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REFRESHER COURSE

The Bleeding Parturient – Current Transfusion Recommendations

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Introduction

Obstetric haemorrhage is one of the leading causes of maternal mortality worldwide.[1,2] In South Africa, according to the National Committee for Confidential Enquiry into Maternal Deaths (NCCEMD), obstetric haemorrhage was the second most common cause of maternal deaths in the triennium 2008 – 2010. The report showed that obstetric haemorrhage contributed 14.1% of all maternal deaths in that period and it continues to be the most common cause of avoidable maternal mortality.[3]

Definitions

Bleeding in pregnancy can occur prior to (antepartum), during (intrapartum) or after delivery (postpartum).[4]

Antepartum haemorrhage occurs after 24 weeks gestation. Postpartum haemorrhage (PPH) can further be classified as primary or secondary, occurring within 24 hours of delivery and between 24 hours to six weeks post delivery respectively.[1,4]

Aetiology of obstetric haemorrhage

Haemorrhage early in pregnancy can be a result of abortions or ruptured ectopic pregnancy. [4] Antepartum haemorrhage may occur as a result of placental or uterine abnormalities. Abruptio placentae and placenta praevia are the most common placental abnormalities causing significant haemorrhage.[1,4]

The aetiology of postpartum haemorrhage can be classified into the following major categories: tone (uterine atony), placental abnormalities (retained placenta), trauma (genital tract lacerations), or coagulation abnormalities (coagulopathy).[1,4-6]

In South Africa the major causes of obstetric haemorrhage are abruptio placentae, uterine rupture, retained placenta, uterine atony, and bleeding during and after caesarian section.[3,7]

Assessment of blood loss

Definitions of haemorrhage vary but it is commonly defined in terms of the volume of blood lost.[8] The World Health Organization (WHO) defines a blood loss of > 500 ml in the first 24 hours after vaginal delivery as primary PPH,[1,5,8-10] or 1000 ml after caesarian section.[5,8,11]

Severe obstetric haemorrhage involves a blood loss of > 1500 ml, with a decrease in haemoglobin > 4 g/dl or requiring > 4 units blood transfusion.[4,5,8,11] Major haemorrhage has been described in certain publications as blood loss > 2500 ml, and massive haemorrhage as the loss of one blood volume or transfusion of at least 10 U of packed RBCs in 24 hours.[5,11,12]

The amount of blood loss is determined by visual estimation using stained maternity pads, surgical swabs, floor spills or suction bottles. Accurate estimation of blood loss can warn of impending haemorrhagic shock. There are various guidelines published to facilitate visual estimation of blood loss.[13]

In addition to volume assessment of blood loss, the rate of blood loss should also be assessed.[5,11] The loss of 50% of blood volume within 3 hours or at a rate of 150 ml/min constitutes massive blood loss.[11,14]

The patient's clinical status should also be taken into account, as the different stages of shock can be determined. Estimated percentage of blood loss and clinical parameters such as, heart rate, arterial pressure, respiration, mental status, urine output and capillary refill can be used to classify haemorrhagic shock into four different stages. The classification aids in the management of haemorrhage.[1]

Management principles of obstetric haemorrhage

It is recommended that all facilities providing care to obstetric patients be prepared to manage obstetric haemorrhage.[15,16] An obstetric haemorrhage protocol outlining each stage of haemorrhage and specific management guideline should be established.[17]

The main therapeutic strategy in the treatment of acute haemorrhage is the prevention or correction of hypovolaemic shock. Crystalloids/colloids are initially infused to restore circulating blood volume and to maintain adequate blood flow and blood pressure.[18] Transfusion of PRBC then follows to correct tissue hypoxia. This initial fluid therapy may lead to dilution of clotting factors increasing the risk of coagulopathy. FFPs are then added in cases of massive haemorrhage, when PT or aPTT is prolonged > 1.5 times. If fibrinogen plasma level is lower than 1g/L, cryoprecipitate use is recommended. Platelet transfusion is also recommended in massive haemorrhage. Regular monitoring of haemoglobin (Hb) and platelet (Plt) count, as well as blood coagulation tests are recommended to aid product administration.[14]

The California Maternal Quality Care Collaborative (CMQCC) has published clear obstetric haemorrhage care guidelines in the form of a table or flow chart. The patients are classified into four groups: stage 0 – 3. Stage 0 being every woman in labour, stage 1: blood loss > 500 ml vaginal or > 1000 ml caesarian, stage 2: continued bleeding with blood loss < 1500 ml and stage 3 total blood loss > 1500 ml. Each step has a management guideline ranging from active management of 3rd stage of labour for stage 0 patients to activation of massive haemorrhage protocol in stage 3.[17]

The protocol includes medical and obstetric interventions, as well as transfusion management. If the haemorrhage is classified as stage 1, obstetric haemorrhage protocol is activated, two units PRBC are typed and crossmatched, then the patient is assessed for continued heavy bleeding. Increased postpartum surveillance is recommended if there is no continued heavy bleeding. Patients who continue to bleed are managed as stage 2/3. Stage 2 patients are transfused 2 units PRBC per clinical signs. The transfusion management of stage 3 patients involves activation of massive haemorrhage protocol, where PRBCs, FFP and platelets are transfused at a ratio of 6:4:1 or 4:4:1.[17]

A massive transfusion protocol is also essential in institutions dealing with obstetric haemorrhage on a regular basis.[5,19-21] Massive transfusion is defined as transfusion exceeding the patient's blood volume, or transfusion of more than 10 units of blood within 24 hours.[22] The criteria for identifying patients experiencing severe haemorrhage need to be outlined. For example the King Edward Memorial Hospital (KEMH) in Western Australia recommend activation of the Massive Transfusion Protocol (MTP) in the patient who continues bleeding with the estimated blood loss of > 2500 ml, four units of packed red blood cells already received with more anticipated and clinical or laboratory evidence of coagulopathy.[23]

According to the KEMP MTP, the senior anaesthetist in charge of the case notifies blood bank once the patient fulfills the abovementioned criteria. Blood component therapy includes 4 PRBC units, 4 FFP units and cryoprecipitate 8 – 10 units. The initial blood component therapy is followed by transfusion of 4 PRBC, 4 FFP and 1 platelet unit. Laboratory monitoring every 60 minutes forms part of the MTP and blood product administration is guided by results. The laboratory tests include haemoglobin (Hb), platelet count, INR or aPTT and fibrinogen.[23]

The Department of Obstetrics at the University of Cincinnati implements MTP when the estimated blood loss > 2000 ml with ongoing blood loss of > 150 ml/min and presence of clinical signs suggesting shock. According to their protocol blood products are prepared in coolers containing 6 PRBC, 4 FFPs and 5 pooled platelets. In addition to the above-mentioned products the 2nd and 3rd cooler will contain 10 pooled cryoprecipitate. The coolers are then issued in three consecutive cycles. Transfusion will proceed in the following order:

- 2 units PRBC
- 2 units FFP
- 5 units pooled platelets
- 2 – 3 units PRBC
- 2 units FFP
- Repeat 1– 5
- 10 pooled cryoprecipitate
- Repeat 6 and 7 as frequently as necessary.[24]

Blood product replacement in obstetric haemorrhage

Life threatening haemorrhage occurs in approximately 1 – 2% of deliveries. Delaying recognition and treatment of haemorrhage frequently result in inadequate blood product replacement and development of disseminated intravascular coagulation (DIC), contributing significantly to maternal morbidity and mortality.[25]

Transfusion of packed red blood cells (PRBC)

The transfusion of PRBC is indicated to correct the inadequate oxygen-carrying capacity of the blood.[11] The decision to transfuse an acutely bleeding patient depends on the haemoglobin (HB) concentration, the amount and rate of blood loss, and signs of reduced oxygenation.[18,26] Transfusion is probably necessary in class III haemorrhage where the blood volume loss is 30 – 40 % and the patient has lost 1500 – 2000 ml. If the patient has lost > 40 % of blood volume or > 2000 ml of blood transfusion becomes a life saving therapy.[14,18]

Transfusion therapy is almost always indicated at Hb values below 6 g/dl and very rarely necessary in patients whose Hb concentration is higher than 10 g/dl. Patients with Hb values between 6 and 10 g/dl require an evaluation of clinical status before the decision to transfuse is made.[14,18,26]

Transfusion of fresh frozen plasma (FFP)

Fresh frozen plasma is the component of whole blood that remains after cellular elements and platelets are removed. It contains all of the coagulation factors and it is used to replenish multiple coagulation factors.[20] Major obstetric haemorrhage is always associated with a reduction in coagulation factor levels and frequently thrombocytopaenia.[11]

FFPs are commonly indicated in the obstetric setting for the treatment of microvascular bleeding due to coagulopathy and factor deficiency following massive transfusion.[15] FFPs are usually transfused at an initial dose of 15 ml/kg.[18,20] The transfusion of FFPs is guided in some centers by the PT/aPTT ratio, infusing FFPs if it is >1.5x normal.[2,8,14,18]

Transfusion of platelets

Transfusion of platelets is indicated for the treatment of thrombocytopaenia or primary and secondary platelet function disorders. A platelet count should be obtained before transfusion of platelets in a bleeding patient, if possible.[26] Platelet transfusion is recommended in patients with platelet count < 50 x 10^9/L in the presence of excessive bleeding.[14, 18, 26] During massive transfusions a threshold of 75 x 10^9/L is recommended, to prevent platelet count falling below 50 x 10^9/L.[18]

Use of cryoprecipitate

Cryoprecipitate is the cold insoluble fraction of FFP and contains 10 times the fibrinogen concentration than FFP.[5] A decrease in fibrinogen is an early predictor for severe PPH. Cryoprecipitate

is administered to maintain fibrinogen levels > 1.5 g/L.[5,8] Cryoprecipitate transfused at 1 – 2 units/10 kg increase plasma fibrinogen concentration by approximately 0.5 g/L.[14]

Current transfusion recommendations

Resuscitation in haemorrhage has classically been centered on administration of crystalloids and packed red blood cells (PRBC). Other blood products like fresh frozen plasma, cryoprecipitate and platelets are used in the presence of abnormal laboratory values. The crystalloid/PRBC – based resuscitation guideline fail to prevent early coagulopathy in massive bleeding cases.[27-29]

Massive crystalloid administration may worsen bleeding before surgical haemostasis is achieved due to dislodgement of clots at sites of endothelial injury and increases in intravascular hydrostatic pressures. Early coagulopathy has also been shown to occur before haemodilution and clotting factor consumption takes place. Activation of certain anticoagulant mechanisms and fibrinolysis has been shown to result in early coagulopathy.[28, 30]

The concept of early coagulopathy studied in trauma patients has resulted in the traditional resuscitation guidelines being challenged. Limited evidence suggests that early aggressive blood product replacement can improve outcomes in the setting of massive haemorrhage. The new recommendations discourage excessive administration of crystalloids. Blood product administration is the cornerstone of resuscitation in the current resuscitation concept, termed haemostatic resuscitation.[27, 31]

Haemostatic resuscitation therapy limits early aggressive crystalloid use and considers permissive hypotension. Early administration of FFP and platelets (with concomitant use of PRBC) is promoted. Blood products are administered at a ratio of 1:1:1 for PRBC, FFP and without waiting for coagulation laboratory results. Early use of recombinant factor VIIa (rFVIIa) is recommended.[27,28] The use of permissive hypotension with systolic blood pressures between 80 – 100 mmHg, before surgical control of haemorrhage may be optimal to limit ongoing blood loss. This is recommended in patients with postpartum haemorrhage, however during the antenatal period uterine perfusion pressure may be compromised.[27,30]

Many centers in the United States have adopted massive transfusion protocols utilising high FFP: PRBC ratios, despite the lack of randomised trials. The rationale behind the move is that such ratio prevents early development of coagulopathy.[27,28] There is no evidence that the 1: 1: 1 FFP: PRBC: platelets ratio should be applied in obstetrics.[5]

The formulaic approach to management of obstetric haemorrhage is however discouraged in other publications because it does not take into account that in the majority of PPH, the parturient's fibrinogen level will be higher than that in the administered FFP, and unmonitored usage will lead to dilution and possibly contribute to pulmonary complications. Point of care testing is encouraged because it allows real time monitoring and a tailored approach to coagulopathy management. Cryoprecipitate use has been shown to successfully increase fibrinogen levels during PPH and the dose should depend on measured and target fibrinogen levels.[8]

The platelet count should be kept > 50 x 10^9/L during ongoing PPH, according to guideline recommendations and should be infused when the count falls < 75 x 10^9/L. The 1: 1: 1 FFP: PRBC: platelets transfusion strategy would result in multiple platelet transfusion and cannot be justified by certain authors.[8]

Another current approach in managing major obstetric haemorrhage is the Major Obstetric Haemorrhage protocol used at the University Hospital of Wales. On activation of major obstetric protocol after 1000 ml of blood loss, blood samples are taken for a FIBTEM assay, a point of care Hb measurement, FBC and coagulation screen. The protocol does not involve empirical early use of FFP because the FIBTEM is available in 10 minutes. If the FIBTEM >/= 16 mm (equivalent to a fibrinogen level of 3 g/L) it is assumed all other coagulation factors will be normal and no FFP or cryoprecipitate is administered. FFP is administered if FIBTEM is < 12 mm and bleeding is ongoing. Platelets are administered if the count is < 75 x 10^9/L and not administered empirically. Cryoprecipitate or fibrinogen concentrate is used to manage severe monitored coagulopathy if FFP has failed.[8]

Conclusion

It is essential for every institution managing obstetric haemorrhage to have a massive transfusion protocol (MTP) (5). Excessive administration of crystalloids should be avoided.[5,27] The protocol may be based on either empiric use of coagulation factor products or point-of-care blood product administration based on facilities available at the institution.

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