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Uterine Atony: Management Strategies

Pei Shan Lim*
Universiti Kebangsaan Malaysia Medical Center,
Universiti Kebangsaan Malaysia
Malaysia

1. Introduction

It is estimated about 529,000 mothers die every year (World Health Organisation [WHO] 2005). Postpartum haemorrhage (PPH), a life-threatening condition, remains the major cause of maternal mortality worldwide (Pahlavan et al., 2001). Majority of these mortalities are from Asia (48%) and Africa (47.5%) with only the minority (less than 1%) from developed countries.(Ramanathan & Arulkumaran, 2006) In Malaysia, the Confidential Enquiry into Maternal Deaths (CEMD) from 1991 to 2005 revealed that PPH attributed 13-27% of all reported deaths(Division of Family Health Development, Ministry of Health, 1994; Division of Family Health Development, Ministry of Health, 1996; Division of Family Health Development, Ministry of Health, 2000; Division of Family Health Development, Ministry of Health, 2005).

Although PPH is no longer the leading cause of maternal mortality in the developed countries, it still remains as one of the most important causes of maternal morbidity. Recently, two reports from Canada and United States (Joseph et al. 2007; Callaghan, Kuklina & Berg 2010) reported a 23-26% increase in the rate of PPH. Despite reports of an increasing rate, maternal mortality in these two countries remained low indicating the effective management of PPH. Nevertheless, in developing countries, PPH related maternal mortality remains a serious concern due to limited health care facilities, underdeveloped management strategies and deprivation of trained health care personnel.

Disastrously massive PPH can lead to coagulopathy, pituitary ischaemia, cardiovascular insufficiency, and multi-organ failure. It is also associated with an increased need for blood and blood products transfusion, intensive care admission, peri-partum hysterectomy and its related intra- or post-operative complications. Even in a milder form of haemorrhage, anaemia itself would interfere with bonding and care for the newborn (Devine, 2009).

Uterine atony is identified as the main cause of PPH accounting for about 90% in most reports (Bateman et al., 2010; Carroli et al., 2008; Combs et al., 1991; Doran et al, 1955). In developing countries like Malaysia, uterine atony contributed 37.5% to 67.7% of PPH

* Mohamad Nasir Shafiee, Nirmala Chandralega Kampan, Aqmar Suraya Sulaiman,
Nur Azurah Abdul Ghani, NorAzlin Mohamed Ismail, Choon Yee Lee,
Mohd Hashim Omar and Muhammad Abdul Jamil Mohammad Yassin
Universiti Kebangsaan Malaysia Medical Center, Universiti Kebangsaan Malaysia, Malaysia

associated mortality between 1994-2005 (Division of Family Health Development, Ministry of Health, 1994; Division of Family Health Development, Ministry of Health, 1996; Division of Family Health Development, Ministry of Health, 2000; Division of Family Health Development, Ministry of Health, 2005).

2. Definition

2.1 Postpartum haemorrhage

Postpartum haemorrhage is defined as blood loss of 500ml or more from genital tract in the first 24 hours of delivery. Massive PPH is defined as blood loss of 1000ml or more (Carroli et al., 2008).

Conventionally, PPH is classified according to the timing of its occurrence. Bleeding within 24 hours of delivery is defined as the primary postpartum haemorrhage. Secondary postpartum haemorrhage is defined as bleeding that occurs after 24 hours until six weeks postpartum.

Assessment of blood loss during delivery is commonly performed using visual estimation. This is often inaccurate and underestimated (Prasertcharoensuk et al., 2000). The traditional assumption of transfusing a pint of red blood cells in a patient who has bled 500 ml blood will increase the haemoglobin to 1 gm is only accurate if not actively bleeding. Estimation of blood loss as well as amount to be transfused is impossible to gauge in an ongoing PPH (Gutierrez et al., 2004). Some centres advocate PPH to be significant with a 10% drop in haematocrit from antenatal to postpartum. Nevertheless this requires laboratory facilities which impose delay in the diagnosis and further management of PPH.

The ability of women coping with haemorrhage largely depends on their health status as well as the severity of bleeding. Most healthy pregnant women can tolerate blood loss up to 1500ml as the result of blood volume increment during pregnancy (Bonnar, 2000). However, in the presence of pre-existing anaemia or hypovolaemia, compensatory mechanism will be jeopardised. Individual responses towards blood loss limit the use of clinical signs and symptoms in defining PPH and determining its severity.

2.2 Uterine atony

Uterine atony is defined as failure of myometrium to contract and retract following delivery (Cunningham et al., 2005). Powerful and effective myometrial contractions are vital to arrest bleeding. Uterine atony in contrary, the uterus is soft and 'boggy' with presence of excessive bleeding from genital tract. A prompt recognition followed by uterine massage and administration of uterotonic agents often arrest the bleeding. However, in the presence of already well contracted uterus, any persistent bleeding should prompt exploration for other causes of postpartum haemorrhage such as retained placental fragments or genital tract injuries.

3. Risk factors for uterine atony

Identification of women at risk of uterine atony is of utmost importance to allow optimisation and preventive measures to be taken. Hence, a well-arranged delivery plan

and appropriate referral to a well-equipped centre should be done. The recognised risk factors that are associated with uterine atony are listed in Table 1.

Factors associated with uterine over distension
• Multiple pregnancy
• Polyhydramnios
• Fetal macrosomia
Labour related factors
• Induction of labour
• Prolonged labour
• Precipitate labour
• Oxytocin augmentation
• Manual removal of placenta
Use of uterine relaxants
• Deep anaesthesia
• Magnesium sulphate
Intrinsic factors
• Previous postpartum haemorrhage
• Antepartum haemorrhage
• Obesity
• Age > 35 years

Table 1. Risk factors for uterine atony. (Breathnach & Geary, 2006)

Multiple pregnancies, polyhydramnios and fetal macrosomia cause uterine over-distension. The odds ratio to develop PPH from fetal macrosomia and multiple pregnancies are 1.8 (95% CI 1.4 to 2.3) and 2.2 (95% CI 1.5 to 3.2) respectively (Magann et al., 2005). In the presence of twin-twin transfusion syndrome, the odds ratio increases to 5.1 (95% CI 1.5 to 15.7) (Magann et al., 2005). On contrary, Carroli et al. did not find any relationship between multiple pregnancies with occurrence of uterine atony (Carroli et al., 2008). A study based data obtained from Nationwide Inpatient Sample (NIS), a large public use administrative dataset in the United States, had reported an association of polyhydramnios with uterine atony requiring blood transfusion in the odds ratio of 1.9 (95% CI 1.2-3.1) (Bateman et al., 2010).

Intrapartum factors such as induction of labour, prolonged labour, oxytocin exposure and abnormal third stage are also recognised to associate with uterine atony. Induction of labour had an odds ratio of 1.5 (95% CI 1.2 to 1.7) (Magann et al., 2005) and was the cause of 17% of uterine atony requiring blood transfusion (Bateman et al., 2010) .

Prolonged usage of oxytocin in labour contributes to uterine atony. Grotegut et al. had demonstrated that massive PPH secondary to uterine atony was significantly higher in women who were exposed to oxytocin (Grotegut et al., 2011). The authors proposed that persistent oxytocin administration causes desensitisation of oxytocin receptors which further contributed into uterine atony.

The presence of uterine fibroids or connective tissue disorders may hinder the myometrium contractility thus leading to uterine atony. However, the existing data are conflicting with regards to relationship between uterine fibroids and uterine atony (Hasan et al., 1991;

Qidwai et al., 2006; Roberts et al., 1999; Vergani et al., 1994). Patients with connective tissue disorders are at a higher risk of PPH as compared to the general population (Kominiarek & Kilpatrick, 2007) which is explained by poor connective tissue support. Hence, uterotonic agents would be the first-line treatment for these conditions.

Though identification of risk factors is essential, they have only moderate positive predictive value (Callaghan et al., 2010) as uterine atony can happen in any women with no apparent risk factor. Therefore, although early detection is important, timely and appropriate management is also crucial.

4. Management strategies

4.1 Prevention of PPH

Post-partum haemorrhage is preventable in many ways. Prevention begins early in high-risk women, as early as in preconception period. Prevention and optimisation of anaemia allows better tolerability to variable severity of PPH. Induction and augmentation of labour should be made with clear indications, performed judiciously by skilled birth attendants. Women at high-risk of PPH should be delivered at tertiary centres with well-equipped operation theatre, intensive care unit and blood transfusion services. The International Federation of Gynaecology and Obstetrics (FIGO) promotes active management of the third stage of labour (AMTSL) in all women in order to reduce the incidence of postpartum haemorrhage (Leduc et al., 2009).

4.1.1 Family planning

Low contraceptive prevalence rate leads to high fertility among women. In 2007, based on the United Nation Statistics Division report, contraceptive prevalence rate among married Malaysian women (aged 15 to 49 years old) was at 54% (Department of Economic and Social Affairs, United Nations Statistics Division, United Nation, 2010). In the Malaysian CEMD report from 2001 to 2005, up to 70% of maternal deaths were recognised in women who did not practise contraception. This reflects high parity contributing to more than half of maternal deaths was due to PPH during the same period (Division of Family Health Development, Ministry of Health, 2005).

4.1.2 Risk assessment and stratification

Uterine atony, the commonest cause of PPH, is best prevented by ensuring that immediate haemostasis is achieved by effective myometrial contractility (Mukherjee & Arulkumaran, 2009). Uterine blood vessels supplying the placental bed pass through the myometrium. However, in uterine atony, there is failure of myometrial contractions leading to impaired vasoconstriction of these blood vessels, resulting in excessive blood loss.

Nevertheless up to 60% of women with PPH have no identified risk factors (Mukherjee & Arulkumaran, 2009). Thus, constant awareness, early detection, timely resuscitation and management skills are necessary to overcome this problem.

4.1.2.1 Colour coding system

Colour coding system which was initially introduced by the Ministry of Health of Malaysia in 1989 is a risk stratification method used among women receiving antenatal care. (Table 2)

Prenatal assessment is applied in determining the level and place of antenatal care. Four colour codes are used: red indicates immediate hospital referral or admission, yellow indicates antenatal review by a doctor, green indicates antenatal care can be rendered by a senior nurse and white indicates women with no or low risk who may receive antenatal care in local clinics and can deliver in a low risk birthing centres (Ravindran et al., 2003). These codes are attached to the women's antenatal card using coloured sticker. Women with PPH in previous pregnancies have an increased risk of haemorrhage by 2 to 4 folds when compared to women with no previous history (Waterstone et al., 2001).They are coded red.

Colour codes	Associated risk factors
WHITE	primigravida, age <18 or >40,gravida 6 and above, spacing < 2years or >5years, short stature <145cm, single mother
YELLOW	Mothers with HIV positive or Hepatitis B positive, blood pressure >140/90 and <160/110mmHg with no proteinuria,diabetes, gestation >EDD+7 days.
GREEN	Rhesus negative, pre-pregnancy weight <45kg,medical problem excluding diabetes and hypertension,previous gynaecological surgery, drug/tobacco/alcohol addiction, unsure of last menstrual period, recurrent miscarriage, previous obstetrics history (previous caesarean section, gestational hypertension, diabetes, intrauterine death, baby <2.5 or >4kg, third degree perineal tear, retained placenta.
RED	eclampsia, pre-eclampsia, heart disease, breathlessness on exertion, uncontrolled diabetes, antepartum haemorrhage,symptomatic anaemia, prelabour rupture of membrane, preterm contractions, abnormal fetal heart rate <110/min after 26 weeks and >160/min after 34 weeks

Table 2. Colour coding system based on risk factors, used in antenatal clinics in Malaysia as cited by Ravindran et al. in 2003 (Ravindran et al., 2003)

Although used extensively, the actual value in predicting outcomes is not reflected in clinical practice as reported in the CEMD 2001 to 2005. Maternal deaths in women whom were tagged green actually increased from 13.5% in 2001 to 28.8% in 2005. This is in contrast to deaths among women tagged yellow which decreased from 45.3% in 2001 to 16% in 2005. This was probably due related to these codes (green and white) were considered to be 'low risk' leading to lesser attention given (Division of Family Health Development, Ministry of Health, 2005). Limitation to the colour coding system is that occasionally when the newly onset current problems are overlooked and could have added risks later in pregnancy, e.g. polyhydramnios leading to PPH.

Reliability of colour coding system in Malaysia needs to be reviewed as recommended by Ravichandran et al in 2003. The author reported that the accuracy of the codes in predicting morbidity and mortality were only about 50% in a retrospective cohort of 1122 among 8388 women from several districts in peninsular Malaysia (Ravindran et al., 2003).

4.1.3 Optimisation prior to onset of labour

4.1.3.1 Treatment of anaemia

World Health Organisation defined anaemia in pregnancy as haemoglobin level below 11g/dL (WHO, 1992; WHO, 2007). Iron deficiency anaemia is the commonest cause of

anaemia in pregnancy, being in mild, moderate or severe forms. In developing countries, anaemia is usually associated with malnutrition and concurrent medical disorders which may potentially reduce women's tolerance to PPH (WHO, 1992). Despite its association with serious morbidity and mortality, there is a paucity of data assessing clinical outcomes of mothers and neonates with anaemia. Treatment with oral iron reduces the incidence of anaemia (RR 0.38; 95%CI 0.26-0.55) (Reveiz et al., 2007). Haemoglobin optimisation antenatally is important in an attempt for safe delivery. Women with optimal haemoglobin level are able to tolerate blood loss. The MMR of women with haemoglobin of less than 5g/dL was reported to be increased by 8 to 10 fold (Kalaivani, 2009).

4.1.4 Safe delivery

4.1.4.1 Judicious oxytocin usage

Prolonged usage of oxytocin paradoxically causes uterine atony and PPH (Grotegut et al., 2011). Judicious use of oxytocin during induction and augmentation of labour may prevent uterine atony. A correct diagnosis of labour is of utmost importance in avoiding unnecessary and prolonged exposure to oxytocin. A clear guideline should be drawn for indications of induction of labour.

4.1.4.2 Active management of the third stage of labour

Active management of the third stage of labour is the crucial step in avoiding PPH secondary to uterine atony. AMTSL reduces the incidence of PPH compared to women who were managed expectantly (RR 0.34; 95%CI 0.14-0.87) (Begley et al., 2010) .

The definition of AMTSL varies from use of uterotonic agents immediately after baby is delivered, delivery of the placenta by controlled cord traction (CCT) and early cord clamping and cutting (Prendiville et al., 2000). The International Federation of Obstetrics and Gynaecology (FIGO) and International Confederation of Midwives (ICM) recommended similar approach followed by uterine massage without early cord clamping (ICM and FIGO, 2003). Previous studies have recommended that active versus expectant management which showed significant reduction in the incidence of PPH. Prendiville et al. concluded that expectant management in comparison with AMTSL is three times more likely to result in PPH (OR 3.1; 95%CI2.3-4.2) (Prendiville et al., 1988). Prophylactic administration of uterotonic agents as part of AMTSL has significantly reduced the amount of blood loss (RR 0.5; 95%CI 0.43-0.59) with less requirement of therapeutic oxytocin (RR 0.5; 95%CI 0.39-0.64) (Elbourne et al., 2001).

4.1.5 Skilled birth attendants

Presence of skilled birth attendants in dealing with PPH proved to reduce maternal morbidity and mortality up to 30% (Carlough & McCall, 2005). WHO defines skilled birth attendants to be those with the minimum knowledge and skills to manage normal childbirth and provide basic (first line) emergency obstetric care (Carlough & McCall, 2005). They should be familiar with early identification of uterine atony and are able to initiate basic intervention such as uterine massage and administration of intramuscular/intravascular oxytocin. Prefilled oxytocin (Uniject™) with easy administration is available in low resource countries and is recommended to be in the bags of birth attendants.

Based on the Safe Motherhood Initiative report from 1987 to 2005, the number of deliveries in developing countries attended by skilled birth attendants has increased significantly from 41 to 57% (Safe Motherhood Initiative, 2005). In low resourced settings, skilled birth attendants' knowledge in PPH however was found to be at an average of 60% and less than one- third of them were able to perform bimanual uterine compression (Harvey et al., 2007). Hence, further training, regular drills and audits are needed to enhance their skills and knowledge.

4.1.6 Training

Suboptimal obstetric care has been shown to cause maternal death from PPH. Delay in establishing diagnosis, failure to carry out appropriate intervention and lack of team effort had been associated with poor maternal outcomes (Siassakos et al., 2009). Lombard et al. reported PPH related deaths among women in South Africa from 2002 to 2006 with 2.25 errors per death as compared to 0.61 errors per death in the near missed group (Lombaard & Pattinson, 2009).

Implementation of the training programme has been shown to reduce in the incidence of substandard care (Hofmeyr et al., 2009). Training includes in-service training and drills. In-service training programme involves induction training for all new staffs inclusive of labour ward management. Regular training in the form of continuous medical education sessions (CME), lectures and scientific meetings will ensure updates the knowledge of all staffs.

In obstetrics drills, staffs are trained to be familiar with simulated obstetrics emergency scenarios. Clinical algorithm and action plans are practised either individually or as a team activity. Accurate blood loss estimation enables early recognition of PPH. Ability to perform initial fluid resuscitation, measures on initial ways to stop bleeding such as bimanual uterine and aortic compression, prevent women from further developing hypovolaemic shock.

However, a Bristol based study analysing a cohort of midwives who had undergone training in Practical Obstetrics Multi professional training (PROMPT) revealed a significant reduction in Apgar score of less than 6 at 5 minutes and neonatal encephalopathy (Draycott et al., 2006). However, there is no available published data on the outcome of staff training to reduction of PPH. In Malaysia, joint efforts between the Obstetrics and Gynaecology Society Malaysia, Ministry of Health and Royal College of Obstetricians and Gynaecologists have successfully delivered several obstetrics emergency and live saving courses since 2008. This programme has expanded throughout the whole country as far as invitation to train personnel in Myanmar. A study on the effectiveness of this training programme is currently ongoing.

4.1.7 Facilities

4.1.7.1 Maternal child health clinic

Since introduction of the Maternal and Child Health (MCH) services in 1957, extensive development towards improving access and quality of care had been well established in Malaysia. Majority of women in Malaysia are able to have easy access to healthcare facilities, family planning services and upgraded essential care in obstetrics service. In developing countries, recent estimation of MMR has seen a reduction by 34% from 1990 to 2008, from 440 deaths to 290 deaths per 100,000 live births (Department of Economic and Social Affairs, United Nations Statistics Division, United Nation, 2011). Over the past two decades, improvement in maternal health is reflected by reduction in the trend of MMR

from 47.8 in 1991 to 26.6 per 100,100 live birth in 2005 (Department of Economic and Social Affairs, United Nations Statistics Division, United Nation, 2010). MCH services in Malaysia are inclusive of antenatal care, postnatal home visits, family planning consultation, nutrition support, and immunisation programmes.

4.1.7.2 Red alert system

A designated system to respond to emergency situations allows prompt mobilisation of health personnel to institute timely and optimal patient management. (Gosman et al., 2008). The emergency team is alerted via a paging system simultaneously. In dire emergency such as massive PPH, this system has successfully delivered early interventions hence improving maternal outcomes (Gosman et al., 2008). A delay in intervention of 20 minutes or more had led to a poorer outcome. (Korhonen & Kariniemi, 1994) All the major hospitals in Malaysia with obstetrics unit are equipped with the red alert system.

4.1.8 Risk management and monitoring system

Risk management includes incidence reporting, clinical practice guidelines review, near miss audits and CEMD. Standardised practice among all healthcare personnel is achievable by complying the clinical practice guidelines and hospital protocols. Incidences reporting involving a retrospective detailed documentation of adverse events are done by staffs. The whole document is reviewed by the risk management team to determine any preventable or substandard care. This is followed by a series of event including audit, re-audit, staff-education and training to improve in subsequent care.

Obstetrics near miss events are inclusive of massive PPH and peri-partum hysterectomy (Upadhyay & Scholefield, 2008). Audits of these events allow risk identification and implementation of preventive measures. Brace et al. reported that massive PPH was the major maternal morbidity in Scotland from 2003 to 2005 with the incidence of 3.7 per 1000 births (Brace et al., 2007). Up to 40% of near missed events received suboptimal care (Upadhyay & Scholefield, 2008).

Implementation of CEMD has allowed access of information with regards to the cause of death, areas of substandard care and identification of high risk women (Neilson, 2009). Each maternal death is studied and analysed in detail followed by expert's recommendation. Malaysia CEMD was introduced back in 1991. To date there has been several published reports over the past two decades. This allows identification of deficiency in the health care system. The MOH had put tremendous efforts and resources allocation into improvising the health care system. This is evident by a marked reduction in MMR in recent years (Division of Family Health Development, Ministry of Health, 2005).

4.2 Non-pharmacological/ Mechanical strategies

Varatharajan et al. evaluated the outcome of management for massive PPH using the algorithm `**HAEMOSTASIS**' (**H**elp; **A**ssess and resuscitate; **E**stablished diagnosis; **M**assage of uterus; **O**xytocin infusion and prostaglandins; **S**hift to operation theatre; **T**amponade test; **A**pply compression sutures; **S**ystematic pelvic devascularisation; **I**nterventional radiology and **S**ubtotal/total hysterectomy) (Varatharajan et al., 2011). The algorithm was found to provide a logical management pathway to reduce blood transfusions, hysterectomy, admissions to intensive care units and also maternal deaths (Varatharajan et al., 2011).

4.2.1 Uterine massage

Uterine massage is performed by rubbing or stimulating the fundus of the uterus. It is hypothesised that massage releases local prostaglandins that promote uterine contractility hence reduces bleeding (Abdel-Aleem et al., 2010). Systematic review has shown that uterine massage is effective in preventing PPH. Abdel-Aleem et al. conducted a randomised controlled trial involving 200 women who were allocated to either uterine massage or no uterine massage following active management of third stage (Abdel-Aleem et al., 2006). Women who received uterine massage had lesser amount of bleeding and requirement for additional uterotonic agents (Abdel-Aleem et al., 2006).

In another randomised trial by Abdel-Aleem et al., 1964 women were randomised into 3 groups; intramuscular oxytocin after delivery of the anterior shoulder, sustained uterine massage for 30 minutes followed by delayed oxytocin or received oxytocin and uterine massage immediately after delivery (Abdel-Aleem et al., 2010). It was found that oxytocin was more superior in controlling haemostasis as compared to sustained uterine massage. Uterine massage performed immediately after administration of oxytocin did not show significant additional benefit as compared to oxytocin alone (Abdel-Aleem et al., 2010). The limitation of this trial was that, it was unable to demonstrate the effect of uterine massage on the amount of blood loss in the absence of oxytocin as this was non-ethical.

4.2.2 Aortic compression

Aortic compression can assist in controlling the amount of blood loss by decreasing the blood flow at the distal end including uterine artery (Riley & Burgess, 1994). Aortic compression is achieved via applying pressure with the flat surface of the knuckles above the contracted uterus and slightly to the left (Figure 1). Absence of femoral pulse indicates correct and complete occlusion of the aorta. It is crucial to release and re-apply the pressure every 30 minutes to allow intermittent blood flow to the lower limbs. Aortic compression is a simple intervention that can be used while preparing for a definitive management or during the transfer of patient from a district hospital to another tertiary hospital.

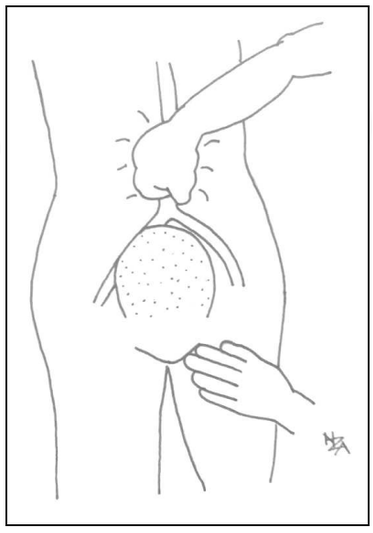


Fig. 1. Aortic compression

External aortic compression devices have been described by several authors (Winter, 1939; Soltan et al., 2009). These have been shown to be effective in reducing the resuscitation time and also the amount of blood being transfused with minimal side-effects reported. However, these devices are not readily available in Malaysia. There is a potential use of this device in our setting especially in district hospital setting. According to CEMD report in the year 2000, 6.6% of PPH mortality had occurred during transfer of patients. Such simple device can be applied by any health care provider (with minimal training) would be of great value in reducing maternal morbidity and mortality.

4.2.3 Bimanual compression

Bimanual compression is performed by inserting the right hand into vagina at anterior surface of the uterus and the left hand is on abdomen at the fundus towards the posterior surface of uterus. The uterus is compressed between the two hands to minimise bleeding (Figure 2). This technique can be used as a temporary measure while patient is being stabilised for definitive treatment.

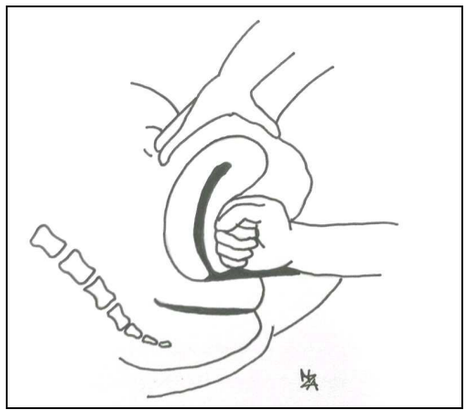


Fig. 2. Bimanual compression

4.2.4 Uterine tamponade

In the past, sterile roller gauze had been used to pack the uterine cavity to reduce blood loss during massive PPH caused by uterine atony (Douglass, 1955). Despite its effectiveness, the popularity of uterine packing has dramatically declined with the wide availability of uterotonic agents (Douglass, 1955).

Nowadays, balloon devices have been recognised as an effective adjuvant strategy for achieving haemostasis in massive PPH in uterine atony. It was hypothesised that intra-uterine balloon exert hydrostatic pressure on the uterine arteries resulting in reduced blood loss (Georgiou, 2009). The most commonly described balloon devices are Bakri balloon, Rusch catheter, Sengstaken-Blackmore catheter, Foley catheter and Condom catheter (Airede & Nnadi, 2008; Keriakos & Mukhopadhyay, 2006; Marcovici & Scoccia, 1999; Majumdar et al., 2010; Vitthala et al., 2009).

Bakri balloon is the only device that is specifically designed for uterine tamponade in massive PPH. It is equipped with large drainage channel that allow drainage of blood from

the uterine cavity (Georgiou, 2009). Although both Sengstaken-Blackmore and Foley catheter have drainage channel, they are small in size thus prone to blockage by blood clots. In addition, the distal tip of Sengstaken-Blackmore catheter would deter the contact between the balloon surface and the fundus of uterus. The other two catheters (Rusch and Condom catheter) do not have drainage channel and thus result in difficulty in drainage of blood from the uterine cavity (Georgiou, 2009).

The capacity of balloon insufflations differs between various types of balloons. Rusch catheter has the largest capacity of 1500 ml of fluid (Keriakos & Mukhopadhyay, 2006) followed by Bakri balloon with 500 ml (Georgiou, 2009) while both Sengstaken-Blackmore catheter and Condom catheter have the capacity to accommodate 300 ml (Georgiou, 2009). Foleys catheter has the smallest capacity with 30 ml and the use of multiple Foley catheters have been described (Marcovici & Scoccia, 1999).

Tamponade test' is used to determine the success of controlling the haemostasis in atonic PPH. A negative `tamponade test' indicate inadequate control of bleeding thus require additional strategies such as applying compressive sutures, systematic pelvic devascularisation or hysterectomy.

The use of concomitant uterotonic agents such as oxytocin and Carbetocin while the balloon is still in-situ is recommended to maintain the tamponade effect (Georgiou, 2009). Antibiotic therapy is also recommended to reduce ascending infection during balloon placement (Keriakos & Mukhopadhyay, 2006). However, there is no consensus on duration of its usage. Most authors remove the balloon within 48 hours. However, variations in the rate of deflation have been reported (Georgiou, 2009).

The adverse effects of the balloon devices reported so far were mainly due to over-distension of the balloon which includes pressure necrosis and uterine rupture. Other reported complications were uterine perforation and air embolism especially if air was used to inflate the balloon. Due to this risk, insufflation of balloon with air is not recommended. With regards to subsequent fertility, successful pregnancies have been reported following the use of these balloon devices (Georgiou, 2009).

As uterine atony is a significant contributing factor in PPH, balloon tamponade devices may play a major role in pre-hospital emergency management prior to safe transfer to tertiary centre in reducing blood loss, hence lowering morbidity and mortality. However, to date there is paucity of data in addressing this issue.

4.3 Pharmacological strategies

Effective uterine contractions are crucial to ensure adequate haemostasis following delivery. Several uterotonic agents have been described to be effective in promoting myometrium contractility hence avoiding the need for surgical intervention.

4.3.1 Oxytocin

Oxytocin is the first line therapy for uterine atony. It acts by stimulating rhythmic uterine contraction particularly in the upper segment. It is administered intramuscularly or intravenously; however the onset of action is delayed if given intramuscularly (3-7minutes)

as compared to immediate onset if given by intravenous route. Furthermore, due to its short plasma half-life of 3minutes, continuous intravenous infusion is preferred (Breathnach & Geary 2009).

Most centres use the regime of 20 IU oxytocin in 500 ml of crystalloid solution (Breathnach & Geary, 2009; Rajan & Wing, 2010). In Malaysia, 40 IU oxytocin in 500 ml of crystalloid solution is given over the duration of 6 hours. In certain circumstances, 80 IU oxytocin in 500 ml of crystalloid solution has been used effectively.

Adverse effects of oxytocin infusion were mainly related to its anti-diuretic properties resulting in water intoxication, manifesting as headache, vomiting, drowsiness and convulsions (Breathnach & Geary, 2009b). In cases where fluid restriction is indicated, concentrated oxytocin via infusion pump is recommended.

4.3.2 Ergometrine

As opposed to oxytocin, ergometrine results in sustained myometrial contraction. As it also acts on the vascular smooth muscle, it is not suitable for those with hypertension, migraine, heart disease and peripheral vascular disease such as Raynaund's syndrome. It is given as 0.25 mg intramuscularly or intravenously with rapid clinical effect within 2 to 5 minutes that can persist up to 3 hours. Ergometrine is metabolised in the liver and has a plasma half-life of 30 minutes. A repeat dose of ergometrine can be given after 5 minutes if the uterus is still not well contracted. Nausea, vomiting and dizziness are commonly reported side-effects (Breathnach & Geary 2009b).

Syntometrine consists of 5 IU oxytocin and 0.5 mg ergometrine in a single preparation. This preparation results in a rapid onset of uterine contraction due to its oxytocic properties and sustained contractility from the ergometrine component (Rajan & Wing, 2010).

4.3.3 Carbetocin

Carbetocin is a long-acting synthetic oxytocin analogue that is administered via intramuscular or intravenous route. The recommended dose is 100 μg. Carbetocin has the advantage of rapid onset of action, within 2 minutes, similar to oxytocin with additional benefit of longer duration of action. These actions do not differ by the route of administration. However, intramuscular Carbetocin (120 minutes) had been reported to give a longer uterine contraction as compared to intravenous route (60 minutes) (Rath, 2009).

Side effects of carbetocin include headache, hypotension, tremor, flushing, abdominal pain and nausea. Rarely, it was associated with dizziness, chest pain, dyspnoea, metallic taste, vomiting, back pain and chills (Rath, 2009).

Randomised controlled trials have found Carbetocin to be associated with lesser requirement for additional uterotonic agents and uterine massage in high risk patients after caesarean deliveries (Su et al., 2007). However, there was no significant difference in the amount of blood loss and rate of PPH between Carbetocin and oxytocin in these women. Furthermore, a single dose of Carbetocin was found to be more convenient than oxytocin infusion that require intravenous line and is time-consuming (Su et al., 2007).

There are three randomised controlled trials assessing the use of Carbetocin following vaginal delivery. Boucher et al. compared Carbetocin with 2-hour 10 IU oxytocin infusion in 160 women with at least one risk factor for PPH (Boucher et al., 2004). The number of women requiring uterotonic intervention (either additional uterotonic agents or uterine massage) was significantly lower in the Carbetocin group (Boucher et al., 2004). Leung et al. randomised 329 women to intramuscular Carbetocin and intramuscular syntometrine and found no difference in the decline of haemoglobin two days after delivery (Leung et al., 2006). Although the rate of PPH was lower in the Carbetocin group, it was not statistically significant (Leung et al., 2006). About 120 women were randomised to Carbetocin and Syntometrine groups had showed lower haemoglobin drop in the Carbetocin group (Nirmala et al., 2009). All three studies had shown Carbetocin to be associated with lower incidence of adverse effects.

Carbetocin is not widely available in developing countries. In Malaysia, though it is available, its use is restricted to high risk cases due to its higher cost.

4.3.4 Misoprostol

Misoprostol is a synthetic analogue of prostaglandin E_1 that has uterotonic properties (Hofmeyr & Gulmezoglu, 2008). Although it has been used widely as uterotonic agents in certain developed country misoprostol has only been registered for therapeutic use in refractory gastro-duodenal ulcers, and has not been made legally available for pregnancy in view of safety concerns in pregnancy (Health Technology Assessment Unit, Ministry of Health Malaysia, 2003).

Misoprostol is a cheap and effective uterotonic agent that can be administered via oral, sublingual, vaginal or rectally. The onset of action is slower if given rectally with more favourable side effects. Adverse effects of misoprostol are dose-related and commonly reported are diarrhoea, shivering and pyrexia (Breathnach & Geary, 2009).

A Cochrane review has concluded that misoprostal administered at a dose of 600 mcg was effective in reducing blood loss after compared to placebo (Gulmezoglu et al., 2007). However, it was found to be less superior to oxytocin in preventing PPH. More recent trials have challenged the superiority of oxytocin. Several studies have shown that there were no difference in the amount of blood loss between misoprostol and oxytocin (Hofmeyr & Gulmezoglu, 2008; Parsons et al., 2006). In fact, Parsons et al. found that those who received misoprostol required less additional uterotonic (Parsons et al, 2006).

Due to its cost and easy storage, misoprostol may indeed be of value to prevent PPH in low resource setting where oxytocin may not be readily available (Mobeen et al., 2011; Nasreen et al., 2011).

4.3.5 Carboprost/Haemabate

In Malaysia, carboprost is used as second-line therapy for uterine atony-related PPH that has failed to respond to either oxytocin or syntometrine. It is an analogue of PG $F_{2\alpha}$ and acts on smooth muscle resulting in myometrial contractions. The recommended dose is 0.25 mg and it can be given as intramuscular or intramyometrial injection. Intramyometrial administration can be performed trans-abdominally or under direct vision during caesarean deliveries (Breathnach & Geary, 2009).

The clinical effect is faster if given intramyometrial (peak within 5 minutes) as compared to intramuscularly (peak within 15 minutes). A maximum dose of 2mg (8 doses) can be given at 15 minutes interval (Breathnach & Geary, 2009).

Commonly reported adverse effects are nausea, vomiting, diarrhoea, pyrexia, bronchospasm and systemic hypertension. Therefore contraindication to its usage would be those with cardiac and pulmonary disease (Breathnach & Geary, 2009).

4.4 Surgical intervention

In most cases, the use of non pharmacological approach and uterotonic agents are able to curb massive bleeding due to uterine atony. Those who are not responding to these interventions may require surgical interventions. Multidisciplinary support involving anaesthetists and haematologists expertise is essential to ensure an optimal outcome.

4.4.1 B-Lynch compression sutures

In the atonic uterus, the vessels especially at the placental bed are unable to contract to secure bleeding. B-Lynch suture, which was first reported in 1997, comprises of vertical compression suture on the uterine vascular system. The reported success rate was 91.7% (95% CI 84.9%-95.5%) (Doumouchtsis et al., 2007). It is a simple, quick and life-saving procedure to combat bleeding from a lax uterus.

Before performing this procedure, its efficacy should be predicted by doing manual compression of the uterus. The surgeon's left hand is placed behind the uterus while the right hand compresses the lower segment of the uterus just above the bladder reflection. If the amount of bleeding reduces, the compression suture is likely to be effective.

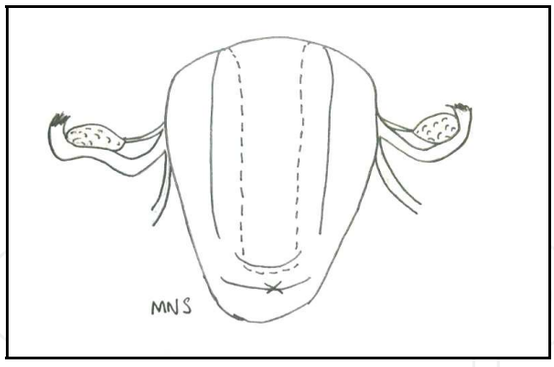


Fig. 3. A puncture 3 cm from the right lower edge of the uterine incision and 3 cm from right lateral border made and threaded through the uterine cavity to emerge at the upper incision margin 3 cm above and its lateral border. Then, the suture is looped over the uterine fundus 3-4 cm from the right border before it being pulled downward vertically to enter the posterior uterine wall at the same level of the first puncture site. The suture is passed through the cavity and emerged on the left uterine border horizontally before it is brought up to the fundus and looped anteriorly. After the needle has passed through the uterine cavity and brought out 3 cm anteriorly and below the incision margin on the left, the two lengths of catgut are pulled tight, while the assistant continuously compressed on the uterus. A knot applied anteriorly to secure the tension.

Lloyd-Davis position is preferred when performing this procedure as the vaginal bleeding can be assessed simultaneously. B-Lynch suture is performed by using absorbable sutures with round bodied needle. The technique B-Lynch suture application is described in Figure 3. B-Lynch surgical technique is relatively safe and allows fertility preservation. Two uterine necroses were reported. (Joshi & Shrivastava M, 2004; Treloar et al., 2006) However, these two cases had received numerous comments and queries regarding the suturing techniques. In one of the comments, B-Lynch had stated among 948 successful cases of B-Lynch sutures worldwide only seven cases failed. (B-Lynch, 2005) Allam et al reviewed 10 case reports involving a total of 38 women who underwent B-Lynch surgical technique for massive PPH. There were 36 successful cases with 2 failures reported. Till date, no known post-operative mortality reported (Allam & B-Lynch, 2005).

4.4.2 Hayman suture

Hayman uterine compression suture (Figure 4) is another method which has been described to arrest bleeding in uterine atony. This technique does not require lower segment hysterotomy therefore it is a good option when PPH occurs following vaginal delivery (Hayman et al., 2002). It is faster, easier and less traumatic to the uterus. The success rate of this procedure is approximately 93.75% (Nanda & Singhal, 2011). However, it may entrap blood within the uterine cavity and subsequently induces haematometra, pyometra and uterine necrosis (B-Lynch, 2005)

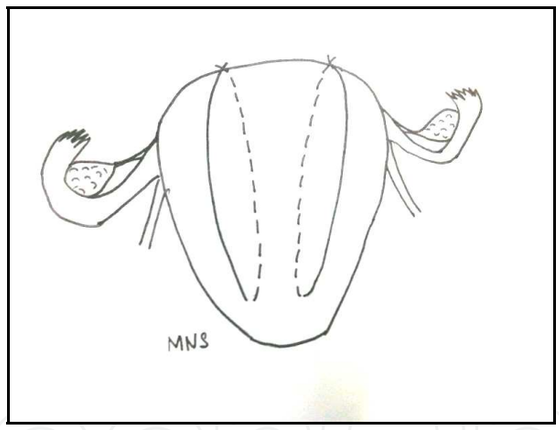


Fig. 4. This procedure involves making two stitches approaching from below the bladder reflection anteriorly to the posterior wall of the uterus at the same level. The knots are placed at the fundus while the uterus is being compressed by an assistant simultaneously.

4.4.3 Vascular ligation/ Occlusion

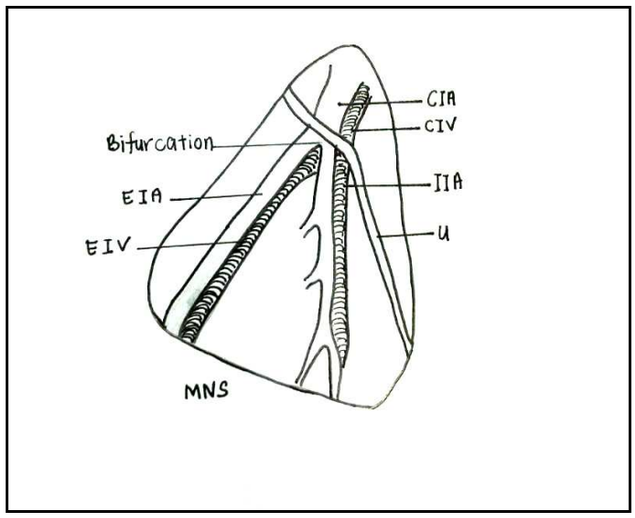
Currently there is no evidence or consensus regarding the superiority of one treatment to another in massive PPH. The limitations are depending on the availability and experience of surgeons, facilities, and local policies. In the past, laparotomy has been advocated to facilitate devascularisation. Vascular ligation is advocated following failure of compression sutures before resorting to hysterectomy is considered, especially when fertility is of concern. However with recent advancement of less invasive radiological intervention, it has become a viable alternative to vascular ligation.

4.4.3.1 Bilateral uterine artery ligation

This easier technique with fewer complications was first described by Waters in 1952 (Waters, 1952). It involves a low abdominal approach like in Pfannenstiel incision. The uterus is exteriorised and pulled upward to facilitate identification of uterine vessels. An absorbable suture is placed 2 cm below the bladder reflection on both sides of the uterus avoiding the ureters. This technique occludes the ascending branch of uterine vessels, with reported success rate of 80-96% (Morel et al., 2011). This procedure is technically safe other than possible risk of ureteric injury.

4.4.3.2 Bilateral internal iliac (hypogastric artery) ligation

This is one of the oldest surgical technique (Figure 5) introduced as early as 1960's (Sziller et al., 2007). It requires a good knowledge of anatomy to avoid inadvertent injuries to the external iliac vessels and ureters. The success rate of internal iliac artery ligation varies between 42-93% (Morel et al., 2011). Incorrect ligation entails high risks of limbs ischaemia, gluteal claudication, further bleeding and possible ureteric and nerve injury.



(EIA: external iliac artery; EIV: external iliac vein; CIA: common iliac artery; CIV: common iliac vein; IIA: internal iliac artery; U: ureter)

Fig. 5. The broad ligament is opened and traced upward until at the level of bifurcation of common iliac artery parallel to the sacroiliac curvature. The ureter is commonly on the medial leaf of the broad ligament after crossing the bifurcation of common iliac artery. The vascular sheath needs to be cleared for better visualisation and recognition, minimising inadvertent ligature and venous injury. The internal iliac is a branch of medio-inferior after the bifurcation of common iliac artery. By using a right angle forceps to isolate this vessel, an absorbable ligature is placed 1 to 2 cm below the bifurcation. Following this, a distal pulse at femoral artery is checked to ensure its patency. The same procedure is repeated to the contra-lateral side (Given et al., 1964).

4.4.3.3 Other type of vascular ligation

Many other vascular ligation techniques had been described. For example, triple ligations (Tsirulnikov, 1979) and stepwise sequential ligation (AbdRabbo, 1994).

4.4.4 Embolisation

Uterine artery embolisation is relatively a new technology in managing PPH. It is only available in tertiary hospitals and it requires an interventional radiologist with the attending obstetrician. This procedure requires haemodynamic stability. Ideally, anticipation of its role is best done pre-operatively example in morbidly adherent placenta. However, uterine atony related PPH often unpredictable hence its use is limited. In cases where balloon tamponade has partially reduced bleeding, concurrent use of uterine artery embolisation may be of value to avoid hysterectomy for conserving fertility.

The success rate of emergency uterine artery embolisation for refractory uterine atony ranges from 70 to 100% (Soncini et al., 2007). As pelvic vasculature is very rich in anastomosis, both sides of uterine artery occlusion are required to ensure its effectiveness.

Possible complications include procedure failure with persistent bleeding, infection, vascular injury, postoperative pain and fever. The overall risk is approximately 5% (Soncini et al., 2007). However the reproductive function following this procedure is maintained (Soncini et al., 2007) but may be associated with malpresentation, preterm delivery and PPH.

4.4.5 Hysterectomy

Peri-partum hysterectomy for PPH is a difficult decision to make but a life saving definitive procedure. Although this is usually the last resort however early consideration should be given in selected cases especially when fertility is of less concern and in morbidly adherent placenta. The incidence varies up to 8 per 1,000 deliveries (Lone et al., 2010).

Peri-partum hysterectomy has a morbidity rate of 30-40% (Christopoulos et al., 2011). Complications include ureteric and bladder injury, persistent bleeding requiring re-exploration, pneumonia, and urinary fistula (Christopoulos et al., 2011).

Peri-partum hysterectomy can be performed either as total or subtotal hysterectomy. A total hysterectomy reduces risk of cervical stump malignancy (El-Jallad et al., 2004), but requires longer operating time and has higher rate of urinary tract injuries. A subtotal hysterectomy is faster and safer (Rahman et al., 2008) but regular cervical screening is mandatory.

5. Role of intensive care management

5.1 Intensive care unit (ICU)

Critical care management is an essential component in the management of PPH. A timely management with early involvement of a multidisciplinary team is likely to result in a better maternal outcome by arresting the progression to multi-organ failure, hence lowered morbidity and mortality (Demirkiran et al., 2003; Price et al., 2008; Price et al., 2009).

Postpartum haemorrhage, which contributed to 15% of maternal deaths, has been reported in CEMACH as preventable death or morbidity in some cases. Only a third of mothers who died had received some form of intensive care management (Wong, 2011).

For deaths attributable to PPH, which occurred outside the ICU, the main contributory factors were:

1. Failure to recognise the severity of PPH.
2. Delay in referral to anaesthetist and ICU.
3. Sub-optimal management of PPH while awaiting ICU transfer.

In contrast to the obstetric management of PPH, the critical care management is likely independent of its cause. The majority of obstetric patients who require ICU admission suffer from complications of PPH, sepsis and hypertensive disorders (Naylor & Olson, 2003; Williams et al., 2008).

5.2 High dependency unit (HDU)

The HDU is a specific area in a hospital that provides either a 'step-up' or 'step-down' care as compared to a general ward or ICU respectively. It provides an intermediate care for invasive monitoring and support for patients at risk of developing organ failure. Patients who require mechanical ventilation or suffer multiple organ failure or dysfunction are best managed in ICU (Price et al., 2009).

Early involvement of the anaesthetist at this stage allows assessment to determine if there is a need to 'step-up' to ICU care. Indications for ICU transfer in PPH are shown in Table 3.

Indications for transfer to ICU	
Respiratory	Need for mechanical ventilation Severe respiratory acidosis (uncorrected) Airway protection
Cardiovascular	Inotrope support Pulmonary oedema
Renal	Renal replacement therapy Severe metabolic acidosis (uncorrected)
Neurological	Deteriorating / Poor Glasgow coma scale (GCS)
Others	Multi-organ failure Hypothermia

Table 3. Indications for transfer to ICU

5.3 Transport of the critically ill

When transfer is needed in severely ill patients, it should be done without any delay. This is to ensure closer or more intensive monitoring, rapid resuscitation and more detailed assessment and therapy. A pre-planned and well-prepared transfer reduces the morbidity of patient and allows rapid and safe transfer. Sufficient notice is necessary to the recipient unit to allow adequate time for assembly of equipment and monitors as well as allocation of staff and presence of intensivist on site for rapid assessment upon arrival. In an unstable patient, the minimum team for transfer should consist of a trained and skilled doctor who is able to re-intubate a ventilated patient and to detect any change in condition, a nurse and two assistants to manoeuvre the bed (Guise & Segel, 2008; Haupt et al., 2003; Price et al., 2009; Price et al., 2008).

5.4 Staffing for critical care management team

Early multidisciplinary involvement and planning for critical care is crucial in the management of PPH. This should involve the obstetricians, midwives, physicians, intensivists, anaesthetists, haematologists, blood bank technicians, nursing and other allied health professionals. The role of each of the main personnel in ICU is defined below.

Early combined care of high-risk patients with intensivist/anaesthetist, as early as antenatal period, is prudent in reducing morbidity. Intensivist/anaesthetist plays a key role in the critical care management. This enables immediate detection and early management of complications, hence, may prevent or lower morbidity and mortality. (Guise & Segel, 2008; Martin & Foley 2006; Plaat & Wray, 2008)

Nursing the critically ill is a complex job. Their main role is to provide continuous close monitoring of the patient. They are able to analyze patient's clinical changes, anticipate possible complications leading to shorter recovery period and better emotional support for both the patient and family members. (Price et al., 2008; Simpson & Barker, 2008; Guise & Segel 2008)

Physiotherapist plays an important role in reducing overall morbidity of the patient. Post-operative physiotherapy enables a faster recovery phase, lower risk of ventilation-associated sepsis or pneumonia, and a shorter ICU stay. (Daber & Jackson 1987; Skinner et al., 2008; Thomas et al., 2006)

5.5 Blood bank

Blood bank facilities in a hospital are essential for immediate provision of blood in cases of massive PPH. Adherence to blood bank policies and guidelines is necessary to avoid injudicious use of blood and blood products. Liaison with haematologist will go a long way to ensure appropriate handling and usage of blood and blood products.

5.6 Haemodynamic monitoring

Acute circulatory failure or shock is a condition in which there is inadequate tissue perfusion. The main aim of management is to restore perfusion to the compromised areas in order to provide adequate oxygenation to the affected tissue. In situations where the diagnosis is in doubt, resuscitation is initiated to improve the patient's haemodynamic status before appropriate definitive therapy is rendered (Wise & Clark 2010b).

Identification of patients who require resuscitation, and assessment of its adequacy thereof, is essential in critical management. Clinical assessment of patient's haemodynamic status is easy to perform and rapidly informative. This includes clinical parameters such as conscious level (Glasgow Coma Scale), pulse rate, respiratory rate, capillary refill and urine output (Pearse & Rhodes, 2004; Price et al., 2008).

Monitoring equipment provides additional information to assess adequacy of resuscitation efforts. This can be broadly categorised into non-invasive and invasive types of monitoring. The former includes continuous electrocardiography, non-invasive blood pressure monitoring, pulse oximetry and capnography, while the latter includes direct measurements of intra-arterial blood pressure, central venous pressure, pulmonary artery pressure, central venous

oxygen saturation, and cardiac output. In massive obstetric haemorrhage, invasive monitoring may be crucial to allow continuous assessment of the haemodynamic status until clinical improvement occurs. However, not all sophisticated monitoring equipment may be available in every hospital, in which case management decisions may need to be based on clinical assessment (Martin & Foley, 2006; Moore & Chandraharan, 2010; Pearse & Rhodes, 2004).

5.7 Haemodynamic management

Cardiovascular support may be required in women with PPH to maintain an adequate cardiac output and blood pressure. This includes fluid administration, treatment of abnormal heart rate and rhythm, use of vasoactive agents, thrombolysis, ventilatory support and uncommonly other mechanical devices, such as pacemaker, ventricular assist devices, or extracorporeal membrane oxygenator (Pearse & Rhodes, 2004; Price et al., 2008).

Rapid intravenous infusion is the key to initial resuscitation. The aim is to improve microvascular blood flow to provide tissue oxygenation by expanding the intravascular volume and improving cardiac output. The type and amount of fluid used is dependent on the underlying aetiology of circulatory insufficiency, and to a lesser extent the availability of any particular fluids. The choice between crystalloid and colloid during resuscitation remains a debate. Excessive use of normal saline has been reported to result in hyperchloraemic acidosis. The composition of Ringer lactate solution closely resembles that in the plasma and is considered to be one of the most "physiological" cystalloids available for use. In contrast to crystalloid, colloid remains longer in the intravascular compartment and therefore may be more effective in severe hypovolaemia (Bauer et al., 2009; Shoemaker & Kram, 1988).

A useful guide is to infuse an initial amount of 10 ml/kg of colloid or 20 ml/kg of crystalloid followed by clinical and haemodynamic assessment of the response. More fluids should be administered if the patient remains hypovolaemic. Approximately three times the volume of crystalloid is required to achieve blood volume expansion to the same degree as colloid. Large volumes of intravenous fluids may have to be administered while awaiting the availability of cross-matched blood (Price et al., 2008; Shoemaker & Kram, 1988).

Coagulopathy may ensue during massive blood loss or as a result of massive blood transfusion. Correction of hypothermia is essential to prevent exacerbation of coagulopathy. Severe acidosis may warrant correction with sodium bicarbonate to prevent acidosis-induced myocardial depression, provided ventilation is not compromised (Bauer et al., 2009; Price et al., 2009).

Patients who have no prior cardiac disease usually respond to volume resuscitation with intravenous fluids, blood and blood products. However, a small percentage of patients, especially those with pre-existing cardiovascular compromise, may require vasoactive agents to improve cardiac function and peripheral circulation. Cardiac failure secondary to coronary artery insufficiency may require vasodilator therapy using glyceryl trinitrate. Loop diuretics may be needed to reduce pulmonary congestion in acute pulmonary oedema associated with left ventricular failure. Infusion of a positive inotrope (e.g. epinephrine, dobutamine) and/or a vasoconstrictor (e.g. norepinephrine) should be considered to provide circulatory support and maintain adequate renal perfusion. Mechanical devices such as ventricular assist devices and intra-aortic balloon pumps to improve cardiac output

have been advocated in critically ill patients unresponsive to pharmacologic therapy. (Pearse & Rhodes, 2004; Price et al., 2008).

5.8 Respiratory management

Acute respiratory distress syndrome is one of the complications of massive haemorrhage, which may require ventilatory support. The aim of respiratory management is to maintain adequate gas exchange by ensuring a patent airway, sufficient oxygen therapy and sustainable ventilation. Airway management is a challenge in pregnant women due to a combination of factors such as weight gain, fluid retention, and enlarged breasts resulting in difficult laryngoscopy. The patient may rarely present with stridor, and difficult endotracheal intubation may complicate airway management. (Price et al. 2009)

5.9 Renal management

Acute renal failure is one of the main causative factors of maternal deaths following massive PPH. The mainstay of treatment is aimed at providing support by minimising damage to the surviving nephrons till the kidneys recover. Restoration of circulation by fluid or blood together with the judicious use of vasopressors will improve perfusion pressure and maintain adequate urine output (> 0.5-1 ml/kg/hour). Electrolyte derangement, especially involving potassium, needs to be corrected. Severe acidosis may require sodium bicarbonate therapy. Renal replacement therapy, if indicated, should be started without delay following early nephrology consultation. (Demirkiran et al., 2003; Anthony & Johanson, 1996)

5.10 Others

Prevention of venous thrombo-embolism is necessary in view of the hypercoagulable state during post-partum period. This can be achieved with compression stockings, adequate hydration, thromboprophylactic agents, limb physiotherapy and early mobilisation (Price et al., 2009).

6. Transfusion of blood & blood products

According to British Committee for Standards in Haematology, the therapeutic aim for management of massive blood loss is to maintain:

- Haemoglobin ≥ 8.0 g/dl
- Platelet count ≥ 75 x 10^9/l
- Prothrombin time ≤ 1.5 mean control
- Activated prothrombin time ≤ 1.5 mean control
- Fibrinogen ≥ 1.0 g/l

Massive PPH would require blood and blood products to replace the clotting factors, fibrinogen and platelets. There are various definitions on massive blood transfusion. These include replacement of the full circulating volume within 24 hours, loss of 50% of circulating blood volume within 3 hours, estimated blood loss of more than 5000 ml, or transfusion of more than 4 units of blood in an hour with ongoing blood loss (Moore & Chandraharan, 2010; Wise & Clark, 2010a).

Massive transfusion may be complicated by citrate toxicity, acid-base and electrolyte disturbances, and hypothermia. Other risks of transfusion include haemolytic reactions, anaphylactic reactions, febrile non-haemolytic reactions, transmission of infectious disease, and alloimmunisation (Moore & Chandraharan, 2010; Padmanabhan et al., 2009).

6.1 Red cell transfusion

Concentrated red blood cells (RBC) is the first line therapy in massive PPH. The aim is to improve oxygenation in the peripheral tissues. Each unit of concentrated RBC improve haemoglobin by 1.0 g/dl as well as haematocrit by 3%. Commencement of blood transfusion should be guided by clinical assessment rather than result of full blood count (Bolan & Klein, 2007; Klein, 2006; Padmanabhan et al., 2009).

6.2 Management of coagulopathy

Management of transfusion-associated coagulopathy entails anticipation, prompt recognition and early initiation of therapy. Late detection of disseminated intravascular coagulation (DIVC) results in systemic bleeding which may lead to multi-organ failure and poor prognosis. Hence, it is not necessary to wait for laboratory results if coagulopathy is suspected and clinical bleeding is present. The management of coagulopathy should be in liaison with the haematologist. Blood components that are required in management of DIVC include fresh frozen plasma, cryoprecipitate and platelet (Bolan & Klein, 2007; Chandraharan & Arulkumaran, 2007; Klein, 2006; Moore & Chandraharan, 2010;).

Fresh frozen plasma (FFP) is derived from whole blood. It contains all the coagulation factors, main inhibitors, anti-thrombin III and protein C. A prothrombin time (PT) and APTT ratios of >1.5 are significantly associated with an increased risk of clinical coagulopathy. About 5 to 10 units of cryoprecipitate (containing Factor VIII, fibrinogen, factor XIII and fibronectin) should be infused following FFP used to correct hypofibrinogenaemia. Platelet transfusion is required when the count is lower than 50 $x10^9/l$ in the context of persistent bleeding (Key & Negrier, 2007; Klein, 2006).

Recombinant Factor VIIa (rFVIIa) is an activated form of Factor VII. It is licensed for use in haemophilia but not in massive PPH due to paucity of data on its use. There are currently no guidelines for its use in obstetric haemorrhage, although proposals for guidelines are starting to appear. However, it may have a role in the management of massive PPH refractory to conventional treatment. Recombinant Factor VIIa was found to be effective in a review of 65 case studies of women with massive PPH. There are limitations to its use, including limited information about safety when used in obstetric patients, cost and non-response in a minority of patients. Further evaluation is required (Haynes et al., 2007; Karalapillai & Popham, 2007; Searle et al., 2008).

6.3 Jehovah witness

It is important to identify women who refuse blood and blood products, e.g. Jehovah's Witnesses. These patients will not accept either the whole blood or its other main components i.e. packed red cells, white blood cells, platelets, or plasma. Consent or advanced directive' should be obtained with regards to the acceptability of types of blood

products or other recombinant factors. (Moore & Chandraharan, 2010; Wise & Clark, 2010a). Various strategies have been employed to prevent PPH and requirement of blood transfusion in these high-risk patients.

Correction of anaemia prior to delivery is of utmost importance. Use of iron supplementation and good nutrition with appropriate dietician referral are usually employed. In selected cases, erythropoietin may be given after discussion with haematologist.

The use of Carbetocin as the first line uterotonic agent at AMTSL had been shown to be associated to lesser blood loss (Nirmala et al., 2009); In the event of uterine atony, early involvement of senior personnel and a more aggressive approach to definitive treatment i.e. hysterectomy; in cases with retained placenta, intra-umbilical oxytocin injection instead of manual removal of placenta has been shown to reduce the amount of blood loss though not at a significant level (Lim et al., 2011). These intra-partum strategies will reduce the risk of massive blood loss and hence reducing the need for transfusion.

When operative intervention is needed, certain steps to minimise bleeding may be employed. The use of diathermy or blunt dissection to open the layers of abdominal wall will reduce bleeding as compared sharp dissection. Appropriate autologous blood transfusion techniques, such as normovolaemic haemodilution, pre-operative autologous blood donation, intra-operative red cell salvage, should be considered in this group of women to avoid blood transfusion (Moore & Chandraharan, 2010; Wise & Clark, 2010a; Heard & Quinn, 2010). However, these services are not readily available in all centres. Hence these women should have their deliveries in centres that provide this particular service.

The use of cell salvage may be acceptable by Jehovah's Witness as the blood remained in continuity with their body circulation (King, 2009; Remmers & Speer, 2006). However, its use in obstetric cases due to PPH is still viewed negatively for the potential fear of amniotic fluid embolism due to fetal cells, fat or faecal matter contamination. This potential risk has to be communicated to the patient.

Acute normovolaemic haemodilution may be used by the anaesthetist intra-operatively during either elective or emergency cases. Following anaesthesia, a total of 15 to 20 ml/kg of blood is withdrawn from the patient and is replaced by either crystalloid or colloid. The blood is kept and re-transfused after completion of operation. The re-transfused blood will contain clotting factors and platelets. This procedure is also acceptable to the Jehovah's Witness as the replaced blood is in continuity with body circulation. However, this procedure is not without complication as it may cause cardiovascular instability (Remmers & Speer, 2006).

Pre-operative autologous blood donation involves repeated donation of blood by the patient at least 4 to 6 weeks prior to the delivery or operation. The blood is kept and transfused if necessary. Though this method can reduce risk of transfusion related infection and reaction, it is not acceptable among Jehovah's Witness. This is in view of discontinuity of blood from their circulation (Heard & Quinn, 2010; Remmers & Speer, 2006).

Other methods acceptable to Jehovah's Witness include the use of antifibrinolytics (aprotinin and tranexamic acid) and Perfluorocarbon-based or haemoglobin-based oxygen-carrying compounds (Hemopure, Oxygent or PolyHeme). These products have been shown to reduce the risk of re-laparotomy for bleeding and the need for blood transfusion (Heard & Quinn, 2010).

7. Conclusion

PPH is a major cause of maternal deaths worldwide and uterine atony is the main attributor. In order to reduce maternal mortality, one of the strategies should be towards primary, secondary and tertiary prevention of uterine atony. Close relationship with ancillary support i.e. blood bank facilities, intensivists and ICU care completes the team in management of atonic PPH.

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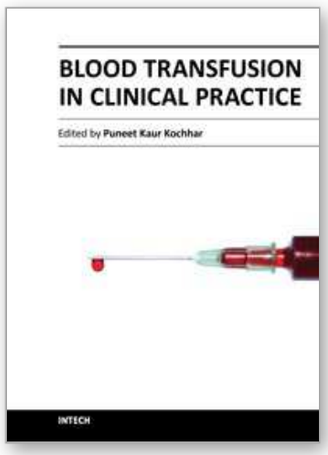

Blood Transfusion in Clinical Practice

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Blood Transfusion in Clinical Practice focuses on the application of blood transfusion in different clinical settings. The text has been divided into five sections. The first section includes a chapter describing the basic principles of ABO blood group system in blood transfusion. The second section discusses the use of transfusion in various clinical settings including orthopedics, obstetrics, cardiac surgery, etc. The third section covers transfusion transmitted infections, while section four describes alternative strategies to allogenic blood transfusion. The last section speculates over immunomodulatory effects of blood transfusion.

InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
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Unit 405, Office Block, Hotel Equatorial Shanghai
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中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
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