

Postpartum hemorrhage management: the importance of timing

Clinical Management

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Abstract

Postpartum hemorrhage is defined as a blood loss equal to or greater than 500 ml, which can occur from 24 hours to six weeks after delivery. It is a critical event with a rapid and devastating evolution, which can quickly lead to maternal shock and death.

Many efforts have been made to create international and multisectoral guidelines that allow to face an event that represents the cause of about one quarter of maternal deaths. It is crucial to create a team able to act promptly in accordance with shared protocols. The availability of shared guidelines and protocols and the organization of periodic simulations and teamwork training are part of the fundamental initiatives that can promote the safety of perinatal care. The purpose of this document is to give clinicians the tools to minimize the risks associated with inadequate management of hemorrhagic emergency, avoiding the risk of "too little or too late" and giving patients maximum safety.

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INTRODUCTION

Obstetric hemorrhage remains one of the major causes of maternal mortality in both developing and industrialized countries, representing a clinically and socially significant problem. Given the critical nature of the problem, it is particularly important to effectively manage the clinical risk and respond aggressively at the beginning of a potentially dramatic event. The creation of a multidisciplinary team trained to act quickly to identify and treat the causes of hemorrhage according to shared protocols remains crucial. The availability of shared guidelines and of protocols, together with the organization simulations and training, are initiatives of the utmost importance in the promotion of the safety of perinatal care.

This protocol is intended to provide all the specialists involved with clear guidelines on prophylaxis and therapy, implemented in compliance with national and international literature as well as the regulations in force in Italy [1,2].

ISSUE DESCRIPTION

According to the World Health Organization, postpartum hemorrhage (PPH) causes about one quarter of the maternal deaths each year [3]. In most cases, deaths occur in the first 24/48 hours after delivery and, despite the significant improvements in the last three years, 66% of deaths due to PPH are still due to substandard care, according to the latest report of the Center

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for Maternal and Child Inquiry on maternal mortality [4]. In addition, numerous studies have shown, in industrialized countries, an increase in the incidence of postpartum hemorrhage in recent years [5], reflecting in part the changes in obstetrical practice of the last decade (for example, the increase in the rate of caesarean sections or the increased trend toward practice of spontaneous delivery after caesarean section).

DEFINITION

Postpartum hemorrhage is defined as a blood loss equal to or greater than 500 ml, occurring early in the first 24 hours after delivery (primary postpartum hemorrhage) or up to six weeks postpartum (secondary postpartum hemorrhage), and which, if not identified and treated, can quickly lead to mother shock and death [6]. We talk about **minor PPH** if the estimated blood loss is between 500 and 1000 ml, but if the loss exceeds 1000 ml, it is defined as **major PPH**, which can be defined as **controlled** in the case of controlled blood loss, with impairment of maternal clinical conditions requiring thorough monitoring, or massive or **persistent PPH** in case of blood loss over 1500 ml and/or signs of clinical shock and/or transfusion of 4 or more packed red blood cells units, with impairment of maternal conditions which poses an immediate threat to the woman's life.[7,8]

The pregnant woman undergoes a series of physiological modifications that allow her to withstand substantial blood loss effectively, and is generally a young patient with good cardiovascular reserve; this condition, associated with the difficulty of correctly and timely estimation of blood loss, can lead to an underestimation of the problem. It is always important to consider that significant blood loss, > 2000 ml, can induce a rapidly worsening condition, with an inexorable decrease in blood pressure and signs and symptoms of severe shock (paleness, agitation, oliguria, followed by mood and collapse), while these symptoms might be absent in significant but less severe blood loss.

ETIOLOGY

There are many alterations that can lead to a PPH, but the main causes of postpartum hemorrhage are: uterine atony (90%), cervical and/or perineal lacerations (5%),

placental fragments retention (4%), coagulation deficiencies or alterations, uterine inversion, uterine rupture. The morbidly adherent placenta, i.e. placenta accreta, increta or percreta, is nowadays an important cause of primary hemorrhage. Previous uterine surgery, such as caesarean section, significantly increases the risk of morbidly adherent placenta [9]. Attention must also be paid to the assessment of possible clotting disorders and the prevention and treatment of anemia. According to the authors, there are other important risk factors to be considered: multiple pregnancy, previous PPH, preeclampsia, birth weight above 4000 g, failure to progression of the second stage, prolongation of the third stage of labor, episiotomy [9,10].

In clinical practice, the multiple causes of PPH are briefly synthesized through the formula "4T" [11]:

1. tone (uterine atony);
2. tissue (placenta-related problems: placental, placental implants, etc.);
3. trauma (uterine rupture, lacerations, uterine inversion); and
4. thrombin (in relation to clotting disorders).

PPH MANAGEMENT PROTOCOL

Crucial in postpartum hemorrhage management is prophylaxis and, eventually, therapy of anemia or congenital clotting disorders, treated in collaboration with the hematologist.

The PPH treatment hubs are:

- identification of the cause of PPH (4T);
- maintenance of uterine contractility, obtained through physical or pharmacological means;
- maintaining and supporting cardiovascular parameters with appropriate rehydration and volume expansion; maintaining physiological parameters, such as temperature and acid/base status; and
- prevention or therapy of hemorrhagic coagulopathy [1].

Management in the "golden hour" is particularly important to increase patient survival. If possible, in patients with high hemorrhagic risk it is advisable the use of the cell separator (cell sorter with continuous flow) and the presence of an interventional radiologists in the surgery room (with portable digital angiography).

A - Blood loss between 500 and 1000 ml without signs of hemodynamic imbalance

- Ask for the collaboration of all paramedical and medical figures, alert the Transfusion Centre, the operating room and, if available, interventionist radiology. Contemporary involve the whole team ensuring the highest level of consultation.
- Ensure two large caliber venous accesses.
- Estimate blood loss as soon as PPH is diagnosed and monitor vital parameters every 10 minutes at least initially on appropriate graphics. A graduate sterile bag for the evaluation of blood loss is recommended.
- Administer tranexamic acid 30 mg/kg [12] (ClinicalTrials.gov registration number: NCT00872469; ISRCTN76912190, and PACTR201007000192283).
- Send request for availability of blood products to the Transfusion Centre.
- Increase prophylactic oxytocin at therapeutic dose (20 IU in 500 ml saline in two hours). If after 20 minutes there is no effect, go to second line uterotonic agents (ergometrine: 2 vials 0.2 mg IM; sulprostone: 1 vial 0.50 mg in 250 ml IV, then with a controlled infusion: 0.1 to 0.4 mg/h up to a maximum of 1.5 mg in 24 hours).
- Effectuate a Type&Screen test, recurrent blood count, and coagulation tests (fibrinogen by Clauss method or, if available, point-of-care coagulation tests such as thromboelastography—TEG or rotational thromboelastometry—ROTEM).
- Avoid or correct hypothermia, acidosis, and desaturation.
- Look for the origin of bleeding through the rule of the four T:
 1. tone (evaluation and measures for atony/uterine inversion: bimanual uterine compression, endocavitary uterine infusion by hydrostatic balloon catheter and uterotone drug use). In the absence of the hydrostatic balloon, it is possible to use a latex glove or a condom with good results, as suggested by the International Federation of Gynecology and Obstetrics (FIGO) 2012 guidelines [13]. It is important to note that uterine gauze packing is not recommended today;
 2. tissue (exploration and evacuation of the uterus);

3. trauma (repairing vaginal tears, cervix, and/or uterine tears);
 4. thrombin (evaluate and correct any coagulopathy defect, if available, with Thromboelastometric/Graphic Evaluation via point-of-care monitoring).
- Targeted transfusion therapy: packed red blood cells to maintain hematocrit between 21% and 27% and hemoglobin between 7 and 9 g/l.
 - Evaluate fibrinogen infusion 30-50 mg/kg or fresh frozen plasma 20-30 ml/kg if fibrinogen is below 200 mg/dl.

B - Blood loss greater than 1000 ml, hemodynamically unstable patient

Do all the operations under point A.

- Reintegrate circulating volume with crystalloids or, if necessary, colloid by evaluating sensory, diuresis, lactate, and excess bases level.
- Maintain transfusion therapy and hemostatic support.
- Transfusion in the presence of PPH is performed by clinical indication and not on the basis of information derived from hematocrit examinations. Keep in mind that a packed red blood cells unit contains 280 ml and increases the hematocrit of 2-3%:
 - it is advisable to use a 1:1:1 ratio of units of plasma and platelets to red blood cells administered, pending laboratory values;
 - for the constitution of the package to be transfused, depending on the availability of blood products, the following alternatives are suggested:
 - 4 packed red blood cells units : 4 single dose donor or industrial plasma units; or
 - 4 packed red blood cells : 2 plasma units from apheresis;
 - platelet concentrates, it is recommended to use 1 unit from apheresis or from buffy coat every 8 unit of packed red blood cells.

It is worth emphasizing the suggestion of the alternatives mentioned above, whose application may vary depending on the different realities present on the territory and the availability of the components and monitoring tools. It is also desirable that each hospital prepares a mass transfusion protocol to be activated in case of critical hemorrhage

with signs of hemodynamic instability and hypoperfusion.

- When the result of the hemocoagulatory examinations is available, if the prothrombin time ratio—PTTr or International Normalized Ratio—INR is > 1.5 , it is necessary to infuse the plasma at the initial dose of 20 ml/kg with the packed red blood cells, up to 30 ml/kg in case of persistent or ingraining coagulopathy.
- Use heating and infusion devices.
- Always guarantee basic conditions: hematocrit $> 21\%$, temperature $> 34^\circ\text{C}$, pH > 7.20 , $\text{Ca}^{++} > 1$ mmol/l.
- Cases nonresponders to the aforementioned therapies require a conservative surgical-intervention approach: compression sutures, uterine tamponation with hydrostatic balloon, association of devascularizing sutures of uterine, ovarian or internal iliac arteries, selective embolization of pelvic vessels.
- If no response to the therapy, use recombinant activated clotting factor VII—rF-VIIa (60-90 $\mu\text{g}/\text{kg}$ bolus repeated within 15-30 min) as an extrema ratio, before performing hysterectomy. Keep in mind that rFVIIa to function requires: normal pH, temperature, adequate levels of platelets ($> 50,000/\text{mm}^3$), and fibrinogen (> 200 mg/dl).
- If no response occurs, proceed to subtotal or total hysterectomy.
- There is no agreement in the literature on the use and choice of thromboprophylaxis

after major bleeding. There are different clinical protocols depending on the different realities [14] and the reluctance for a predetermined plan of thromboprophylaxis reflects the awareness that women following intractable hemorrhage are at increased risk for disseminated intravascular coagulopathy rather than deep vein thrombosis [15].

CONCLUSIONS

In conclusion, we want to emphasize the importance of the rapidity of action and the management organization of the obstetric emergency. Given the dramatic nature of the hemorrhagic event in the postpartum, it is important that all women with known risk of uterine bleeding should be directed to a hospital equipped with a transfusion center and laboratory analysis. It is imperative to never overlook the assessment of blood loss in order not to delay the beginning of care procedures, which, if performed at the first hour, “golden hour”, ensure to the woman a better chance of survival. It should always be kept in mind that one of the main causes of death for PPH in Western countries is the delay in blood transfusion. Last but not least, it is important to emphasize the importance of creating a dedicated and well-trained team, even through simulation scenarios, who can rapidly implement the previously shared guidelines and protocols.

Key Points

- *Given the rapid and devastating evolution of postpartum hemorrhage, it is critical to act quickly and aggressively in the first hour to avoid maternal shock*
- *To create an efficient team, sharing management protocols and periodic simulation are of paramount importance*
- *The multiple causes of PPH are briefly synthesized through the formula “4T”:*
 - *tone (uterine atony);*
 - *tissue (placenta-related problems: placental, placental implants, etc.);*
 - *trauma (uterine rupture, lacerations, uterine inversion); and*
 - *thrombin (in relation to clotting disorders)*
- *The key points for PPH treatment are:*
 - *maintenance of uterine contractility;*
 - *maintaining and supporting cardiovascular parameters; and*
 - *prevention or therapy of hemorrhagic coagulopathy*

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Conflicts of interests

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