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Massive Postpartum Hemorrhage: Protocol and Red Code

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Abstract

Postpartum hemorrhage (PPH) is the leading cause of maternal death. In developing countries, approximately 8% of maternal death is caused by PPH. Protocols should provide a standardized approach to evaluate and monitor the patients. A standard protocol must be recognized by the institution and must be accepted and known by all team members. Additionally, it is important to have a massive obstetric hemorrhage protocol (red code) for those patients with an important bleeding who require blood products available as soon as possible. In the red code activation protocol there are several key points to consider: the management algorithm must be known and accepted by all team members, a clear and effective communication between the team must be established and all the participants must know the role they play. Massive obstetric hemorrhage has a multidisciplinary implication: obstetricians, anesthesiologists, pediatricians, midwife, nurses, auxiliary staff, and laboratory blood bank staff. The active participation of the multidisciplinary team in simulations before the protocols implementation facilitates the evaluation of critical points and subsequent changes before their final application, the assessment of the adequacy of circuits and infrastructure, as well as a better protocols compliance.

Keywords: postpartum hemorrhage, red code, massive blood transfusion, protocol, multi-professional simulation training

1. Introduction

Postpartum hemorrhage (PPH) is commonly defined as a blood loss of 500 ml or more within 24 h after birth, whereas major PPH is defined as a blood loss of 1000 ml or more within the

same time frame. Major PPH can be further subdivided into moderate (1001–2000 ml) and severe (more than 2000 ml). Secondary PPH is defined as abnormal or excessive bleeding from the birth canal between 24 h and 12 weeks postnatally [1]. The quantification of postpartum blood loss is a subjective parameter that hinders the application of this definition and usually there is an underestimation of the loss.

It has recently been proposed to define PPH as a blood loss that may lead to hemodynamic instability [2].

2. Epidemiology

PPH affects approximately 2% of all women who gave birth: it is associated not only with nearly one quarter of all maternal deaths globally (around 125,000 deaths per year), but is also the leading cause of maternal mortality in low-income countries. PPH is the primary cause of nearly one quarter of all maternal deaths globally. PPH is a significant contributor long-term disability as well as to a number of other severe maternal conditions generally associated with more substantial blood loss, including shock and organ dysfunction [3].

Maternal collapse rate due to major PPH lies somewhere between 0.14 and 6/1000 (14 and 600/100,000) births [4].

3. Etiology of PPH

The causes of PPH can be simplified under the acronym “4T”: tone (atony), trauma (trauma of the birth canal), tissue (retention of remains), and thrombin (clotting disorders). Multiple predisposing factors can be related to these causes (**Table 1**).

The assessment of antenatal risk factors predicts only 40% of PPH cases, with placenta praevia and placenta accreta being the most important identifiable risk factors for severe bleeding. Therefore, 60% of PPHs occur in women with unknown risk factors. Before a primary PPH, a correct etiological diagnosis will be important, since the management will depend on the cause of the hemorrhage.

4. Prevention

Uterine atony is the most common cause of PPH, since it accounts for 80% of it. Therefore, the most effective preventive measure is the active management of the third phase of delivery, which has been shown to reduce PPH by 60% of cases, a significant reduction in postpartum anemia and the need for transfusion [5].

4T's	Etiology	Risk factor
Tone	Overdistension	Multiple pregnancy Fetal macrosomia Polyhydramnios Fetal congenital defects Hydrocephalus
	Muscle fatigue	Prolonged labor Multiparity
	Infection Chorioamnionitis	Prolonged PROM Fever
	Tocolytic drugs	Betamimetics Nifedipine SO ₄ Mg Anesthetics
Trauma	Laceration of cervix, vagina, or perineum	Instrumental delivery Episiotomy
	Injury during cesarean section	Malpresentation Fetal intrauterine manipulation Advanced Hodge line presentation
	Uterine rupture	Previous uterine surgery
	Uterine inversion	Fundal placental implantation Excessive cord traction Multiparity
Tissue	Retained placental products	Previous uterine surgery Placental abnormalities (placenta accreta, increta, percreta) Placenta abruptio Placenta praevia
Thrombin	Congenital coagulation disorders	Hemophilia Von Willebrand disease
	Acquired coagulopathy	Placental abruptio Pre-eclampsia Sepsis Amniotic fluid embolism DIC Hyperfibrinolysis Pharmacologic anticoagulation

Table 1. Postpartum hemorrhage etiology.

The current definition of active management of the third phase of delivery proposed by the World Health Organization (WHO) includes the administration of uterotonics, late cord clamping, and controlled cord traction to obtain the placenta. The uterine massage does not offer benefits in the prophylaxis of PPH, but in the treatment [3].

Most PPHs occur during or immediately after delivery, but a significant proportion of them occur during the first few hours postpartum, so it is necessary to maintain prevention for a few hours. Therefore, it is necessary to use uterotonic drugs with long half-life or forms of administration that maintain the effect during these hours.

The first-line drug is oxytocin, the most effective treatment with fewer side effects [6]. The appropriate dose is 3–5 IU in slow bolus for 1–2 min to avoid undesirable effects or 10 IU intramuscularly. Its administration should start with the output of the anterior shoulder, just after birth or upon exiting the placenta. Because of its short half-life (10–15 min), it is recommended to maintain continuous oxytocin infusion for about 4 h.

Carbetocin is a synthetic analog of oxytocin whose principal advantage is its longer half-life compared with oxytocin (40 min vs. 10–15 min). It has the same side effects and its main indication is the prevention, not the treatment of PPH in elective cesarean sections. The appropriate dose is 100 µg by slow intravenous route. The scientific evidence has shown no differences in the prevention of PPH, only an improvement in relation to the use of additional uterotonics [7].

The use of ergometrine 0.2 mg intramuscularly is an alternative in cases of high risk of PPH. Although slightly more effective than oxytocin, because its half-life is 2–3 h, it has more side effects, especially the risk of hypertensive crisis in hypertensive patients. Its administration must be after the delivery of the placenta [8].

It can be considered as the use of misoprostol 400–600 µg orally or rectally, although it is less effective and has more effects than the previous ones, if no parenteral agents are ready for use or in settings where venous access, needles, or a refrigerator is not available [9].

Administration of tranexamic acid (0.5–1 g intravenously) appears to decrease blood loss following vaginal delivery and after cesarean delivery. In spite of this, more information is needed on its effectiveness and safety profile [10].

5. Maternal collapse

Maternal collapse is defined as an acute event involving the cardiorespiratory systems and/or brain, resulting in a reduced or absent conscious level (and potentially death), at any stage in pregnancy and up to 6 weeks after delivery [4].

The common reversible causes of collapse in any woman can be remembered using the well-known 'aide memoire' employed by the Resuscitation Council of the 4 T's and the 4 H's (Table 2). In a pregnant woman, eclampsia and intracranial hemorrhage should be added to this list, and obstetric-specific causes are clearly more likely and must also be considered systematically. Owing to the lack of robust morbidity data regarding collapse, maternal deaths are often used as a reference point [4].

Hemorrhage is the most common cause of maternal collapse. Causes of major obstetric hemorrhage include postpartum hemorrhage, major antepartum hemorrhage from placenta praevia/

Reversible cause	Cause in pregnancy
4H's	
Hypovolemia	Bleeding (may be concealed) (obstetric/other) or relative hypovolemia of dense espinal block, septic or neurogenic shock
Hypoxia	Pregnant patients can become hypoxic more quickly Cardiac events: peripartum cardiomyopathy, myocardial infarction, aortic dissection, large-vessel aneurysms
Hypo/hyperkalemia and other electrolyte disturbances	No more likely
Hypothermia	No more likely
4T's	
Thromboembolism	Amniotic fluid embolus, pulmonary embolus, air embolus, myocardial infarction
Toxicity	Local anesthetic, magnesium, other
Tension pneumothorax	Following trauma/suicide attempt
Tamponade (cardiac)	Following trauma/suicide attempt
Eclampsia and pre-eclampsia	Includes intracranial hemorrhage

Table 2. Reversible causes of maternal collapse.

accreta, placental abruption, uterine rupture, and ectopic pregnancy. In most cases of massive hemorrhage leading to collapse, the cause is obvious, but concealed hemorrhage should not be forgotten, including following cesarean section and ruptured ectopic pregnancy. Other rarer causes of concealed hemorrhage include splenic artery rupture and hepatic rupture. Blood loss is often underestimated; especially slow, steady bleeding and fit healthy women can tolerate significant loss prior to showing signs of decompensation.

5.1. Hypovolemic shock

Hypovolemic shock due to hemorrhage is defined as the blood loss that results in tissue hypoperfusion, with a maintained deficit of oxygen transport to tissues. The injury suffered by the organs marks the prognosis of bleeding, causing a disruption of metabolism and function of tissues, which brings up metabolic acidosis and contributes to the development of coagulopathy.

6. Diagnosis

Clinical symptoms of hypovolemia may not be present until 10–20% of total whole blood volume is lost.

	Stage 1	Stage 2	Stage 3	Stage 4
Blood loss	Up to 15% (750 ml)	15–30% (750–1500 ml)	30–40% (1500–2000 ml)	Over 40% (over 2000 ml)
Blood pressure	Normal (maintained by vasoconstriction)	Increased diastolic BP	Systolic BP < 100	Systolic BP < 70
Heart rate	Normal	Slight tachycardia (>100 bpm)	Tachycardia (>120 bpm)	Extreme tachycardia (>140 bpm) with weak pulse
Respiratory rate	Normal	Increased (>20)	Tachypneic (>30)	Extreme tachypnea
Mental status	Normal	Slight anxiety, restless	Altered, confused	Decreased LOC, lethargy, coma
Skin	Pallor	Pale, cool, clammy	Increased diaphoresis	Extreme diaphoresis, mottling possible
Capillary refill	Normal	Delayed	Delayed	Absent
Urine output	Normal	20–30 ml/h	20 ml/h	Negligible

Table 3. Signs and symptoms of the major stages of hypovolemic shock.

Hypovolemia can be recognized by tachycardia, diminished blood pressure, and the absence of perfusion as assessed by skin signs (skin turning pale) and/or capillary refill on forehead, lips, and nail beds. The patient may feel dizzy, faint, nauseated, or very thirsty. These signs are also characteristic of most types of shock.

Obvious signs of external bleeding should be noted while remembering that people can bleed to death internally without any external blood loss.

6.1. Stages of hypovolemic shock

Hypovolemic shock can be classified in four stages depending on its severity (**Table 3**).

6.2. Laboratory diagnosis

A single hemoglobin and hematocrit value is not useful for assessing bleeding and its severity. These parameters are poorly sensitive for the early detection of significant bleeding. However, the serial determinations of hemoglobin and hematocrit have very good specificity.

Lactate and pH are analytical parameters that are altered when the metabolism becomes anaerobic. They are sensitive measures to monitor the importance of bleeding and shock. A lactate lower than 22 mg/dL and a pH lower than 7.20 are indicators of hypoperfusion and tissue distress.

7. Management in major obstetric hemorrhage

Hemorrhage is the most common cause of maternal collapse and a consequence of other causes of collapse. There must be a high index of suspicion for bleeding and awareness of the limitations of clinical signs.

The management of PPH requires a multidisciplinary approach: midwives and obstetric first-line staff who must be awarded of important bleeding, senior obstetric staff, and anesthetist, that plays a crucial role in maintaining hemodynamic stability.

Communication with the patient and her birthing partner is crucial, and clear information about what is happening from the outset must be given.

There is limited evidence on appropriate intervention points and management strategies related to the hemostatic management of obstetric hemorrhage.

A primary survey of sever obstetric bleeding should follow a structured approach of simple “ABC”, including evaluation and resuscitation simultaneously.

7.1. A and B: assess airway and breathing

A high concentration of oxygen (10–15 l/min) should be administered, regardless of maternal oxygen concentration. Anesthetic assistance should be requested in case of impaired consciousness [1].

7.2. C: evaluate circulation

Two intravenous lines must be taken and sent blood for diagnostic tests. Full blood count, coagulation, urea, electrolytes, and cross match must be evaluated [1].

Resuscitation management is based on both blood volume and oxygen-carrying capacity. Volume replacement must be undertaken on the basis that blood loss is often underestimated [11]. Compatible blood, supplied with the form of red cell concentrate (RCC), is the best fluid to replace major blood loss and should be transfused as soon as available, if necessary.

Resuscitation based on fluid replacement, blood transfusion, and drug therapy must be guided by hemodynamic goals, regardless of the moment it starts (**Table 4**).

7.3. Monitoring hemostasis

Routine coagulation tests are the most common methods for monitoring hemostasis during PPH, with the advantage of well-regulated quality control [12]. Their main drawback is that

Goals	Value
Arterial blood pressure	90–100 mmHg
Cardiac frequency	<100 hb
Central venous pressure	>6 mmHg
Cardiac index	>2.5 l/min/m ²
Serum lactate	<2 mmol/l
pH	>7.20

Table 4. Hemodynamic and analytic goals in resuscitation.

Immediate venepuncture for cross-match, full blood count, coagulation screen (and fibrinogen), renal and function liver for baseline
Monitor temperature every 15 min
Continuous pulse, blood pressure recording, and respiratory rate
Foley catheter to monitor urine output
Two peripheral cannulae (14G)
Consider arterial line monitoring
Consider transfer to a intensive therapy unit
Documentation of fluid balance, blood, blood products, and procedures

Table 5. Protocol for monitoring in major PPH.

they are too slow to be clinically useful in an acute and evolving situation. In addition, PT/aPTT ratios have limited sensitivity to a developing coagulopathy associated with PPH, and are often normal, despite very large volumes of blood loss [13]. If laboratory-based tests are used, a Clauss fibrinogen must be measured rather than a PT-derived fibrinogen level.

Based on recent studies, point-of-care (POC) testing of coagulation using thromboelastography or thromboelastometry (TEG® and ROTEM®) can provide early feedback to care providers about key changes in the maternal hemostatic profile during PPH. POC testing can be considered for rapid hemostatic assessment during PPH and these technologies have been endorsed in guidelines from the Obstetric Anaesthetists Association (UK) [14], the European Society of Anaesthesiology [15], and the American Society of Anaesthesiologists [16] (Table 5).

8. Fluid replacement

Fluid replacement is based on crystalloids and colloids. There have been no randomized controlled trials comparing the use of colloids with other replacement fluids for resuscitation of women with PPH. There is indirect evidence from a Cochrane review that evaluated 78 trials on the use of colloids in the resuscitation of critically ill patients who required volume replacement secondary to trauma, burns, surgery, sepsis, and other critical conditions. No evidence that resuscitation with colloids reduces the risk of death, compared to resuscitation with crystalloids was found [17]. Furthermore, the use of hydroxyethyl starch might increase mortality. And colloids are more expensive than crystalloids.

Based on the actual evidence, World Health Organization Guidelines recommend that intravenous fluid replacement in severe PPH must be with isotonic crystalloids in preference to colloids [18].

Rapid administration and warming of the infusion are essential issues in fluid therapy in severe PPH. But great amount of fluid replacement must be avoided because they can cause hemodilution and can deteriorate coagulopathy.

By consensus, total volume of 3.5 l of clear fluids (up to 2 l of warmed Hartmann's solution as rapidly as possible, followed by up to a further 1.5 l of warmed colloid if blood still not available) comprises the maximum that should be infused while awaiting compatible blood. The woman needs to be kept warm using appropriate measures.

9. Blood transfusion

9.1. Red cell concentrates and fresh frozen plasma

Transfusion rates have been increasing during recent years, likely due to the increases in rates of PPH [19]. Transfusion is an important indicator of severe obstetric morbidity and women who received four or more units of blood products should be reviewed [20].

The objective of resuscitation is to maintain hemoglobin at 9–10 mg/dl [21]. Early and rapid red cell concentrate (RCC) and fresh frozen plasma (FFP) transfusion in 1:1 rate (RCC: FFP) is the most recommended at the moment to improve hemostasis in severe PPH refractory to medical treatment [22].

If no hemostatic results are available and bleeding is continuing, then, after 4 units of red blood cells, FFP should be infused at a dose of 12–15 ml/kg until hemostatic test results are known [1].

The only strong recommendation on blood transfusion in PPH is that women receive RBCs as soon as possible in case of massive PPH. Because cross-matched blood is not always available, maternity units should have immediate access (within 5 min) to O-negative blood. If the need is less pressing, group-specific blood can be made available more quickly than fully cross-matched blood. Consequently, all maternity units should have their own reserve of blood products if there is no blood bank on-site [23].

FFP is frequently issued as “shock packs” on an activation of major obstetric hemorrhage protocol. The objective is to maintain thrombin generation and fibrinogen by the replacement of coagulation factors as early as possible. The disadvantage is that most women will have normal coagulation and platelets at the time of transfusion and will be receiving blood products with fewer fibrinogen and other coagulation factors than they have been circulating.

If no hemostatic tests are available, early FFP should be considered for conditions with a suspected coagulopathy, such as placental abruption or amniotic fluid embolism, or where detection of PPH has been delayed [1].

9.2. Platelets

Guidelines recommend that the platelet count should be kept more than 50,000/mm³ during active PPH and to achieve this, they should be infused when the count falls below 75,000/mm³ [24]. Except for placental abruption, amniotic fluid embolus, severe preeclampsia, or inherited or immune thrombocytopenia, a platelet count less than 75,000/mm³ is uncommon during PPH.

9.3. Fibrinogen

The clinician should be aware that fibrinogen normally increases during pregnancy; thus, normal ranges for nonpregnant adults often printed on hospital laboratory reports have little relevance to obstetrics. While a fibrinogen level in the immediate postpartum period <4 g/l is reassuring in terms of immediate clotting capacity, it is abnormal and should alert the clinician to the presence of either significant blood loss or ongoing intravascular consumption. A fibrinogen level <3 g/l in a bleeding post-partum patient calls for preparation of both red cells and FFP or cryoprecipitate and, as outlined in this volume, a level of <2 g/l is generally considered an indication for component replacement [25].

The fibrinogen plasma level has been demonstrated to be a good predictor of PPH severity [26]. A fibrinogen plasma level of 2 g/l or less had a 100% positive predictive value for severe PPH [27]. Therefore, a plasma fibrinogen level of greater than 2 g/l should be maintained during ongoing PPH.

Increasing the fibrinogen level by 1 g/l requires about 60 mg/kg fibrinogen [28], although if there is ongoing consumption or dilution, smaller increments would be expected [29]. The guidelines recommend fibrinogen concentrate use when fibrinogen is ≤ 1 g/l. Nevertheless, in an active bleeding is possible to start when fibrinogen is ≤ 1.5 –2 g/l.

In the past, fibrinogen therapy was usually given as cryoprecipitate, but owing to the potential viral contamination and variable concentration of fibrinogen in cryoprecipitate, human plasma-derived fibrinogen concentrates are now available in most countries but not everywhere. Similar clinical outcomes and increments in fibrinogen have been reported for cryoprecipitate and fibrinogen concentrates, but these are based on limited data [30].

Fibrinogen concentrate significantly reduced the need for massive transfusion of RBCs, plasma, and platelets [31]. Nevertheless, weak evidence supports the use of fibrinogen concentrate in bleeding patients [32] and there are currently some prospective, randomized studies investigating the role of fibrinogen concentrates in PPH [33, 34].

9.4. Prothrombin complex concentrate

Prothrombin complex concentrate contains clotting factors II, IX, and X \pm VII and occasionally used off-label during PPH. Given the current lack of evidence to support their use in PPH, we do not recommend their use outside patients under dicumarinic treatment or clinical trials, because their side effects may outweigh their benefits.

9.5. Recombinant factor VIIa

Recombinant activated factor VII (rFVIIa) was developed for the treatment of hemophilia. It has been used off-label in life-threatening PPH or to prevent hysterectomy [35].

In a recent systematic review about the use of rFVIIa in severe PPH refractory to uterotronics, it was showed that rFVIIa reduce the need for specific second-line therapies in about 1 in 3 patients, with the occurrence of nonfatal venous thrombotic events in 1 in 20 patients [36].

The World Health Organization argues that it is not possible to reach meaningful conclusions from current literature [18] and clinical trials are needed (**Table 6**).

Unfortunately, blood transfusion has its own adverse consequences. To decrease transfusion exposure and to control the bleeding, pro-hemostatic agents are used more and more often in women with PPH.

9.6. Tranexamic acid

Tranexamic acid (TXA) is an antifibrinolytic agent that inhibits the activation of plasminogen into plasmin. It has been shown to reduce bleeding and transfusion requirement in massive hemorrhage secondary to a number of nonobstetric causes and it seems that is also effective in obstetric bleeding, decreasing the postpartum blood loss and preventing PPH and blood transfusions [10].

There appeared to be no increased risk of venous thromboembolism and no difference in length of hospital stay associated with TXA use. Although the prophylactic TXA administration may be associated with improved peripartum bleeding, existing evidence is insufficient for any definitive recommendations secondary to the poor to moderate quality of the literature [37].

The double-blinded WOMAN study [38] aims to investigate the role of TXA in early PPH. This study will provide valuable information on the role of early TXA in reducing progression from mild to severe PPH. There are other open studies to determinate the role of TXA as a complementary treatment of third stage of labor, in addition to prophylactic uterotonic drugs [39].

However, owing to its low cost and low rate of side effects, the use of TXA is currently recommended by several academic societies. For example, the most recently updated PPH treatment guidelines prepared by the World Health Organization state that TA (1 g over 5 min, repeated within 30–60 min if necessary) is recommended for the treatment of PPH if oxytocin and other uterotonics fail to stop bleeding or if it is thought that the bleeding may be partly due to trauma (weak recommendation) [40].

TXA is a promising candidate drug, inexpensive, easy to administer, and simple to add to the routine management of deliveries in hospitals.

Hemoglobin/hematocrit	9–10 g/dL/ 27–30%
Platelets	>50,000
Fibrinogen	1.5–2 g/l
Ionic calcium	Normocalcemia
Temperature	>35°C

Table 6. Goals of transfusion for an obstetric patient.

10. Etiologic treatment

10.1. Mechanical measures

The simple mechanical and physiological measures of 'rubbing up the fundus', bimanual uterine compression, and emptying the bladder to stimulate uterine contraction represent the first-line management of PPH. No published studies were identified to provide an evidence base for these interventions; nevertheless, professional consensus supports their continued use.

10.2. Uterotonic drugs

The use of uterotonics has a central role in the treatment of PPH. Treatment must be accompanied by careful clinical examination to ascertain that the uterus is indeed atonic and that other sources of bleeding, such as genital tract lacerations or uterine inversion have been excluded.

10.2.1. Oxytocin

Intravenous oxytocin is the first-line uterotonic; this recommendation also covers women who have already received this drug for PPH prophylaxis [40]. When given as an intravenous bolus, the drug should be given slowly in a dose of not more than five units.

Easier methods for oxytocin administration have been developed for use in resource-poor settings, but a systematic review fails to demonstrate that oxytocin administered by community health officers reduces the incidence of severe PPH (>1000 ml), severe maternal morbidity, or maternal deaths [41].

10.2.2. Ergometrine

In settings in which IV oxytocin is not available or if the bleeding does not respond to oxytocin, ergometrine, oxytocin-ergometrine fixed dose, or a prostaglandin drug (including 800 µg of sublingual misoprostol) is considered a valid alternative.

10.2.3. Prostaglandin: carboprost and misoprostol

Carboprost (15 methylprostaglandin F2) was more effective than oxytocin in preventing PPH in high-risk patients undergoing cesarean delivery [42]. If the bleeding occurs at the time of cesarean section, intramyometrial injection of carboprost may be used.

The recommended dose is 250 µg intramuscularly. This may be repeated every 15 min to a total dose of 2 mg (eight doses). However, if significant atonic hemorrhage continues after a third dose of carboprost, without significant improvement (i.e., 30 min or more after the first dose was given), the team should consider transfer to the operating theater for examination under anesthesia, with an awareness of the impending need for laparotomy and/or hysterectomy.

Misoprostol (prostaglandin E1) is appropriate if carboprost is not indicated, as asthma patients or not available. A systematic review suggests that among women who received oxytocin for the treatment of primary PPH, adjunctive use of misoprostol confers no added benefit [43].

Misoprostol does not appear to increase or reduce severe morbidity (excluding hyperpyrexia) when used to prevent or treat PPH, does not modify maternal mortality, but is associated with an increased risk of pyrexia, particularly in dosages of 600 µg or more. Therefore, it is recommended to use the lowest effective dose [44].

A study [45] of women in early pregnancy demonstrated that regardless of the route of administration (vaginal, sublingual, or rectal), misoprostol took 1.0–2.5 h to increase uterine tone. Clinicians should be aware of this delay in the clinical effect of misoprostol. Sublingual administration is recommended by WHO guidelines [40] (Table 7).

10.3. Surgical treatments

If pharmacological measures fail to control hemorrhage, surgical interventions should be initiated sooner than later. The most appropriate choice of treatment will depend, in part, on the team experience.

10.3.1. Uterine balloon tamponade

Intrauterine balloon tamponade has been suggested as an effective, easily administered minimally invasive treatment option to control uterine bleeding while preserving the mother's ability to bear additional children [46]. In terms of mechanism of action, the intrauterine balloon is believed to act by exerting inward to outward pressure against the uterine wall, resulting in a reduction in persistent capillary and venous bleeding from the endometrium and the myometrium [47].

Multiple types of balloons are available, including Bakri balloon, BT-cath balloon tamponade catheter, Foley catheters, Rusch balloon, condom catheters, and the Sengstaken-Blakemore tube. The Bakri postpartum balloon [48] and the BT-cath balloon tamponade catheter [49] are specifically designed for postpartum intrauterine tamponade. However, in settings where these are unavailable, other balloons can be used to achieve a similar effect.

Bakri balloon must be filled with 300–500 ml of sterile saline. There is no clear evidence on how long the tamponade should be left in place, but its effects can be observed after 4–6 h in most cases. In a small case series, success rates of uterine balloon catheters for controlling hemorrhage ranged from 57% after cesarean delivery to 100% after vaginal delivery [50, 51].

Balloon tamponade also allows maternal stabilization, necessary for embolization or for transfer to an intensive unit care.

10.3.2. Uterine hemostatic sutures

In recent years, uterine compression sutures, in particular B-Lynch suture, described in 1997 [52] and Hayman suture [53], have been developed for ease and rapidity even in less expert hands. Both are considered easy-to-apply conservative techniques, regarding to reduce the arrival of blood from the uterine vessels to the bleeding zone. Sutures are allocated around the uterus with thick absorbable material causing contact and compression of the uterine anterior and posterior walls.

Drug	Dose	Route of administration	Frequency	Secondary effects	Caution/contraindication
Oxytocin Syntocinon®	10–40 UI	IV (Saline 0.9% 125 ml/h)		Unusual: antidiuretic effect (cerebral or pulmonary edema) nausea, vomiting—quick infusion: hypotension, arrhythmia, stroke.	Pneumopathy cardiopathy nephropathy hepatic disease
Ergometrine Methergine®	10 UI 5 UI	IM/IMM Bolus iv slow (3–5 min)	/2–4 h (max. 5 doses)	Hypertensive crisis, vasoconstriction, nausea, vomiting	Hypertension, cardiopathy or cardiovascular risk factor, nephropathy, liver disease, systemic infection
Carboprost (15-methyl PGF _{2α}) Hemabate®	0.2 mg 0.125 mg	IM IMM	/15–90 min max. 2 mg (8 doses)	Bronchospasm diarrhea, nausea and vomiting hypertension or hypotension headache, flushing	Pneumopathy (asthma), cardiopathy, nephropathy, severe liver disease. -CI related: HTA, glaucoma, bronchial asthma -Epilepsy
Misoprostol (PGE ₁) Cytotec®	600–1000 µg	Sublingual-rectal	/2–6 h	Fever Diarrhea Nausea and vomiting	

Table 7. Uterotonic drugs.

B-Lynch suture requires hysterotomy for its realization and in Hayman suture is not necessary. Its overall efficacy ranged from 81 to 91.7% and gestations after its application have been described [50, 54].

Main complications include ischemia and uterine infection, especially in transverse sutures, because of difficulty to drain uterine contents, as in the case of the Cho technique. A risk of intestinal strangulation in the space between the suture and the uterus after the uterine involution must be awarded. Therefore, absorbable sutures should be used.

10.3.3. *Pelvic artery embolization (PAE)*

The largest study with 251 patients treated with arterial embolization observed that this technique is safe and effective for managing primary PPH. However, patients with disseminated intravascular coagulation and massive transfusion of more than 10 red blood cell units were more likely to have failed embolization [55].

PAE is found to be a minimally invasive, highly successful, and safe technique for the management of PPH in a recent systematic review of 21 studies, being successful in 89.4% of cases. The mortality rate was 0.9% and other major complications were uncommon (1.8%). It should be considered in PPH refractory to initial treatment [56].

Another recent systematic review, including 28 small studies about procedures, as embolization or uterine tamponade, or surgeries, arterial ligation or uterine compression sutures, concluded that given the insufficient evidence, clinicians must continue to make individual care decisions based on each woman's clinical situation and available management options [57]. Some studies with longer term follow-up reported infertility in women undergoing embolization.

10.3.4. *Artery ligation*

Uterine artery ligation depends on gynecology expertise. It may include the terminal part of the uterine branch, a second lower suture involving cervical branches or mass ligation of the uterine arteries and veins, including part of the myometrium (O'Leary's suture) [58].

Effectiveness is between 40 and 100% can preserve the uterus and subsequent fertility and is simpler than the ligation of hypogastric arteries, although it is associated with an increased risk of ureteral injury.

Internal iliac artery ligation is technically more complicated. Opening of the peritoneum from the bifurcation of the iliac vessels, identifying and separating the ureter medially are required and then individualizing the internal iliac artery proceeding to the double ligation of its branch (about 2–3 cm from the bifurcation) without sectioning the vessel [59].

The efficacy of the technique is similar to uterine artery ligation, although it may also be used in cases of traumatic uterine injury or even after hysterectomy [60]. Possible complications are uterine necrosis, vascular perforation, and ureteral injury.

It should be borne in mind that it may hinder further embolization. Its complications include necrosis (rare), either uterine or other neighboring territories, vascular perforation (mainly iliac vein), and ureteral lesion.

A systematic review [61] of fertility outcomes following the surgical management of PPH concluded that uterine devascularisation techniques, including internal iliac artery ligation, did not adversely affect future fertility, although, the number of studies and quality of evidence were limited.

10.3.5. Hysterectomy

Hysterectomy is the most radical therapeutic option and definitively compromises fertility. The decision and procedure must be carried out by an experienced clinician and surgeon. It should not be considered a first-choice technique except in some situations, as placenta accreta or uterine rupture [62]. It is considered in case of failure of conservative techniques, but an excessive delay has to be avoided.

11. Use of protocols

Protocols should provide a standardized approach to evaluate and monitor the patients, involving a multi-professional team. The protocols must be founded on literature review according to evidence-based medicine. Each maternity unit should have its own protocol adapted to the particularities of its organization. The protocol must be able to respond to cases of major hemorrhage. The multi-professional team together with hematology and blood bank staff should update and test this protocol regularly. The protocol must be updated every few years with recent publications.

Summarizing protocols in algorithms improve its application. Algorithms reflected in posters must be located at critical points of obstetric spaces for easy reference. Some publications [63, 64] show that the new application of a PPH protocol was associated with the resolution of maternal bleeding at an earlier stage or the use of fewer blood products.

There is a growing awareness of the importance of a checklist for assisting healthcare providers during medical crises. Checklists together with simulation training improve multi-professional team performance. It is recommended to use a checklist reader: a person who reads out loud the checklist to the team leader. It has been observed that the checklist reader can decrease task saturation experienced by the team leader thereby, increasing the likelihood that all critical tasks are completed [65].

In obstetrics, the patient safety checklist has been promoted as an important tool for improving perinatal care and reducing maternal and neonatal mortality. The World Health Organization [66] has developed a 29-item checklist to promote the delivery of key maternal and perinatal care practice. The use of checklist could be a prospective way to help to do things or using it retrospectively, to verify if all points are done. However, it is necessary to standardize how teams use checklists during obstetric crises.

Poor team organization and task assignment have also been reported in a simulation study [67] of how physicians perform during simulated obstetric emergencies, including PPH. This shows the importance of effective communication among care providers during obstetric crises. Mistakes in communication are recognized as the root cause of many sentinel events on

the labor unit [68]. Accordingly, periodic training to improve and maintain effective communication between providers should be encouraged [69].

Goldhaber and Howard [70] proposed four elements for implementing a crisis checklist:

- To create or customize the checklist.
- To familiarize providers in using the checklist effectively.
- To use checklists in clinical practice.
- To integrate into a hospital safety culture.

Improving PPH recognition and response times along with improved team communication may significantly improve patient outcomes and decrease maternal mortality. The Joint Commission (JC) [68] has recommended team training and clinical drills for high-risk events including maternal hemorrhage. The JC report also emphasized the importance of team training and communication skills when it reported that communication issues were the root cause of perinatal death or permanent infant disability in 72% of cases.

A systematic review of multi-professional team simulation training with integrated acute obstetric training interventions in a simulation setting [71] is potentially effective in the prevention of errors, thus improving patient safety in acute obstetric emergencies. Studies on its effectiveness and cost-effectiveness are needed before team training can be implemented on a broad scale.

In addition to a protocol and checklist, it is also useful to have a PPH emergency kit. This kit should include emergency equipment, treatment algorithms, and medications required for the immediate management of PPH.

Another tool that helps to early recognize bleeding is the modified early obstetric warning score (MEOWS) charts. The modified early obstetric warning score (MEOWS) has been designed to allow early recognition of physical deterioration in women by monitoring their physiological parameters. MEOWS is a score attributed to these parameters and documented on the MEOWS observation chart [72]. It is believed that small changes in the combined physiological variables measured by MEOWS may pick up deterioration earlier than an obvious change in an individual variable. Early detection will trigger subsequent prompt intervention that will either reverse further physiological decline or facilitate timely referral to appropriate personnel. The use of an early warning score is also supported by NICE in the guideline 'Acutely ill patients in hospital: recognition of and response to acute illness in adults in hospital' [73].

12. Red code

PPH is a typical obstetric emergency that can develop rapidly and unexpectedly. In case of need, it is imperative to adopt an obstetric hemorrhage massive transfusion protocol (red protocol) for obstetric patients with massive hemorrhage and continued bleeding. This must be able to respond to the need to have blood products as soon as possible. In the red code activation, several key points are identified. Grating roles and developing an action algorithm

known for all team members (obstetricians, anesthesiologists, midwives, auxiliary staff, and laboratory blood bank staff) is the key to success.

The use of in situ simulation before the implementation of a new health care protocol can be useful to facilitate finding previously not valued critical points, allowing make changes before final application. Creation of PPH training drills has allowed identifying the most common mistakes. Some of them are:

- Underestimate the blood loss.
- Delay in recognition of the severity of the bleeding until the patients become shocked.
- Failure to promptly recognize concealed bleeding.
- Delay in starting adequate fluid resuscitation.
- Ignorance about how to access blood products rapidly.

In the case of the red code protocol, the use of simulation allowed to change the shipping and collecting sample circuit, improving time reception of first unit of blood. The active participation of the multidisciplinary team can provide point improvement in the proposed protocols and, subsequently, it can generate greater compliance with them.

However, maternity wards have relatively few opportunities to train by self-experience and to evaluate and discuss how previous cases have been managed. During any emergency situation, communication and organizing the process of care are difficult tasks. It has been recognized that in many cases there is no clear leadership [74], and poor teamwork has been recognized as a major cause of poor outcome [75].

The team training based on a simulation is effective because it allows a deeper analysis of knowledge, attitudes, and behavior in professional teams. This simulation methodology has shown to improve patient safety in acute obstetric emergencies [76].

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