Recent advances in the management of major obstetric haemorrhage

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Introduction

Major Obstetric haemorrhage (MOH) remains one of the leading causes of maternal mortality & morbidity worldwide. In the 2003-2005 report of the UK Confidential Enquiries into Maternal Deaths, haemorrhage was the third highest direct cause of maternal death (6.6 deaths/million maternities) with the rate similar to the previous triennium. Postpartum haemorrhage (PPH) accounts for the majority of these deaths. This triennium, 2006-2008, unlike in previous reports there has been a change in the rankings of direct deaths by cause. Deaths from haemorrhage have dropped, to sixth place, following genital tract sepsis, preeclampsia, thromboembolism, amniotic fluid embolism and early pregnancy deaths. A well-defined multidisciplinary approach that aims to act quickly has probably been the key to successful management of MOH. In the developing world, several countries have maternal mortality rates in excess of 1000 women per 100,000 live births, and WHO statistics suggests that 25% of maternal deaths are due to PPH, accounting for more than 100,000 maternal deaths per year. The blood loss may be notoriously difficult to assess in obstetric bleeds. Bleeding may sometimes be concealed & presence of amniotic fluid makes accurate estimation challenging.

Definition

MOH is variably defined as blood loss from uterus or genital tract >1500 mls or a decrease in haemoglobin of >4 gm/dl or acute loss requiring transfusion of >4 units of blood. Blood loss may be:

1. **Antepartum**: Haemorrhage after 24th week gestation & before delivery; for example: placenta praevia, placental abruption, bleeding from vaginal or cervical lesions.

2. **Postpartum**: Haemorrhage after delivery
   - **Primary PPH**: Within 24 hours of delivery, which is >500 mls following vaginal delivery & >1000 mls following a caesarean section.
   - **Secondary PPH**: 24 hours to 6 weeks post-delivery; for example: Uterine atony, retained products of conception, genital tract trauma, uterine inversion, puerperal sepsis, uterine pathology such as fibroids.

PPH can be minor (500-1000 mls) or major (> 1000 mls). Major PPH could be divided to moderate (1000-2000 mls) or severe (>2000 mls).

Causes

Causes of PPH may be conveniently remembered using 4 T’s as a mnemonic:

- **Tone** (Uterine atony)
- **Tissue** (retained products)
- **Trauma** (cervical & genital tract trauma during delivery)
- **Thrombosis** (coagulation disorder)

Other Risk factors include: Prolonged labour, multiple pregnancy, polyhydramnios, large baby, obesity, previous uterine atony & coagulopathy.

Prevention

The most significant intervention shown to reduce the incidence of PPH is the active management of the third stage of labour (see below). Other measures to prevent or reduce the impact of MOH include:

- Avoidance of prolonged labour
- Minimal trauma during assisted vaginal delivery
- Detection & treatment of anaemia during pregnancy
- Identification of placenta praevia by antenatal ultrasound examination.
- Where facilities exist, magnetic resonance imaging (MRI) may be a useful tool and assist in determining whether the placenta is accreta or percreta. Women with placenta accreta/percreta are at very high risk of major PPH. If placenta accreta or percreta is diagnosed antenatally, there should be consultant-led multidisciplinary planning for delivery.

Active management of the third stage

This represents a group of interventions including early clamping of the umbilical cord, controlled cord traction for placental delivery & prophylactic administration of uterotonic at delivery (e.g. oxytocin). Active management of the third
stage is associated with a lower incidence of PPH and need for blood transfusion.11 A longer acting oxytocin derivative, carbetocin, is licensed in the UK specifically for the indication of prevention of PPH in context of caesarean delivery. Randomised trials suggest that a single dose (100 mcg) of carbetocin is at least as effective as oxytocin by infusion.12, 13

Management of MOH

Pregnant women are often young, healthy & have an increased blood volume of up to 20% at term and therefore likely to compensate well to haemorrhage until the circulating blood volume is very low.14 MEOWS are a useful bedside tool for predicting morbidity. A validation study of the CEMACH recommended modified early obstetric warning system (MEOWS) in all obstetric inpatients to track maternal physiological parameters, and to aid early recognition and treatment of the acutely unwell parturient. In addition, blood loss may sometimes be concealed and difficult to calculate. More commonly massive haemorrhage may be obvious; signs other than revealed haemorrhage include:

- Tachycardia
- Hypotension (BP may not drop until significant blood is lost)
- Pallor
- Oliguria
- Cool peripheries
- Lower abdominal pain

Management of anticipated MOH

On some occasions, cases at high risk of MOH can be predicted; e.g. caesarean section in a lady with a low lying placenta and previous uterine scar. These cases may be at a risk of placenta accreta and massive blood loss.

- 2 large bore IV cannulae
- Rapid infusion device or pressure bags in theatre
- Blood warmer & warming blanket
- Blood cross-matched & available
- Consider preoperative invasive monitoring
- Consider cell salvage if available (see below)
- Consider interventional radiological procedures if available (see below)

Management of unanticipated MOH

Management involves four components, all of which must be undertaken SIMULTANEOUSLY: communication, resuscitation, monitoring and investigation, arresting the bleeding.9,15 Most maternity units in UK have CODE RED bleep system for alerting MOH.

Communication & teamwork:

Communication and teamwork are essential in cases of both anticipated & unanticipated maternal haemorrhage. This includes:

- Call for help. Alert the midwife-in-charge, senior obstetrician & anaesthetist.
- Alert Blood transfusion service & haematologist.
- Alert portering service for transport of blood samples & collection of blood products
- Check blood is available. In the UK 2-4 units of O-neg blood is kept on labour ward for emergency use.
- Allocate roles to team members.
- Ensure departmental guidelines exist for the management of MOH & regularly practice ‘fire drills’.
- Alert one member of the team to record events, fluids, drugs and vital signs.
- The use of standard form of words (such as ‘on going major obstetric haemorrhage’, ‘we need compatible blood now or group specific blood’).9

Goals of management:

- Early identification of maternal bleed and institution of major haemorrhage drill
- Rapid access to infusion of fluid in first instance with rapid availability & administration of blood.
- Efficient team working & management decision making.

Resuscitation & immediate management:

- ABC, 100% oxygen
- 2 large bore cannulae & bloods for X-match
- Fluid resuscitation; crystalloid/colloid 2000mls via rapid infuser or pressure bags e.g. Level 1 Rapid infuser (can achieve >500mls/min warmed fluid flow)
- Fluid therapy and blood product transfusion
- Crystalloid Up to 2 litres Hartmann’s solution
- Colloid up to 1–2 litres colloid until blood arrives
- Blood Crossmatched
- If crossmatched blood is still unavailable, give uncrossmatched group-specific blood OR give ‘O RhD negative’ blood
- Fresh frozen plasma 4 units for every 6 units of red cells or prothrombin time/activated partial thromboplastin time > 1.5 x normal (12–15 ml/kg or total 1litres)
- Platelets concentrates if platelet count < 50 x 109
- Cryoprecipitate If fibrinogen < 1 g/l
- Thromboelastography and rotational thromboelastometry coagulation tests: In most cases, medical and transfusion
therapy is not based on the actual coagulation state because conventional laboratory test results are usually not available for 45 to 60 minutes. Thromboelastography and rotational thromboelastometry are point-of-care coagulation tests. A good correlation has been shown between thromboelastometric and conventional coagulation tests, and the use of these in massive bleeding in non-obstetric patients is widely practiced and it has been proven to be cost-effective.

- A 2006 guideline from the British Committee for Standards in Haematology summarizes the main therapeutic goals of management of massive blood loss is to maintain:
  - Haemoglobin > 8g/dl
  - Platelet count > 75 x 10⁹/l
  - Prothrombin < 1.5 x mean control
  - activated prothrombin times < 1.5 x mean control
  - Fibrinogen > 1.0 g/l.

- In addition, the Confidential Enquiry into Maternal and Child Health recommends that women with known risk factors for PPH should not be delivered in a hospital without a blood bank on site.

- Transfer to theatre.
- Non-surgical intervention for uterine atony.
- Bimanual uterine compression (rubbing up the fundus) to stimulate contractions.
- Ensure bladder is empty (Foley catheter, leave in place). Rub up the uterus
- Syntocinon 5 units by slow intravenous injection (may have repeat dose).
- Ergometrine 0.5 mg by slow iv/im injection (contraindicated in women with hypertension).
- Syntocinon infusion (40 units over 4 hours).
- Carboprost 0.25 mg by intramuscular injection repeated at intervals of not less than 15 minutes to a maximum of 8 doses (contraindicated in women with asthma).

- Direct intramyometrial injection of carboprost 0.5 mg (Haemobate or Prostaglandin F2α) with responsibility of the administering clinician as it is not recommended for intramyometrial use. Can be repeated up to 5 doses (contraindicated in women with asthma, may cause bronchospasm, flushing & hypertension).

- Misoprostol 1000 micrograms rectally.
- If pharmacological measures fail to control the haemorrhage, initiate surgical haemostasis sooner than later.

Surgical treatment and other interventions

The most common cause of primary PPH is uterine atony. However, clinical examination must be undertaken to exclude other or additional causes:

- Retained products (placenta, membranes, clots)
- Vaginal/cervical lacerations or hematoma
- Ruptured uterus

- Broad ligament hematoma
- Extra genital bleeding (for example, subcapsular liver rupture)
- Uterine inversion.

Intrauterine balloon tamponade is an appropriate first line ‘surgical’ intervention for most women where uterine atony is the only or main cause of haemorrhage. If this fails to stop the bleeding, the following conservative surgical interventions may be attempted, depending on clinical circumstances and available expertise:

- Balloon tamponade (Bakri/Rusch balloon, Foley's/condom catheter, Sengstaken-Blakemore tube).

- Haemostatic brace suturing (such as B-Lynch or modified compression sutures).

- Bilateral ligation of uterine arteries.

- Bilateral ligation of internal iliac (hypogastric) arteries.

- Selective arterial embolisation or balloon occlusion radiologically.

- Compression/ clamping aorta to buy time.

- Uterine replacement if uterine inversion

It is recommended that a laminated diagram of the brace technique be kept in theatre. Resort to hysterectomy sooner rather than later (especially in cases of placenta accreta or uterine rupture). A second consultant clinician should be involved in the decision for hysterectomy.

Interventional Radiological techniques

Interventional techniques are gaining popularity if the facilities & expertise exist and are especially useful for the anticipated massive bleeds e.g. planned LSCS in a woman with anticipated placenta accreta. Though evidence of effectiveness is still limited, there are increasing case reports of its successful use. This suggests that prophylactic arterial catherisation (with a view to embolisation) could be considered where facilities permit until such time as further evidence becomes available.

- Bilateral internal iliac artery balloons may be placed electively & inflated at C. section/ should bleed occur.

- Selective pelvic artery (internal iliac arteries, anterior division of internal iliac or uterine artery) embolisation can be performed.

- Complications appear rarely & include: haematoma, false aneurysms & lower limb ischemia.

Interventional radiology may be considered in cases of placenta praevia with accreta if intra-arterial balloons can be placed in the radiology department before the woman goes to theatre for caesarean section. Follow up studies of women who had undergone arterial embolisation for control of PPH suggest that the intervention does not impair subsequent menstruation and fertility.
Intraoperative cell salvage in obstetrics (ICSO)

Cell salvage has now been used in numerous cases of obstetric bleeds and appear safe. Concerns relate to re-infusion of foetal cells which could theoretically cause haemolytic disease in future pregnancies and also the potential for amniotic fluid embolus. If cell salvage techniques are utilised, separate suction of amniotic fluid is recommended and a leukocyte depletion filter used during re-infusion of salvaged blood. Setting up cell salvage measures should not divert staff an attention from initial resuscitation.

Intraoperative cell salvage (the process whereby blood shed during an operation is collected, filtered and washed to produce autologous red blood cells for transfusion to the patient) is commonly being used in cardiac, orthopaedic and vascular surgery with relative reduction of blood transfusion by 39% and absolute risk reduction by 23%, with cell salvage not appearing to impact adversely on clinical outcomes 51, 32. Although large prospective trials of cell salvage with autotransfusion in obstetrics are lacking, to date, no single serious complication leading to poor maternal outcome has been directly attributed to its use. Several bodies based on current evidence have endorsed cell salvage in obstetrics. Current evidence supports the use of cell salvage in obstetrics, which is likely to become increasingly commonplace, but more data are required concerning its clinical use 33. A National UK survey in 2007 showed that, in 2005–2006, 38% of all UK maternity units were using cell salvage and that 28% incorporated cell salvage into their massive haemorrhage guidelines 36. In particular, this survey showed that a lack of training was the main perceived barrier to its use: 48% of units specifically stated that their reason for not using cell salvage was lack of training and equipment, with fears about safety being expressed by only 10%. However, the potential difficulty is the effective removal of amniotic fluid and the degree of contamination with fetal red cells with potential maternal sensitization, intraoperative cell salvage may be a useful technique in women who refuse blood or blood products (Jehovah’s Witnesses guideline) or those where massive blood loss is anticipated (placenta percreta or accreta). For women who are Rh-negative, to prevent sensitization, the standard dose of anti-D should be given and a Kleihauer test taken 1 hour after cell salvage has finished, to determine whether further anti-D is required 35.

Recombinant activated factor VII (rFVIIa)

Recombinant activated factor VII (rFVIIa) was developed for the treatment of haemophilia. Over the past decade, it has also been used to control bleeding in other circumstances. A 2007 review identified case reports of 65 women treated with rFVIIa for PPH 36. Although the case reports suggested that rFVIIa reduced bleeding, 30 of the 65 women underwent peripartum hysterectomy and particular caution is required in interpreting data from uncontrolled case reports. In the face of life-threatening PPH, and in consultation with a haematologist, rFVIIa may be used as an adjuvant to standard pharmacological and surgical treatments. A suggested dose is 90 micrograms/kg, which may be repeated in the absence of clinical response within 15–30 minutes 37. Although there is no clear evidence of thrombosis with the use of rFVIIa in obstetric practice, there have been case reports of thrombosis with the use in cardiac surgery38-40. Women with PPH are particularly susceptible to defibrination (severe hypofibrinogenemia) and this is particularly relevant to the most severe cases that will be considered for rFVIIa; rFVIIa will not work if there is no fibrinogen and effectiveness may also be suboptimal with severe thrombocytopenia (less than 20 x 10⁹/l). Therefore, fibrinogen should be above 1g/l and platelets greater than 20 x 10⁹/l before rFVIIa is given. If there is a suboptimal clinical response to rFVIIa, these should be checked and acted on (with cryoprecipitate, fibrinogen concentrate or platelet transfusion as appropriate) before a second dose is given 36-40.

Anaesthetic management 35:

- GA with RSI is generally advocated if actively bleeding or coagulopathy.
- Reduce dose of induction agent if severe on going bleeding.
- Regional anaesthesia is relative contraindication but may be maintained if the patient has an epidural insitu & bleeding is controlled.
- Alert Blood bank & haematologist.
- Consider arterial line, central line and urinary catheter but only after definitive treatment has commenced. Their insertion must not delay resuscitation & fluid management.
- Use fluid warmer & aim to keep the patient normothermic.
- Regular monitoring of haemoglobin level and coagulation using near patient devices if available (e.g Haemacue). FFP, platelets transfusion & cryoprecipitate may be necessary if coagulopathy develops. Liaise early with haematology department for optimal & timely product replacement.
- Perioperative monitoring as per AAGBI guidelines.
- Recording of parameters on a flow chart such as the modified obstetric early warning system charts.
- Consider systemic haemostatic agents such as Aprotonin, Vit K, Tranexemic acid, Recombinant factor VII a (Novo seven R). Although evidence is conflicting, there is a consensus view that fibrinolytic inhibitors seldom, if ever, have a place in the management of obstetric haemorrhage 35, 42.
- Postoperative management includes transfer to ITU/HDU.
- Anticipate coagulopathy & treat clinically until coagulation results available.
- It is also important that, once the bleeding is arrested and any coagulopathy is corrected, thromboprophylaxis is administered, as there is a high risk of thrombosis. Alternatively, pneumatic compression devices can be used, if thromboprophylaxis is contraindicated in cases of thrombocytopenia.
Conclusion

Globally, postpartum haemorrhage (PPH) is the leading cause of maternal morbidity and mortality. Major obstetric haemorrhage is managed by multidisciplinary approach. In the current treatment of severe PPH, first-line therapy includes transfusion of packed cells and fresh-frozen plasma in addition to uterotonic medical management and surgical interventions. In persistent PPH, tranexamic acid, fibrinogen, and coagulation factors are often administered. Secondary coagulopathy due to PPH or its treatment is often underestimated and therefore remains untreated, potentially causing progression to even more severe PPH. The most postnatal haemorrhage is due to uterine atony and can be temporarily controlled with firm bimanual pressure while waiting for definitive treatment.

Competing Interests
None declared

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