Obstetric haemorrhage

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Abstract

Obstetric haemorrhage remains a significant cause of maternal morbidity and mortality. It is the leading obstetric cause for admission to intensive care units. Knowledge of risk factors and early recognition of haemorrhage enables rapid activation of a coordinated multidisciplinary team response. Clear unit protocols for the management of massive haemorrhage that are reinforced by team drills help to increase awareness in the multidisciplinary team, improve performance and thus can improve patient outcome. Pharmacological agents and surgical manoeuvres are reviewed in the article, as are blood conservation techniques.

Keywords Cell salvage; interventional radiology; obstetric haemorrhage; resuscitation; uterotonic drugs

Royal College of Anaesthetists CPD Matrix: 1A02, 2A04, 2A05, 2A06, 2B05, 2B06

Learning objectives

After reading this article, you should be able to:

- define postpartum haemorrhage
- classify the aetiology of postpartum haemorrhage
- list two ways to reduce risk of AFE when using intraoperative cell salvage

Background

Obstetric haemorrhage is a significant cause of maternal morbidity and mortality. The Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK (MBRRACE-UK) report published in November 2018, placed obstetric haemorrhage as the second most common direct cause of death and seventh as the overall leading cause of maternal deaths for the period 2014–2016.[1] The mortality rate was 0.78 per 100,000 maternities, which was not significantly different to the previous triennial period (2013–2015).[2] The lack of significant decrease in mortality therefore stresses the need to improve the care of women with haemorrhage.

Paucity of observations following delivery and lack of recognition of haemorrhage were implicated in many of the cases, more evidently when women were being cared for from outside the theatre, such as recovery or postnatal ward. Human factor was identified as a persistent problem, with the lack of leadership and failure to escalate appropriately featuring in many deaths.[1]

Obstetric haemorrhage causes significant morbidity and is the most common cause of obstetric-related intensive care admissions.[3]

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Definitions

Antepartum haemorrhage (APH) occurs prior to delivery in the period of 24 weeks' gestation to full term of pregnancy. It is much less common than postpartum haemorrhage. The common causes include placenta praevia, placental abruption, trauma and uterine rupture.

Postpartum haemorrhage is defined as primary if blood loss from the genital tract occurs within 24 hours of delivery or secondary if blood loss occurs over 24 hours following delivery up to 6 weeks post-delivery. Primary postpartum haemorrhage (PPH) is the most common form of major obstetric haemorrhage.

The Royal College of Obstetricians and Gynaecologists define PPH as minor (with 500–1000 ml blood loss) or major (with over 1000 ml blood loss). Major PPH can be further classified into moderate (with between 1000 ml and 2000 ml blood loss) or severe (with over 2000 ml blood loss).[4]

Other definitions include the need for a transfusion of greater than four units of packed red cells or a haemoglobin fall of greater than 4 g/dl. Definitions based upon physiological changes can be unreliable due to the physiological changes associated with pregnancy.

Postpartum haemorrhage

The aetiology of PPH can be classified as per the 'Four Ts':

- tone – abnormalities of uterine contraction
- thrombin – abnormalities of coagulation
- trauma – genital tract injury
- tissue – retained products of conception, abnormally invasive placenta.

Risk factors are summarized in Table 1.[4] The occurrence of secondary postpartum haemorrhage is associated with retained products of conception or puerperal sepsis.

Management (Figure 1)

Team preparation

Early involvement of appropriate senior staff (including the anaesthetic team and relevant clinicians) is fundamental to the management of PPH, especially those who are at risk of abnormal placentation.[4] There is some evidence that intensive educational programmes, comprehensive obstetric haemorrhage treatment protocols and post-event team review may individually or in combination lead to reductions in the incidence of severe PPH and thus morbidity.[5] The enquiry into maternal morbidity from haemorrhage identified improvements in care for almost 90% of women; in 74% this would have made a difference to their outcome.[1]

Risk factors and the associated levels of risk for PPH

Risk factor	The four Ts	OR (95% CI)
Multiple pregnancy	Tone	3.30 (1.00–10.60)
		4.70 (2.40–9.10)
Previous PPH	Tone	3.60 (1.20–10.20)
Pre-eclampsia	Thrombin	5.00 (3.00–8.50)
		2.20 (1.30–3.70)
Fetal macrosomia	Tone	2.11 (1.62–2.76)
		2.40 (1.90–2.90)
Failure to progress in second stage	Tone	3.40 (2.40–4.70)
		1.90 (1.20–2.90)
Prolonged third stage of labour	Tone	7.60 (4.20–13.50)
		2.61 (1.83–3.72)
Retained placenta	Tissue	7.83 (3.78–16.22)
		3.50 (2.10–5.80)
		6.00 (3.50–10.40)
Placenta accreta	Tissue	3.30 (1.70–6.40)
Episiotomy	Trauma	4.70 (2.60–8.40)
		2.18 (1.68–2.76)
		1.70 (1.20–2.50)
Perineal laceration	Trauma	1.40 (1.04–1.87)
		2.40 (2.00–2.80)
		1.70 (1.10–2.50)
General anaesthesia	Tone	2.90 (1.90–4.50)

Adapted from Green-top Guideline No. 52 published by the Royal College of Obstetricians and Gynaecologists, December 2016.[4]

Table 1

A combination of prediction and prevention, early recognition and rapid coordinated action in treating PPH will aid in pre-empting worst-case scenarios. Excellent communication amongst the multidisciplinary obstetric team is paramount.

Recognizing the haemorrhage

As placental blood flow at term can exceed 750 ml/min, obstetric haemorrhage can be rapid and catastrophic. Failure to recognize the severity of the situation was identified in 26% of deaths in the MBRRACE-UK report.[1] This was more evident when the patient was being cared for out of theatre.

The initial recognition of obstetric haemorrhage is often challenging. The haemorrhage may be concealed or in the case of an overt haemorrhage, estimation of total loss is notoriously inaccurate. Amniotic fluid, loss of blood into sheets and pads, blood loss occurring out of hospital and operator underestimation of blood loss are all causes of inaccuracies.

The ability of the pregnant patient to compensate for haemorrhage with an increase in heart rate, stroke volume and vascular tone mean that haemorrhage may go unrecognized until physiological extremes have been reached. In some cases, more than 40% total blood loss can occur before the physiological signs of haemorrhage become recognizable.

The use of standardized observation systems such as modified early obstetric warning scores (MEOWS) can be vital in recognizing evolving physiological trends over time. These observation systems allow signs such as tachypnoea, poor urine output, temperature, change in pallor, pathological cardiotocography due to placental hypoperfusion to be monitored and detected, along with the basic observations of tachycardia and hypotension.

Pathways such as massive haemorrhage protocols allow the obstetric MDT to obtain blood products quickly to enable rapid empirical treatment of major blood loss when necessary.

Resuscitation should be informed by laboratory results where possible, and there is an increased awareness of the importance of correcting hypofibrinogenaemia in obstetric haemorrhage.[6]

More appropriate administration of red cells, blood components and coagulation factors may be guided by point-of-care testing of haemoglobin values, e.g. Haemocue, and thromboelastography (TEG) or thromboelastometry (ROTEM). Evidence has stated that the use of such tests have an increased sensitivity in identifying deficits in the coagulation cascade when compared to laboratory based tests and an increase in accurate assessment of the deficit phase of coagulation cascade.[7]

Maintenance of normothermia is also important as both sepsis and hypothermia increase the oxygen demand of the women and may lead to disseminated intravascular coagulation. Calcium must also be replaced to support the coagulation system.

Pharmacological management

Alongside the initial resuscitation of the patient, the first-line treatment for obstetric haemorrhage is pharmacological intervention to encourage uterine contraction (Table 2).

Haemostatic agents

Additional agents can be used to promote haemostasis when treating life-threatening haemorrhage.

Tranexamic acid is a synthetic derivative of the amino acid lysine. It is an anti-fibrinolytic agent that competitively inhibits the activation of plasminogen to plasmin, which causes fibrin degradation. Tranexamic acid reduced death due to bleeding in women according to the WOMAN Trial Collaborators.[8] The risk of serious adverse events is minimal. The use of tranexamic acid should be considered in addition to oxytocin, at caesarean section to reduce blood loss in women who are at increased risk of PPH.[4]

Fresh frozen plasma is a blood product that contains all coagulation factors. If there is ongoing bleeding without imminent haemostatic results, FFP should be infused at a dose of 12–15 ml/kg after 4 units of red blood cells transfusion. If prothrombin time/activated partial thromboplastin time is more than 1.5 times normal and haemorrhage is continuing, volumes of FFP in excess of 15 ml/kg are likely to be needed to correct coagulopathy.

Fibrinogen is a glycoprotein that is converted to fibrin and subsequently a blood clot. During ongoing PPH, a plasma fibrinogen level of greater than 2 g/l should be maintained with the use of cryoprecipitate which contains fibrinogen, von Willebrand factor, factor VIII, factor XIII and fibronectin.

The routine use of **recombinant factor VIIa** (rFVIIa) is not currently licensed for use in obstetrics. Although there is some positive results in case studies, the use of rFVIIa is limited to patients with refractory haemorrhage; where embolization is

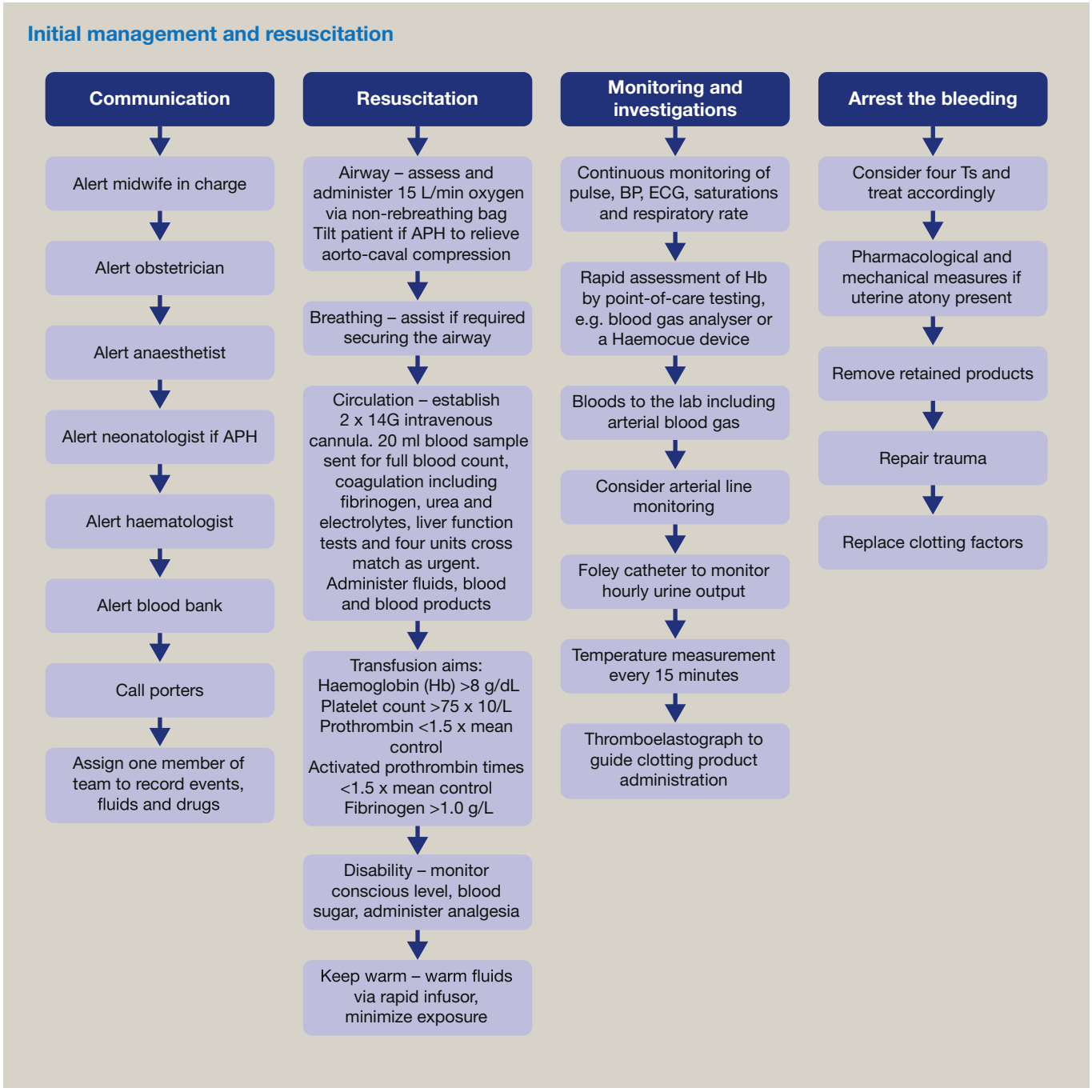

Figure 1

unavailable; or hysterectomy is the only alternative. The initial dose administered is 90 mg/kg, and it is specified that prior to administration the patient must have a fibrinogen level of greater 1 g/dl, adequate platelets, normal calcium levels, correction of acidosis and be normothermic. The main side effects are the occurrence of a thromboembolic event or absence of response.

Surgical intervention

Surgical manoeuvres and pharmacological agents are used side by side in the treatment of persistent haemorrhage.

Retained products of conception should be removed and any genital tract trauma should be identified and repaired.

If uterine atony is the cause of the haemorrhage, uterine compression should be initiated. Emptying the bladder is also advocated.[4]

External uterine tamponade by means of bi-manual uterine compression should be initiated. If this manoeuvre is successful, a B-Lynch suture can be sited.

Internal uterine tamponade can be achieved using a Bakri or Rusch Balloon. The balloon is placed inside the uterus and is

Pharmacological management

Drug name	Action	Dose and frequency	Side effects	Contraindications
Oxytocin	A naturally occurring polypeptide Acts on oxytocin-specific receptors in uterine myometrium promoting uterine smooth muscle contraction	Bolus dose 5 IU slow IV (bolus can be repeated if needed) Short acting so often administered as 10 IU/hr infusion over 4 h	Reflex tachycardia Hypotension	Caution in hypovolaemic and cardiac patients due to vasodilatation and hypotension
Ergometrine	Acts on α-adrenergic, dopaminergic and serotonin 5-HT_2 receptors Uterine smooth muscle contraction not clearly associated with a specific receptor	250–500 μg IV or IM	Tachycardia Hypertension Vomiting Nausea	Avoid in patients with pre-eclampsia and cardiovascular disease
Carboprost	Prostaglandin $F_{2\alpha}$ analogue Profound smooth muscle contractor	250 μg IM. Dose can be repeated every 15 min (maximum of eight doses)	Bronchospasm Intrapulmonary shunting Hypoxia Vomiting Diarrhoea Shivering Pyrexia	Avoid in asthmatics and pre-existing respiratory and cardiac disease (not for IV administration)
Misoprostol	Prostaglandin E_1 analogue	800–1000 μg rectally/vaginally/sublingually	Shivering Pyrexia Diarrhoea	Allergy to misoprostol or other prostaglandins

Table 2

inflated with 500–1000 ml of sterile water. The balloon should be used alongside an oxytocin infusion to further promote uterine contraction.

Uterine artery ligation

Ligation of the bilateral uterine or internal iliac arteries may help to reduce haemorrhage. Ligation of the arteries can be technically difficult, and the presence of collateral vessels may reduce effectiveness. Early senior involvement is essential. Interventional radiology can be utilized to facilitate cannulation of the internal iliac arteries. This allows catheterization of the uterine arteries, which enables uterine artery balloon occlusion or selective uterine artery embolization. This specialist interventional radiology procedure can be used in either elective cases (placenta praevia or accreta) or in the emergency setting. Due to its specialist nature this service may not be available in all hospitals, particularly out of hours.

Hysterectomy

In drastic cases where uterine bleeding cannot be controlled by any of the above measures, emergency hysterectomy may be needed.

Blood conservation techniques

Early replacement of blood products should be considered. However, transfusion of blood and blood components are not without complications.[9] There are the associated risks of blood transfusion-related immunosuppression, microchimerism, alloimmunization and the potential of an increase in blood-borne cancers in recipients.[10]

Transfusion-related acute lung injury (TRALI) is another real risk and the most common cause of death following transfusion, accounting for 51% compared with 27% caused by non-ABO and ABO-related haemolytic transfusion reactions.[9]

Risks aside, the availability of blood is also reducing as more donor restrictions are enforced.

For all of these reasons blood conservation techniques should be embraced commencing with the recognition of antepartum anaemia and treatment aimed at replenishing iron stores.

Cell salvage

Intraoperative cell salvage (IOCS) have been endorsed by several authoritative bodies including CEMACE, Obstetric Anaesthetists' Association and NICE guidelines. It is considered as a clinically effective and cost-effective means of providing autologous red cells.[4] The NICE guideline[11] addressing intraoperative blood cell salvage in obstetrics also acknowledges that it may also be useful when there are difficulties with cross matching. However, there was no statistically significance in the overall reduction observed in donor blood transfusion associated with the routine use of cell salvage during cesarean section in the SALVO study, a randomized controlled trial of IOCS during caesarean section in 3028 women.[12]

The theoretical safety concerns include infusion of fetal cells (which could potentially cause haemolytic disease in future pregnancies) and the potential risk of amniotic fluid embolism (AFE).[10]

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When considering AFE, the risk can be reduced by the use of two suctions, with cell salvage commencing after the majority of the amniotic fluid has been suctioned away to a separate container. Leucocyte depletion filters should also be used.

The risk of maternal alloimmunization is also considered to be small. Fetal red cells may be entrained into the mother's circulation at any time antenatally or during intrapartum. As such, any incompatibility between maternal and fetal red cell antigens risks maternal alloimmunization, with the risk of haemolytic disease in future pregnancies. Rhesus factor incompatibility is a common problem for Rhesus-negative mothers who therefore routinely receive anti-D immunoglobulin to counteract this. Kleihauere Betke testing post-natally enables the appropriate titration of the anti-D dosage.

The use of IOCS in obstetric haemorrhage is recommended particularly in consenting patients who refuse blood products. Ideally obstetric units would have access to a cell salvage service provided by adequately trained personnel available 24 hours a day. Close attention to coagulation is essential as IOCS only contains suspended red blood cells.

Anaesthetic considerations

Senior anaesthetists must be involved in the early management and resuscitation of patients suffering a major haemorrhage.

In many cases, the emergent nature of the case predisposes the use of general anaesthesia. The degree of haemodynamic instability should guide the choice and dose of induction agent. Steps should be taken to reduce the risk of aspiration with antacid prophylaxis (ranitidine, metoclopramide and sodium citrate) and rapid sequence induction.

Arterial line monitoring provides accurate and rapid blood pressure monitoring, access for frequent blood sampling and serial blood gas analysis. Central venous access may be required for vasopressor or inotropic support.

Due to the associated cardiovascular instability and potential coagulopathy, neuraxial anaesthesia may be contraindicated in massive haemorrhage. This should be decided on an individual basis.

In an elective setting where major blood loss is anticipated, the decision between general and regional anaesthesia is decided by the anaesthetist, the patient and the anticipated degree of blood loss.

Postoperative management

Patients who suffer an obstetric haemorrhage will require ongoing monitoring and close observation. This patient group will need level two or three care postoperatively to continue resuscitation and administration of supportive medication and transfusions and to monitor for ongoing bleeding. ◆

REFERENCES

1 Knight M, Bunch K, Tuffnell D, et al. eds. Saving lives, improving mothers' care – lessons learned to inform maternity care from the UK and Ireland confidential enquiries into maternal deaths and morbidity 2014-16. *National Perinatal Epidemiology Unit, University of Oxford Oxford*, 2018.

2 Knight M, Kenyon S, Brocklehurst P, et al. eds. Saving lives, improving mothers' care e lessons learned to inform future maternity care from the UK and Ireland confidential enquiries into maternal deaths and morbidity 2009-12. *National Perinatal Epidemiology Unit, University of Oxford*, 2014.

3 Zwart JJ, Dupuis JR, Richters A, et al. Obstetric intensive care unit admission: a 2 year nationwide population-based cohort study. *Intensive Care Med* 2010; **36:** 256–63.

4 Mavrides E, Allard S, Chandraharan E, et al. on. Prevention and management of postpartum haemorrhage. *BJOG* 2016; **124:** 106–49.

5 Rizvi F, Mackey R, Barrett T, McKenna P, Geary M. Successful reduction of massive postpartum haemorrhage by use of guidelines and staff education. *Br J Obstet Gynaecol* 2004; **111:** 495–8.

6 Collis RE, Collins PW. Haemostatic management of obstetric haemorrhage. *Anaesthesia* 2015; **70:** 78–86.

7 Solomon C, Collis RE, Collins PW. Haemostatic monitoring during postpartum haemorrhage and implications for management. *Br J Anaesth* 2012; **109:** 851–63.

8 WOMAN Trial Collaborators. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomized, double-blind, placebo-controlled trial. *Lancet* 2017; **389:** 2105–16.

9 Banks A, Norris A. Massive haemorrhage in pregnancy. *Cont Educ Anaesth Crit Care Pain* December 2005; **5:** 195–8.

10 Blood transfusions: more is not necessarily better. *Int J Obstet Anesth* October 2009; **18:** 299–301.

11 NICE. Intraoperative blood cell salvage in obstetrics. *Interv procedures guidance* November 2005, https://www.nice.org.uk/guidance/ipg144 (accessed 30 April 2019).

12 Khan K, Moore P, Wilson M, Hooper R, et al. On behalf of the SALVO study group. Cell salvage and donor blood transfusion during cesarean section: a pragmatic, multicenter randomized controlled trial. *PLoS Med* December 2017; **14**: e1002471.

