusion of large volumes of whole blood, irradiated blood and stored blood (10-14 or more days old) is the major cause of hyperkalaemia in paediatric patients and has caused serious arrhythmias and death.[18,19] The rate of rise of serum potassium in children is fast due to small blood volume. Large quantities of packed RBCs when transfused at a rapid rate, can also cause this complication.

Use of blood collected within 7 days and administration slowly with total volume < 1.0 ml/kg/min is recommended. Intravenous sodium bicarbonate 1 m mol/kg and calcium chloride 20 mg/kg or calcium gluconate 60 mg/kg may be used to treat hyperkalaemia causing arrhythmias. Use of intravenous dextrose insulin, hyperventilation and sympathomimetics can be useful.[17]

Hypomagnesaemia

Magnesium ion is essential for normal cardiac electrophysiologic activity. Hypomagnesaemia due to rapid blood transfusion can result in ventricular tachycardia or fibrillation. Calcium treatment is ineffective, however it responds to management with IV magnesium sulphate administered at 25-50 mg/kg.[17]

Acid-base disorders

Rapid transfusion of blood initially causes combined respiratory and metabolic acidosis. Later the carbon dioxide diffuses out and the lactic acid is metabolized, leaving no net effect on the acid-base balance.

Hypothermia

Children are susceptible to heat loss due to relatively large body surface area to weight ratio and larger head size. They are at the risk of hypothermia due to evaporative losses during ventilation and through surgical incisions, use of irrigant fluids, cold temperature of operation theatres (OTs). Hypothermia causes apnoea, hypoglycaemia, decreased drug metabolism and shift of oxygen Hg dissociation curve to the left. A secondary increase in shivering and non-shivering thermogenesis induced increase in oxygen consumption can worsen coagulopathy and increase mortality.

Use of blood warmers, maintaining OT temperature, use of warming blankets and warm fluids for irrigation and intravenous infusion with monitoring of electrocardiogram, SpO_2, skin and core temperature can be helpful in preventing hypothermia and consequent complications.

INFECTIOUS DISEASE TRANSMISSION

There is a risk of transmission of human immunodeficiency virus and hepatitis C virus through blood transfusion. Possibility of infections transmission risk of severe acute respiratory syndrome is a source of concern. Other infections viz., malaria, Creutz-Jacob disease etc., can be transmitted through blood.

ADJUVANT AND PHARMACOLOGICAL INTERVENTIONS TO MINIMIZE PERIOPERATIVE BLEEDING

In surgeries associated with a large amount of blood loss viz., major paediatric surgery, surgery for scoliosis or craniosynostosis and cardiac surgery, following drugs may be used to achieve to manage bleeding.

Antithrombolysis

Tranexamic acid has been found to be as effective as aprotinin in reducing perioperative bleeding after major paediatric surgery,[20] craniosynostosis[21] and scoliosis surgery and paediatric cardiac surgery[20] also.

The recommended dose of tranexamic acid as bolus is 20 mg/kg IV bolus followed by an infusion at 10 mg/kg/h.

Desmopressin

Administered in 0.3 mg/kg dose, desmopressin is effective for up to 10 h after an IV injection in keeping the serum levels of factor VIII and VWF elevated. It also significantly increases the platelet adhesiveness. Caution should be exercised in its use in children below 2 years of age for fear of hyponatraemia. Desmopressin may be used as an adjuvant in congenital (type I only) and acquired VW disease. It is ineffective in type II VW disease and in contraindicated in type IIB. It can facilitate minor surgical procedures and dental extractions in mild haemophiliacs. It is also useful in congenital vascular and platelet function disorders.

Recombinant factor VII

There are issues regarding the safety of use of this drug in paediatric patients. Current evidence of use of off-label recombinant factor VII in paediatric patients is not convincing. Lin Y *et al*.[22] recommend reserving its use only in situations of incontrollable bleeding due to surgery or trauma refractory to management.

Fibrinogen concentrate

Fibrinogen concentrate may be used in doses of 30-50 mg/kg in bleeding diathesis in cases of congenital or acquired hypofibrinogenaemia.

Prothrombin complex

Prothrombin complex contains factor II, VII, IX and X as well as anticoagulant factors viz., protein S, protien C and traces of heparin. It can be used in the management of perioperative bleeding refractory to FFP, platelets and cryoprecipitate. Its major advantage in paediatric patients is decreasing the incidence of volume overload and lowest risk of viral transmission.[7]

Recommended dose of prothombin complex is 20-30 IU/kg calculated with factor II however there is a paucity of literature regarding its use in paediatric patients.[23]

INTERPRETATION OF COAGULATION TESTS IN MANAGEMENT OF PERIOPERATIVE BLEEDING

Giraldo[7] reviewed this subject and emphasized the following important considerations to be kept in mind while interpreting the data obtained from various coagulation tests during management of perioperative paediatric bleeding. Prothombin time, total prothombin time and platelet count are quantitative measurements done *in-vitro* at 37°C. They are done with plasma poor in platelets and do not take into account the complete coagulation cascade or the intervening cell elements and therefore fail to reflect as to what is going on with the patient. Thromboelastography provides the overall information about the haemostasis in each coagulation phase including initial clot formation, retraction of the clot and the fibrinolysis. Its benefits have been vindicated in management of bleeding in liver transplantation, heart surgery and trauma.[24,25]

BLOOD CONSERVATION TECHNIQUES

Pre-operative autologous transfusion, acute normovolaemic haemodilution circulatory manipulations, administration of erythropoietin and use of cell savers have been tried in paediatric cardiac surgery, liver transplantation, craniosynostosis and scoliosis surgery with rewarding results.[26]

SUMMARY

Institutional protocols based on ASA guidelines to manage perioperative bleeding in paediatric patients must be developed keeping consideration of locally available resources. Volaemic status of the patient and target oriented replacement of blood must be done. In the case of massive bleeding, risk of coagulopathy must be anticipated, and haemostasis should be achieved as soon as possible.

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