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Blood and Blood Component Therapy in Obstetrics –A Review

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ABSTRACT

Haemorrhage is the leading cause of maternal mortality. This emphasizes the importance of a updating the knowledge about indications for and complications associated with the replacement of blood components .This article provides current information regarding preparation for and administration of blood products and pharmacological strategies for treatment of haemorrhage.

KEYWORDS Blood, Blood component, Postpartum Haemorrhage

Introduction-

Obstetric haemorrhage remains major cause of maternal mortality worldwide. WHO estimates, over a thousand of all maternal deaths are directly due to obstetric haemorrhage .The obstetric conditions leading to haemorrhage are placenta praevia, placental abruption and postpartum haemorrhage. Massive haemorrhage typically appears in postpartum .The blood flow to the placenta is about 700 ml/min at term, so bleeding is likely to be rapid, often unexpected and difficult to control. Transfusion of blood and it's components is a potentially lifesaving procedure .Although meticulous care is taken in the selection of blood donors , processing , storage and transfusion of blood products, serious transfusion related complications may ensue .It is the incumbent on the physician to be sure that a blood product is indicated ,and standard transfusion practices are observed [1]. Each hospital must take into account the resources available within its own institution and community to design a protocol that will assist them in the optimal management of obstetrical haemorrhage. Each institution is encouraged to review its existing policy and protocols, and modify them if necessary to provide safe patient care, or consider the creation of a policy to optimize the management of obstetrical haemorrhage. The committee believes that all obstetric services must have a written haemorrhage protocol in order to ensure the highest quality of patient care.[2] . Obstetric conditions associated with the need for blood transfusion may lead to morbidity and mortality if not managed correctly. The increasingly important issues in blood transfusion are adverse events associated with transfusion, including potential infection and potential transmission of prions, rising costs and the possible future problems of availability. The aim of this review is to offer guidance about the appropriate use of blood products that neither compromises the affected woman nor exposes her to unnecessary risk.

When is blood transfusion recommended?

Since there are no universally defined criteria, indicating the red cell transfusion, various hospitals do it differently. What is more, the need for transfusion is often not motivated enough. The guidelines for use of blood components, provided in scientific literature, are not always proven by scientific evidence or conclusions of randomized controlled trials; furthermore, they are often based just on best clinical experience[3]

Transfusion of blood products is necessary when the extent of blood loss is significant and ongoing, particularly if vital signs are unstable. The purpose of transfusion of blood products is to replace coagulation factors and red cells for oxygen-carrying capacity, not for volume replacement. To avoid dilutional coagulopathy, concurrent replacement with coagulation factors and platelets may be necessary.[2]

How can the chance of transfusion be reduced-

For reducing the chance of transfusion, strategies should be planned from pre-pregnant state. Her haemoglobin should be more than 11 gm%. If her Hb is less in antenatal period, consider haematinics deficiency once haemoglobinopathies have been excluded. Oral iron should be preferred first line of treatment for iron deficiency. Parentral iron is indicated when oral iron is not tolerated,absorbed,or patient compliance is in doubt .Anaemia not due to haematinics deficiency(for example, haemoglobinopathies and bone marrow failure syndromes) should be managed by blood transfusion where appropriate in close conjunction with haematologist. Blood loss at the delivery should be minimised. AMTSL is recommended to minimise blood loss. Women should be advised to deliver in hospital.

Whole blood and component-

Whole blood –

It contains red cells, clotting factors, and platelets .Whole blood use is to be minimised in modern obstetrics because of its disadvantages like a short storage life (24hours),large volume(350 ml/unit) and potential hypercalcemia.

Packed red Blood Cells (PRBCs)-

PRBCs are the only blood product to provide oxygen carrying capacity and the most appropriate therapy for patients requiring red blood cells due to haemorrhage. Each PRBCs unit will raise the haemoglobin by 1 gm/dl and the haematocrit by 3% .Transfusion of PRBCs should be considered in any gravid with severe anaemia, in haemorrhage, associated coagulopathy and in severe sepsis and septic shock.

Fresh Frozen Plasma (FFP)-

FFP is the plasma that is extracted from whole blood.FFP primarily contains fibrinogen, antithrombin, and clotting factors V, XI, and XII. Each unit contains 150 ml of plasma and assists in coagulation and volume resuscitation. Fibrinogen levels are used to monitor response to FFP. Each unit of FFP should raise the fibrinogen level by 10-15gm/dl.FFP doesn't require being ABO and Rh compatible .FFP should be considered for haem-

orrhaging patients with evidence of coagulopathy, coagulopathic liver disease, or warfarin reversal. The common practice is to administer FFP 12-15 ml/kg to keep aPTT and PT ratios less than 1:5. FFP will require at least 30 min to thaw. There is insufficient evidence to suggest that FFP is useful in major blood loss in the absence of DIC .Its use should be guided by the use of coagulation tests.[4]

Cryoprecipitate-

Cryoprecipitate is the precipitate that results from thawed FFP.It is rich in fibrinogen, von Willebrand factor ,factor VIII ,and factor XIII .Cryoprecipitate can be clinically measured by the fibrinogen response ,which should increase by 5 to 10 mg/dl per unit .Each unit of cryoprecipitate provides minimal volume(10-15 ml).so ,it is an ineffective agent for volume resuscitation .It is indicated in patients with coagulopathy and concerns of volume overload .Fibrinogen level should be maintained above 1 g/l by use of FFP or two pools of cryoprecipitate.[4]

Platelets-

Platelets are separated from whole blood and stored in plasma. The platelet should not be allowed to fall below 5010^9/l in acutely bleeding patients[4]. The platelet should be group compatible. Rh D-negative women should receive Rh D-negative platelets.One unit of platelet provides an increase of only approximately 7500/mm^3 platelet concentrate of 6 to 10 U need to be transfused.[5] Single donor platelets are preferred as they expose the patient to fewer potential antigenic and immunologic risks. Transfusion of a single donor platelet concentrate will increase the circulating platelet count by 30,000-60,000/mm^3.Transfusion of platelets should be considered when the platelet count is less than 20,000/mm^3 for a vaginal delivery, or less than 50,000/$mm^3$for a caesarean section, or if there is evidence of coagulopathy .Platelet should be given by unused blood –giving set.

rFVIIa therapy-

A promising new alternative to blood component therapy is recombinant activated factor VII(rFVIIa). The mechanism of action is to augment the intrinsic clotting pathway by binding with tissue factor and directly activating factors IX and X.The use of recombinant factor VIIa may be considered as a treatment for life-threatening PPH but should not be considered as a substitute for life saving procedures as surgery or embolisation[4]. The most commonly reported effective dose is 50-100 ug/kg intravenously every 2 hours until haemostasis is achieved, with vast majority of patients requiring only one dose.[6] There is no evidence to support the prophylactic use of rVIIa to reduce blood loss for caesarean section.[4] It is important to ensure adequate levels of platelets and clotting factors because rFVIIa increases clotting by acting on these subtrates[6].There is no risk of viral transmission as the drug is derived from recombinant technology. The most commonly reported adverse events associated adverse events are thrombosis, CVAs, myocardial infarction, pulmonary embolism and clotting of indwelling devices. The activity of rFVIIa is reduced during hypothermia and acidosis, highlightening the importance of its use before the patient develops some of the consequences of massive transfusion.[6]

Indications of Transfusion

DISORDER	Whole Blood	PRBCs	FFPs	Cryoprecipitate	Platelets
Haemorrhagic shock(loss of BV>30%)	+	+	±	±	±
Hb<6gm%, Intraparum Hb<7 gm%	-	+	-	-	-
Prior to surgical or invasive procedures, with platelet count of <50×109/L;	–	–	±	–	+
DIC secondary to abruption,PET,amniotic fluide embolism	-	±	+	±	±
Thrombotic thrombocytopenic purpura	–	–	+	±	±
Hemorrhage due to hypofibrinogenemia • DIC syndrome; • Von Willebrand's disease	–	+	±	+	-
In severe sepsis and septicemic shock when Scvo2<70%.	-	+	±	±	±

Planning a Blood Transfusion-

Safety of blood transfusion practice starts from safety of blood donor or to the timely and uneventful recovery of the recipient without leaving any delayed complication. Inform the Patient (or relatives) about blood transfusion, prescribe blood components for transfusion, group and cross match (a fresh sample must be sent to repeat the tests for antibodies if the patient had a RBCs transfusion more than 3 days previously, since the new antibodies may be stimulated).Blood should be warmed before infusion as rapid infusion of cold fluids may cause cardiac arrhythmias and may cause hypothermia which impairs blood clotting .Some blood warmers operate at upto 43^0C but are safe .

In case of reactions:

1. Stop transfusion.
2. Keep IV open with 0.9% NaCl.Give injectible antihistaminic and steroid..
3. Notify Attending Physician and Blood Bank.

If transfusion is terminated:

1. Send freshly collected blood and any necessary urine samples to Blood Bank.
2. Send blood unit and administration set to Blood Bank.
3. Fill out COMPLETELY and send to Blood Bank the Transfusion Reaction section of the blood tag.

Blood component therapy-

PRODUCT	CONTENTS	VOLUME	ANTICIPATED EFFECT
Whole blood	All component	350ml	Used only in emergencies
PRBCs	RBCs	300 ml	Increase Hb by 1 g/dl. or increase haematocrit by 3%
Platelets(single donor pooled)	Platelets	300ml(6U)	Increase platelet by30,000-60,000/mm^3
FFP	All clotting factors	150 ml	Increase fibrinogen byn5-10 mg/dl.
Cryoprecipitate	Fibrinogen, on Willebrand,FactorVIII, Factor XIII.	10-15ml	Increase fibrinogen byn5-10 mg/dl

Transfusion Protocols-

In the past, no consensus existed regarding the optimal ratio of blood product replacement. There is definite improvement in outcome with aggressive use of coagulation factors with PRBCs.Two most common protocols are 1U of PRBCs to 1U of FFP to 1 U of platelets(1:1:1) and 6 U of PRBCs to 4 U of FFP to 1 U of pooled platelets(6:4:1).[5]

If bleeding continues after initial treatment, strong consideration should be given to increasing the amount of FFP to a ratio of 4 units PRBC: 4 units of FFP: 1 unit of pheresis platelets. (4:4:1)[7]

Red cell may be required –
a unit over 5-10 min-in managing major haemorrhage, while in a frail patient at risk of circulatory overload, a slow infusion rate(each pack should not take more than 4 h) is appropriate.

Platelets have a short storage life and generally infused in not longer than 30-60 minutes per dose.

FFP rapid infusion may be appropriate when it is given to replace coagulation factors during haemorrhage.

Transfusion Risks and Reactions-
Incorrect Blood component transfusion- The most frequently occurring adverse event, as proven by Quebec hemovigilance,is incorrect blood component transfusion in which patient receives blood component intended for another patient.

Hypothermia-
hypothermia may complicate the clinical course of massive transfusion and results in cardiac arrhythmias. It can be prevented by warming PRBC units before transfusion.

Metabolic abnormalities-
Leakage of Potassium and ammonia can occur into plasma when PRBCs are stored .This may result in hyperkalemia and high ammonia concentration in patients requiring massive transfusion. As most PRBCs are stored with calcium –chelating agents, hypocalcemia may occur. Serial monitoring with metabolic profiles and ionized calcium levels can be helpful.

Immunological Reaction-
Most common reactions are febrile nonhaemolytic transfusion reactions and urticarial reactions. Rare immunological reactions include anaphylaxis; post-transfusion purpura etc.Transfusion of leukoreduced blood products has been proposed to decrease the frequency of these reactions.

Infection Risk-
Transfusion related infection risk-All blood products have the potential to transmit viral and bacterial infections.[5]

Infection	Transmission risk
HIV-1,HIV-2	1 in 1.5-2.1 million
Hepatitis B	1 in 205000-355000
Hepatitis C	1in 1.1-1.9 million
HTLV I and II	1 in 2 million
Bacterial contamination	
RBCS	1 in 30,000
Platelets	1 in 5000

Nucleic acid amplification technology (NAT), as applied to blood screening, detects the presence of viral nucleic acid, DNA or RNA, in donation samples .In this technology, a specific RNA/DNA segment of the virus is targeted and amplified in-vitro. The amplification step enables the detection of low levels of virus in the original sample by increasing the amount of specific target present to a level that is easily detectable. The presence of specific nucleic acid indicates the presence of the virus itself and that the donation is likely to be infectious. NAT assays can either be performed on individual donations (ID) or on mini-pools (MP) to detect the nucleic acid of the infectious agent. In addition to NAT assays which target individual viral nucleic acids, multiplex NAT screening assays have been developed which can detect DNA or RNA from multiple viruses simultaneously.[8]

Transfusion –Related Acute- Lung Injury (TRALI)-
Acute lung injury is characterized by acute respiratory distress, hypoxemia, hypotension, fever and pulmonary edema. Typically within six hours of a transfusion patient develops breathlessness and non-productive cough.[9] The chest X-ray shows bilateral nodular infiltrates in a batwing pattern, typically of acute respiratory distress syndrome. Loss of circulatory volume and hypotension are common. Treatment consists of supportive care with oxygen administration and diueresis.Sympotoms usually resolves in 96 hours.[5]

Post Transfusion GVHD-
PT-GVHD is a fatal complication of blood transfusion, more likely to occur when blood is taken from first –degree relatives. Partial DNA homology between first-degree relatives is the reason for PT-GVHD.Clinical features include fever, which occurs within 4 to 10 days of transfusion is the result of neutropenia.Skin rash, liver dysfunction, diarrhoea, pancytopenia with bone marrow aplsia.

Blood Conserving Approaches-
Autologous donation and transfusion-
In pregnancy, pre-autologous deposit is not recommended. Blood can be pre-deposited and kept for up to 5 weeks. This procedure is not recommended. In pregnancy ,concerns have been raised regarding placental insufficiency, whether the woman will make up her Hb before delivery and whether the collected units will be sufficient in the event of major obstetric haemorrhage. This procedure does not prevent the most common error in blood transfusion, which is 'incorrect blood component transfused', nor does it alter the risk of bacterial contamination.[4]

Acute Normovolemic Hemodilution-
This refers to a blood conservation technique in which blood is removed from a patient immediately before surgery, the patient is given crystalloid or colloid solution to maintain Normovolemic during surgery, and then the blood is reinfused to the patient after surgery.

Intraoperative and Postoperative blood salvage-
This refers to collecting the patient's blood during or after surgery, filtering the blood and then reinfusing the red cells back to the patient. Cell saver technology is the most widely used blood salvage system. In the past, theoretical concerns regarding the risk for infection and amniotic fluid embolism limited the use of blood salvage technology in obstetrics however, several small studies have documented it's safety and effectiveness.[5]

Alternative Oxygen Carriers-
As some patients refuse to accept blood products(e.g.Jehovah's Witness patients) or unable to receive transfusion due to lack of compatible blood, new oxygen carriers are being developed. The 2 primary products are haemoglobin –based oxygen carriers and perflurocarbons.

Haemoglobin –
based oxygen carriers use haemoglobin from animals, outdated human blood, or recombinant technology. The haemoglobin is separated from the red cell stroma and undergoes multiple filtration and polymerization process before use.[5]

Perflurocarbons are inert compounds that can dissolve gases, including oxygen. Both products have high oxygen carrying capacities and have been used in phase III trials for elective surgery and in patients with haemorrhagic shock.[5]

Key points –
Blood transfusion is a serious decision and should be considered with caution.

Blood components should be used rather than whole blood.

Transfuse the right blood component to right patient at right time.

Most transfusion reactions occur due to clerical errors.

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