Review Article

Blood transfusion practices in obstetric anaesthesia

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ABSTRACT

Blood transfusion is an essential component of emergency obstetric care and appropriate blood transfusion significantly reduces maternal mortality. Obstetric haemorrhage, especially postpartum haemorrhage, remains one of the major causes of massive haemorrhage and a prime cause of maternal mortality. Blood loss and assessment of its correct requirement are difficult in pregnancy due to physiological changes and comorbid conditions. Many guidelines have been used to assess the requirement and transfusion of blood and its components. Infrastructural, economic, social and religious constraints in blood banking and donation are key issues to formulate practice guidelines. Available current guidelines for transfusion are mostly from the developed world; however, they can be used by developing countries keeping available resources in perspective.

Key words: Obstetric anaesthesia, obstetric haemorrhage, postpartum haemorrhage, transfusion practices, transfusion protocol

INTRODUCTION

Blood transfusion is recognised as one of the eight essential components of the Comprehensive Emergency Obstetric Care module, which has been designed to reduce maternal mortality rates. Postpartum haemorrhage is a major contributor which accounts for 25% of all pregnancy-related deaths.[1] Availability of blood transfusion in developing countries depends on infrastructure, economics and social and religious taboos and practices, and this could cause transfusion practices to vary from those in the developed countries.[2]

CHALLENGES OF BLOOD TRANSFUSIONS IN OBSTETRIC PATIENT

Transfusion in obstetric patients poses challenges due to changes in maternal physiology, risk of alloimmunisation and infections in the foetus. While indications for transfusion in obstetrics may be emergent as well as nonemergent, the keystone of transfusion practice is that it should be appropriate that is, not given when not required and not missed when required. Transfusion guidelines have been designed by various organisations in various countries. While the basic tenets remain the same, availability of resources decide the practice.

PROBLEMS SPECIFIC TO THE PREGNANT PATIENT

Physiological changes in pregnancy

Increase in red cell mass (20-30%) and disproportionately greater increase in plasma volume (50%) help the patient stay haemodynamically stable with the normal blood loss during delivery. A hypercoagulable state prevails in pregnancy, with increased fibrinogen and factors VII, VIII, and IX supervening over the rise in the natural anticoagulants, Protein A, Protein C, and Antithrombin III. The fibrinolytic system decreases in activity. Plasminogen is increased, but its activity is dampened by a corresponding increase in plasminogen inhibitor type II. An exception to the general increase in coagulation factors is the fall in platelet levels, the so-called gestational thrombocytopenia.

Difficulty in assessment of blood loss

Assessment of blood loss by vital signs monitoring is unreliable in pregnancy, due to the increased maternal

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plasma volume. The relative haemodilution and high cardiac output allows the large amount of blood loss in a pregnant female before the hypotension and fall in haemoglobin/haematocrit (Hct) ensues. The assessment may also be farce because large amounts of blood lost may be concealed in the uterine cavity.

Associated comorbid conditions like preeclampsia, thrombocytopenia and the HELLP syndrome can bring about catastrophic haemorrhage. While the hypercoagulable state of pregnancy helps limit blood loss, it can tip the mother into disseminated intravascular coagulopathy (DIC) and pulmonary embolism.

Risk to foetus

While managing acute haemorrhagic emergencies, the foetus has to be kept in mind, to prevent infections and avoid Haemolytic Disease of the Foetus and Newborn (HDFN) in the current and future pregnancies.

INDICATIONS OF BLOOD TRANSFUSION IN OBSTETRICS

- Anaemia of pregnancy and Haemoglobinopathies
- Obstetric haemorrhage
- Surgeries where significant blood loss is expected.

BLOOD TRANSFUSION FOR ANAEMIA IN PREGNANCY

Anaemia during pregnancy is responsible for 15% of maternal mortality. Early correction of anaemia avoids the need for transfusion and reduces maternal mortality. The decision for transfusion should not be made on the basis of haemoglobin estimation alone, as healthy and clinically stable women do not require blood transfusion even with Hb of <7 g/dl. To conclude, transfusion is necessary if Hb <6 g/dl and there are <4 weeks for delivery. When Hb is <7 g/dl in labour or in immediate postpartum period, blood transfusion is only indicated if there is previous history of bleeding or patient is prone for bleeding due to some medical condition. Transfusion is also indicated if Hb is 7 g/dl, for women with continued bleeding or at risk of further significant haemorrhage or for those presenting with severe symptoms that need immediate correction (cardiac decompensation).[3,4] Transfusion in patients with sickle disease and thalassaemia should only be reserved for severe situations because prophylactic transfusion is associated with increases in costs, number of hospitalizations, and the risk of alloimmunisation.[5]

OBSTETRIC HAEMORRHAGE

Obstetric haemorrhage continues to be the leading cause of maternal mortality, ranging from 13% in developed countries to 34% in Africa.[6] An obstetric haemorrhage may occur before or after delivery, but >80% of cases occur postpartum, responsible for 25% of the estimated 358,000 maternal deaths each year.[7] [Causes of obstetric haemorrhage are shown in Table 1]. Blood loss results in hypoxia, metabolic acidosis, ischaemia and tissue damage, resulting in eventual global organ dysfunction. Massive blood loss results in consumptive coagulopathy and this is difficult to distinguish from dilutional coagulopathy, caused by transfusion with packed red cells and crystalloids, which in turn is difficult to differentiate in the acute setting from DIC. Dilution impairs coagulation and leads to further blood loss. All soluble clotting factors are absent in packed red blood cells (PRBCs) and stored whole blood is deficient in platelets and factors V, VII and XI. Thrombocytopaenia is the most common defect found in women with blood loss and multiple transfusions.[8]

ESTIMATION OF BLOOD LOSS

As earlier stressed, visual assessment of blood loss is "notoriously" inaccurate and clinicians can underestimate blood loss by 50%.[8] Standard definitions of postpartum haemorrhage, that is, >500 ml after vaginal delivery and >1000 ml after caesarean section, do not adequately reflect the clinical response of the patient. Definitions of massive haemorrhage vary and have limited value. It may arbitrarily be considered a situation where 1-1.5 blood volumes may need to be transfused acutely or in a 24-h period[9] where, normal blood volume in the adult is taken as approximately 7% of ideal body weight. Other

Table 1: Causes of obstetric haemorrhage

Early pregnancy	Abortions Ectopic pregnancy	
Later pregnancy	Antepartum haemorrhage	Placenta praevia, placental abruption, bleeding from vaginal or cervical lesions
	Primary postpartum haemorrhage	Tone (uterine atony)
		Tissue (retained products)
		Trauma (cervical and genital tract damage during delivery)
		Thrombin (coagulation disorder)
	Secondary postpartum haemorrhage	Uterine atony, retained products, genital tract trauma, uterine inversion

definitions include 50% blood volume loss within 3-h or a rate of loss of 150 ml/min.

Immediate Hct will not reflect the actual blood loss. Even a blood loss of 1000 ml will reflect a fall in Hct of only 3% in the 1st h.[8] Urine output, on the other hand, being sensitive to changes in blood volume, can give an early indication of changes in renal perfusion and hence perfusion of other organs.[8] Pulse Oximetry is an imperfect tool in the haemodynamically unstable patient. Use of central venous pressure (CVP) monitoring alone in bleeding obstetric patients with haemodynamic instability[9] is not recommended because it is not a true surrogate of assessment of patient's intravascular status. CVP and its response to fluid challenge or noninvasive cardiac variables using ultrasound can be used for estimation of intravascular status and can guide fluid resuscitation in obstetrics patient with haemodynamic instability. Volumetric/flow bases fluid resuscitation is recommended when compared to pressure based methods. All sources agree that the decision to transfuse is a clinical decision taken on the basis of the individual patient's status.[9-11]

MANAGEMENT OF OBSTETRIC HAEMORRHAGE

Systems based on trauma protocols are increasingly being used to manage obstetric haemorrhage.[10] It is also accepted that a protocol-based, multidisciplinary approach to massive blood loss yields the best results.[7,10-14] A number of protocols for obstetric haemorrhage, particularly postpartum haemorrhage have been designed.[12,14,15] The CMQCC protocol, also adopted by the ACOG District 11, is a step-by-step checklist format, based on the staging of obstetric haemorrhage,[12] whereas the RCOG Green-Top Guideline No. 52 also lays out therapeutic and monitoring guidelines for minor and major postpartum haemorrhage.[14] While there are some individual variations, the broad outlines remain the same. Comparison of two commonly used protocols is given in Table 2.

The mainstay of management of haemorrhage is rapid resuscitation with crystalloids to restore and maintain the circulating blood volume to prevent tissue and organ hypo-perfusion. Role of blood transfusion in acute haemorrhage is to maintain tissue oxygenation and reversal or prevention of coagulopathy using appropriate blood components. Prevention and treatment of hypothermia, acidosis and hypocalcaemia will ensure optimal function of transfused coagulation factors. Simultaneously, the cause of the bleeding should be identified and controlled, by medical means, surgery or invasive radiography.

CONTROVERSIES AND CONSENSUS FOR TRANSFUSION IN OBSTETRICS

The SAFE trial and the CRISTAL trial have shown colloids to have no advantage over crystalloids in the acute setting, and the high cost of colloids makes crystalloids the preferred resuscitative fluid in most centres.[15-17] It should be borne in mind that crystalloids rapidly equilibrate with the extracellular fluid, and only about 20% remains in the circulation after the 1st h. In previous studies it was suggested that, estimated blood loss should be replaced with about 3 times the volume of crystalloids[8] however, this concept has been challenged in recent randomised controlled trial (RCT) like SAFE trial, and starch trials and now, the accepted average ratio of colloid: Crystalloid is 1:1.5.

Whole blood or blood component?

Alexander *et al.*, in an observational study of massive obstetric haemorrhage at Parkland hospital, showed whole blood to be superior to PRBCs or combined transfusions in preventing acute tubular necrosis and other complications.[18] The availability of fresh warm blood in developing countries could provide an alternative to more expensive and infrastructure-dependent blood components.[2] Whole blood replaces many coagulation factors, and its plasma expands blood volume. It has the added advantage of exposing the patient to fewer donors.

To cross-match or not to cross-match?

The chances of a clinically significant red cell antibody being missed in a patient with a negative antibody screen (false negative) are 1-4/10,000.[19,20] Given that the chance of adverse consequences is small, in cases of acute massive haemorrhage, it appears reasonable to transfuse blood without type-and-screened red blood cells.[8,12,13]

CONCERNS REGARDING KELL ANTIGEN AND CYTOMEGALOVIRUS

Haemolytic Disease of the Foetus and Newborn due to Kell antibodies is gaining in importance with the declining incidence of HDFN due to Rh

Table 2: Comparison of two commonly used protocols

CMQCC toolkit 12		RCOG Green-top 5215	
Stage 1: Cumulative blood loss >500 ml vaginal birth or >1000 ml C/S - OR - vital signs >15% change or HR ≥110, BP ≤85/45, O_2 saturation <95% - OR - increased bleeding during recovery or postpartum	Establish IV access if not present, at least 18 gauge Increase IV fluids rates (Lactated Ringers preferred) and increase oxytocin rate (500 mL/h of 10-40 units/1000 mL solution); titrate oxytocin infusion rate to uterine tone Continue vigorous fundal massage Consider methylergometrine 0.2 mg IM per protocol (if not hypertensive); give once If no response, move to alternate agent; if good response, may give additional doses q 2 h Vital signs, including O_2 saturation and LOC q 5 min Weigh materials, calculate and record cumulative blood loss q 5-15 min Administer oxygen to maintain O2 saturation at>95% Empty bladder: Straight cath or place foley with urimeter Type and crossmatch for 2 units red blood cells STAT (if not already done) Keep patient warm Rule out retained products of conception, laceration, hematoma Inspect for uncontrolled bleeding at all levels, especially broad ligament, posterior uterus and retained placenta	Minor PPH: Blood loss 500-1000 ml, no clinical shock	Intravenous access (14-gauge cannula×1) Commence crystalloid infusion Consider venepuncture (20 ml) for Group and screen Full blood count Coagulation screen including fibrinogen Pulse and BP recording every 15 min
Stage 2: Continued bleeding or vital sign instability and <1500 mL cumulative blood loss	Additional uterotonic medication: Do not delay other interventions (see right column) while waiting for response to medications Bimanual uterine massage Move to OR (if on postpartum unit, move to L and D or OR) Order 2 units PRBCs and bring to the bedside Order labs STAT (CBC/PLTs, Chem 12, PT/aPTT, fibrinogen, ABG) Transfuse PRBCs based on clinical signs and response, do not wait for lab results Establish 2nd large bore IV, at least 18 gauge. Maintain adequate fluid volume with Lactated Ringers and adequate uterine tone with oxytocin infusion Assess and announce vital signs and cumulative blood loss q 5-10 min Set up blood administration set and blood warmer for transfusion Administer meds, blood products and draw labs, as ordered Keep patient warm second nurse (or charge nurse): Place Foley with urimeter (if not already done) Obtain portable light and OB procedure tray or haemorrhage cart Obtain blood products from the blood bank Assist with move to OR (if indicated) blood bank: Determine availability of thawed plasma, FFP and PLTs; initiate delivery of PLTs if not present on-site Consider thawing 2 FFP (takes 30 min), use if transfusing >2 units PRBCs Prepare for possibility of massive haemorrhage		

Contd...

Table 2: Contd...

CMQCC toolkit 12		RCOG Green-top 5215	
Stage 3: Cumulative blood loss >1500 ml, >2 units PRBCs given, VS unstable or suspicion for DIC	Establish team leadership and assign roles: Team leader (OB physician+OB anesthesiologist, anesthesiologist and/or perinatologist and/or intensivist) Order massive haemorrhage pack (RBCs+FFP+1 pheresis pack PLT) - Move to OR if not already there repeat CBC/PLTs, Chem 12, PT/aPTT, fibrinogen, ABG STAT q 30-60 min Anesthesiologist (as indicated) ABGs Central hemodynamic monitoring CVP or PA line Arterial line Vasopressor support Intubation Primary nurse: Announce VS and cumulative measured blood loss q 5-10 min Apply upper body warming blanket if feasible Use fluid warmer and/or rapid infuser for fluid and blood product Administration Apply sequential compression stockings to lower extremities Circulate in OR Second nurse and/or anesthesiologist: Continue to administer meds, blood products and draw labs, as ordered Third nurse (or charge nurse): Recorder	Major PPH: Blood loss >1000 ml and continuing to bleed OR clinical shock	Assess airway Assess breathing Evaluate circulation Oxygen by mask at 10-15 L/min Intravenous access (14-gauge cannula×2, orange cannulae) Position flat Keep the woman warm using appropriate available measures Transfuse blood as soon as possible Until blood is available, infuse up to 3.5 L of warmed crystalloid Hartmann's solution (2 L) and/or colloid (1-2 L) as rapidly as required The best equipment available should be used to achieve rapid warmed infusion of fluids Special blood filters should NOT be used, as they slow infusions Consider venepuncture (20 ml) for Crossmatch (4 units minimum) Full blood count Coagulation screen including fibrinogen Renal and liver function for baseline Monitor temperature every 15 min Continuous pulse, BP recording and respiratory rate (using oximeter, electrocardiogram and automated BP recording) Foley catheter to monitor urine output Two peripheral cannulae, 14- or 16-gauge Consider arterial line monitoring (once appropriately experienced staff available for insertion) Consider transfer to intensive therapy unit once the bleeding is controlled or monitoring at high dependency unit on delivery suite, if appropriate Recording of parameters on a flow chart such as the modified obstetric early warning system Documentation of fluid balance, blood, blood products and procedures
In stage 3 for resuscitation: Aggressively transfuse Based on vital signs, blood loss Key: High ratio of FFP to RBC Either: 6:4:1 PRBCs: FFP: PLTs Or: 4:4:1 PRBCs: FFP: PLTs Unresponsive coagulopathy: After 8-10 units PRBCs and coagulation factor replacement may consider risk/benefit of rFactor VII a		Crystalloid up to 2 L Hartmann's solution Colloid up to 1-2 L colloid until blood arrives Blood crossmatched If crossmatched blood is still unavailable, give uncrossmatched group-specific blood OR give 'O RhD negative' blood FFP 4 units for every 6 units of red cells or PT/activated Partial thromboplastin time >1.5×normal (12-15 ml/kg or total 1 L) PLTs concentrates if PLT count <50×109 Cryoprecipitate if fibrinogen <1 g/l Recombinant factor VII a therapy should be based on the results of coagulation Fluid therapy and blood product	

CMQCC – California maternal quality care collaborative; LOC – Level of consciousness; RCOG – Royal College of Obstetricians and Gynaecologists; CBC – Complete blood count; BP – Blood pressure; HR – Heart rate; IM – Initiate massive; PRBCs – Packed red blood cells; PT – Prothrombin time; aPTT – Activated partial thromboplastin time; ABG – Arterial blood gas; FFP – Fresh frozen plasma; PLT – Platelet; CVP – Central venous pressure; PA – Pulmonary artery; DIC – Disseminated intravascular coagulopathy; VS – Vasopressure Support; OR – Operation Room; STAT – Immediately

incompatibility. Donor blood is not routinely tested for Kell antigen in most countries, though it is an NHS recommendation that Kell and Cytomegalovirus screening should be done for blood intended for pregnant women.[13]

O RH D NEGATIVE BLOOD TRANSFUSION

The NHS (National Health Service) recommends that the use of Rh negative red blood cells is mandatory in RhD negative patients with pregnancy, RhD

negative females with child-bearing potential and in an emergency to premenopausal females of unknown blood group. If RhD positive red cells are given to a female of childbearing potential, consideration should be given to the use of anti-D immunoglobulin (plus exchange transfusion for large scale transfusion).[21] All major guidelines recommend the use of O RhD negative transfusion as a life-saving measure in women of unknown blood group, but only as a last resort, in order to conserve this rare resource.

BLOOD TRANSFUSION; HOW MUCH TO GIVE AND WHEN TO STOP?

Most protocols recommend maintaining a target Hct of 21-24%. Hébert *et al*. showed that restrictive transfusions and liberal transfusions were of equivalent value in critically ill patients while relatively stable patients undergoing liberal transfusions had a higher 30-day mortality.[22] The conclusive consensus form various protocols and guidelines suggest that the transfusion is rarely indicated in Hb >10 g/dl. If Hb is <6 g/dl transfusion is indicated irrespective of cause and condition of the patient. If Hb is between 6 and 10 g/dl, the indication will depend upon whether patients is actively bleeding or having history of previous excessive haemorrhage or having some medical condition where optimal Hb is >7 g/dl is required.[9,23] The common goals for transfusion in the obstetric patient[14] is to achieve
Haemoglobin >8 g/dl,
Platelet count >75 × 109/l,
Prothrombin time (PT) <1.5 × mean control,
Activated PT <1.5 × mean control and
Fibrinogen >1.0 g/l.

The risk of dilutional coagulopathy needs to be borne in mind when multiple units of PRBCs and crystalloids/colloids are used. Various recommendations for the proportions of blood components are in effect. While it has been observed that patients receiving <10 units of PRBCs rarely need component replacement, the lowest mortality occurs in the patients where ratio of plasma and PRBCs is 1:1. Both the CMQCC Toolkit and the RCOG Green top Guideline No 52 recommend a ratio of PRBC, fresh frozen plasma and Platelet of 6: 4:1 in cases of massive haemorrhage.[12,14]

ROLE OF RECOMBINANT FACTOR VIIA THERAPY

The role of rVII in primary postpartum haemorrhage is controversial because it may also result in life-threatening thrombosis.[24] When available, its use should be reserved for rescue therapy when conventional therapy has failed.[12,14] It is to be remembered that recombinant factor VIIa (rFVIIa) will not work if there is hypofibrinogenemia, severe thrombocytopenia, acidosis and hypothermia. Therefore, fibrinogen should be above 1 g/l and platelets greater than 20×10^9/l before rFVIIa is given. If there is a suboptimal clinical response to rFVIIa, these should be checked and acted on before the second dose is given.[14] The normal recommended dose is 90 μg/kg[12]

MANAGEMENT OF PATIENTS WITHEXCESSIVE SURGICAL BLOOD LOSS

There are various techniques which can be used either in anticipation of surgical blood loss or used when there is excessive blood loss during surgery.

CELL SALVAGE IN OBSTETRICS

Cell salvage also known as intra-operative blood salvage (IBS) or intra-operative cell salvage is a technique in which patients own blood cells are re-transfused after separation from lost blood.[25] IBS has been used in ectopic pregnancies,[26] caesarean sections,[27] in vaginal deliveries and is acceptable under certain circumstances to Jehovah's witnesses.[27,28]

The safety of cell salvage has been questioned because of the risk of embolism and alloimmunisation. It is recommended that it be carried out in centres with the appropriate experience and adequate infrastructure.[14,26] However, Allam *et al*. in their review could not find a single maternal adverse effect directly related to cell salvage.[26]

PREOPERATIVE AUTOLOGOUS BLOOD DONATION IN OBSTETRICS

Early identification of patients at risk for obstetric haemorrhage and storage of autologous blood has been attempted - preoperative Autologous Blood Donation. Since most patients do not have an identifiable risk factor and many patients do not donate more than the unit of blood, its utility in acute severe haemorrhage is questionable. A study from a Nigerian teaching hospital showed it to be feasible in their Obstetrics and Gynaecology unit, and some authors recommend it as an option in developing countries.[2,29] However, others question its utility and safety as it may cause

anaemia, does not eliminate transfusion risk, cannot be used in an emergency and is not acceptable to Jehovah's Witnesses.[29]

ROLE OF ANTIFIBRINOLYTIC THERAPY IN OBSTETRICS

Antifibrinolytics help in reduction of blood loss during obstetric surgery and other obstetric haemorrhage. Some studies have shown that tranexamic acid reduces postpartum haemorrhage.[30] A larger RCT of 15,000 subjects, the WOMAN trial, is now underway to test the efficacy of tranexamic acid.[31]

SUMMARY

Blood transfusion is an essential component of obstetric care and at times lifesaving. Inappropriate transfusions during pregnancy and the postpartum period expose the mother to the risk of HDFN. In the situation of obstetric haemorrhage early resuscitation is done with crystalloids and/or colloids with oxygenation while simultaneously taking all steps to control bleeding and reduce the transfusion requirement. A preplanned, multidisciplinary protocol yields the best results in the management. The decision to perform a blood transfusion should be made on both clinical and haematological grounds. The majority of protocols recommended that Hct be maintained minimally at 21-24%; however, in actively bleeding patient, target Hct should be 30%. To avoid dilutional coagulopathy, concurrent replacement with coagulation factors and platelets may be necessary. Whole blood may be preferred in acute massive haemorrhage, especially where blood components are not readily available. In an extreme situation and when the blood group is unknown, O RhD negative red cells should be given.

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