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REVIEW ARTICLE

Haemostatic support in postpartum haemorrhage

A review of the literature and expert opinion

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Postpartum haemorrhage (PPH) remains the leading cause of pregnancy-related deaths worldwide. Typically, bleeding is controlled by timely obstetric measures in parallel with resuscitation and treatment of coagulopathy. Early recognition of abnormal coagulation is crucial and haemostatic support should be considered simultaneously with other strategies as coagulopathies contribute to the progression to massive haemorrhage. However, there is lack of agreement on important topics in the current guidelines for management of PPH. A clinical definition of PPH is paramount to understand the situation to which the treatment recommendations relate; however, reaching a consensus has previously proven difficult. Traditional definitions are based on volume of blood loss, which is difficult to monitor, can be misleading and leads to treatment delay. A multidisciplinary approach to define PPH considering vital signs, clinical symptoms, coagulation and haemodynamic changes is needed. Moreover, standardised algorithms or massive haemorrhage protocols should be developed to reduce the risk of morbidity and mortality and improve overall clinical outcomes in PPH. If available, point-of-care testing should be used to guide goal-directed haemostatic treatment. Tranexamic acid should be administered as soon as abnormal bleeding is recognised. Fibrinogen concentrate rather than fresh frozen plasma should be administered to restore haemostasis where there is elevated risk of fibrinogen deficiency (e.g., in catastrophic bleeding or in cases of abruption or amniotic fluid embolism) as it is a more concentrated source of fibrinogen. Lastly, organisational considerations are equally as important as clinical interventions in the management of PPH and have the potential to improve patient outcomes.

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KEY POINTS

- A consensus clinical definition of PPH should consider not only the volume of blood loss but also the vital signs, clinical symptoms, coagulation and haemodynamic changes to improve recognition of PPH and to help determine appropriate and sufficiently intensive treatment.
- Development of standardised algorithms or massive haemorrhage protocols to reduce the risk of morbidity and mortality and improve overall clinical outcomes in PPH is recommended.
- Where available, viscoelastic testing-guided goal-directed haemostatic treatment should be implemented.
- In the presence of evidence of fibrinogen deficiency, cryoprecipitate or fibrinogen concentrate rather than fresh frozen plasma should be used as the initial treatment.
- Organisational aspects of PPH management including implementation of protocols, checklists and simulation training are paramount to improving clinical outcomes of PPH.

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Introduction

Postpartum haemorrhage (PPH) is commonly defined as blood loss from the genital tract of more than 500 ml within 24 h after giving birth.[1] It is the leading cause of pregnancy-related deaths worldwide, responsible for approximately one quarter of maternal deaths.[2] According to a systematic analysis, 34% of the 275 000 estimated global maternal deaths in 2015 were caused by haemorrhage.[3] This means more than 10 deaths each hour worldwide are caused by excessive obstetric bleeding. The majority of these deaths occur in low-income countries;[2] however, women in high-income countries also continue to die from major obstetric hemorrhage.[4–6] In Europe, approximately 13% of obstetric patients will experience PPH (≥500 ml) and about 3% severe PPH (≥1000 ml).[7] Moreover, PPH is associated with significant morbidity including anaemia, the need for blood transfusion, coagulopathy, Sheehan's syndrome (postpartum hypopituitarism), renal impairment and psychological morbidity such as depression and post traumatic stress disorder.[8–10] Active management of the third stage of labour and prophylactic administration of uterotonic drugs are the most effective strategies to prevent PPH and related maternal deaths.[11,12]

There is a lack of consensus on some important topics in the current approaches to the management of PPH, including PPH definition and haemostatic treatment pathway. Therefore, in this review we aim to discuss some of these topics and to develop a simple and clinically relevant definition of PPH as well as to provide practical advice to support efficient, goal-directed coagulation therapy in PPH.

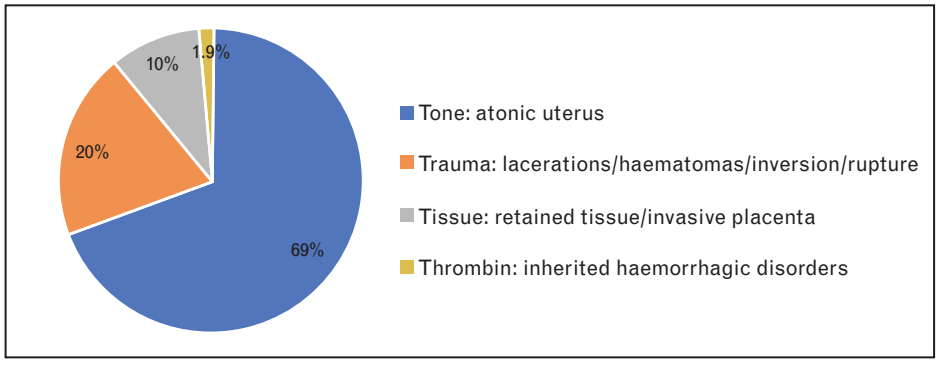
Causes and pathophysiology of postpartum haemorrhage

During pregnancy uterine blood flow increases throughout gestation from about 100 ml min^{-1} before pregnancy to 700 ml min^{-1} at term, representing approximately 10% of the total cardiac output,[13] increasing the risk of massive bleeding after delivery. In addition, other significant physiological changes occur as prophylactic measures to prepare the mother for blood loss and placental separation after childbirth. These include profound changes in haemostasis such as an increase in the concentration of some coagulation factors, *e.g.* FVIII, von Willebrand factor (VWF) and fibrinogen, and a decrease in anticoagulants and fibrinolysis, creating a state of hypercoagulability.[14–16] At the time of delivery, blood loss is controlled by contraction of the myometrium, local decidual haemostatic factors and systemic coagulation factors, and an imbalance of these mechanisms can lead to PPH.[17]

PPH is defined as primary if the bleeding occurs before delivery of the placenta and up to 24 h after delivery of the fetus, or secondary if it occurs more than 24 h after delivery.[9] PPH risk factors include antepartum haemorrhage, augmented or induced labour, instrumental or caesarean delivery, chorioamnionitis, foetal macrosomia, polyhydramnios, maternal anaemia, thrombocytopenia or hypofibrinogenaemia, maternal obesity, multifetal gestation, preeclampsia, prolonged labour, placentation abnormalities and older age.[18–25] Hereditary haemostatic disorders and a history of PPH in a previous delivery also increase the risk.[20,26,27] However, it is estimated that about 40% of PPH cases occur in women who do not have any risk factors, emphasising the importance of surveillance in all women.[28]

The main causes of PPH can be categorised by the four T's: tone, trauma, tissue, thrombin with uterine atony underlying most cases (Fig. 1).[29] Coagulopathies may worsen haemorrhage and contribute to the progression to massive haemorrhage. They represent a state of impaired haemostasis and can include defects known prior to childbirth or which developed during or after childbirth due to other complications. Causes of coagulopathy in massive bleeding include hyperfibrinolysis or dilutional coagulopathy as a result of resuscitation. Consumptive coagulopathy characterised by activation of the coagulation cascade and consequent consumption of coagulation factors and platelets is

Fig. 1 Causes and approximate incidence of postpartum haemorrhage.



less common in PPH, but may contribute to severe cases of bleeding.[30] The onset and mechanism of coagulopathy depend on the aetiology of the PPH.[30–34] In most episodes of PPH (caused by uterus atony, trauma, uterine rupture) early coagulopathy is unusual, whereas PPH that has been diagnosed late or when the volume of blood loss is underestimated may be associated with an apparently earlier onset of coagulopathy.[30,34] Evidence of coagulopathy is found in about 3% of PPH with the incidence increasing with the volume of bleeding.[34] Placental abruption and amniotic fluid embolus (AFE) are often associated with early onset of coagulopathy [34] characterised by disseminated intravascular coagulation and hyperfibrinolysis.[35,36]

Clinical definition of postpartum haemorrhage

The definition of PPH varies across both countries and guidelines and so reaching a global consensus has previously proven difficult.[37,38] Table 1 summarises definitions of PPH from different national and international guidelines. The definition of PPH is generally based on the volume of blood loss; this is because of the historical studies that tried to identify women at the highest risk.[39] There are several methods for measuring blood loss including visual estimation, gravimetric drape measurements and haemoglobin measurements, but there is no solid evidence supporting whether the use of one method over another would lead to improved clinical outcomes.[40] Each method has related difficulties; however, visual methods were shown to almost always underestimate the total blood volume loss.[40] PPH risk is a relative concept and additional factors such as bleeding rate, a patient's body size, and individual tolerance of blood loss are all relevant to its development. Definition of PPH based on blood loss alone can be misleading and more importantly can cause delay in treatment. Pregnant women can lose more than 1000 ml of blood without showing clinical signs of shock, due to the increase in blood volume during pregnancy. Tachycardia is often the only sign, even in cases of blood loss of up to 25–35% of the total blood volume.[41] This masks the extent of the bleeding and is one of the reasons for the great difficulty in the clinical evaluation of obstetric haemorrhage.[41] In addition, the lack of immediate availability of laboratory tests or blood gas analysis in some maternity units represents another difficulty that can cause delay in PPH recognition. Therefore, a multidisciplinary approach in defining PPH is needed, and monitoring of the physical condition, including the vital signs, clinical symptoms, coagulation and bleeding status should all be considered.

A consensus clinical definition of PPH is needed not only for the prompt recognition of PPH but also to distinguish between lesser and more severe bleeding. It thus defines the situation to which the recommendation relates, determines time of treatment initiation and helps to emphasise appropriate and sufficiently intensive treatment. Therefore, PPH should be defined as a cumulative blood loss greater than or equal to 1000 ml or any blood loss associated with clinical and/or laboratory signs of shock/tissue hypoperfusion within 24 h after birth (Table 2). However, blood loss greater than 500 ml should trigger close patient monitoring and alert obstetric and anaesthesia care providers.

Table 1 Summary of PPH definitions based on different guidelines

Organization	Year	Blood volume		Notes	Ref
		Vaginal	Caesarean		
WHO	2012	≥500 ml			1
NATA	2019	≥500 ml, severe ≥1000 ml, massive/life-threatening ≥2500 ml (or hypovolemic shock)			37
ACOG (US)	2017	≥1000 ml		Or blood loss accompanied by signs of hypovolemia within 24 h	9
SCOG (Canada)	2018	≥500 ml	≥1000 ml	For clinical purposes, any blood loss that has the potential to produce haemodynamic instability	76
RANZCOG (Australia/New Zealand)	2017	≥500 ml, severe ≥1000 ml			77
RCOG (UK)	2016	Minor: 500–1000 ml, Major: >1000 ml			78
DGGG/OEGGG/SGGG (Germany/Austria/Switzerland)	2018	≥500 ml	≥1000 ml		79
CNGOF (France)	2016	≥500 ml, severe ≥1000 ml			80
NVOG (Netherlands)	2015	≥1000 ml			81
ISS (Italy)	2018	Minor: 500–1000 ml, Major: >1000 ml		Distinguishes major PPH – controlled vs. persistent	82

ACOG, The American College of Obstetricians and Gynecologists; CNGOF, Collège National Des Gynécologues et Obstétriciens Français (The French National College of Gynaecologists and Obstericians); DGGG, Die Deutsche Gesellschaft für Gynäkologie und Geburtshilfe e.V. (The German Society of Gynaecology and Obstetrics); ISS, Istituto Superiore di Sanità (Higher Institute of Health, Italy); NATA, Network for the Advancement of Patient Blood Management, Haemostasis and Thrombosis; NVOG, Nederlandse Vereniging voor Obstetrie en Gynaecologie (The Netherlands Society of Obstetrics and Gynaecology); OEGGG, Die Österreichische Gesellschaft für Gynäkologie und Geburtshilfe (Austrian Society of Gynaecology and Obstetrics); RANZCOG, The Royal Australian and New Zealand College of Obstetricians and Gynaecologists; RCOG, The Royal College of Obstetricians and Gynaecologists; SCOG, The Society of Obstetricians and Gynaecologists of Canada; SGGG, Die Schweizerische Gesellschaft für Gynäkologie und Geburtshilfe (the Swiss Society of Gynaecology and Obstetrics); WHO, World Health Organisation.

Table 2 Clinical signs that may indicate beginning or undetected PPH within 24 h after delivery and should activate close and active patient monitoring

Symptoms:		
Tachycardia more than 100 bpm, in spite of balanced volume state and adequate pain control	→	**Patient at risk** **Close and active monitoring**
Pallor/Drop in Hb> 2 g dl^{-1} before crystalloid administration		
Hypotension (BP ≤85/45 mmHg or 20% drop in baseline value)		
Critical values in blood gas analysis (e.g., base excess <-4, pH <7.2)		
Shock index of >0.9		
Lactate >4.0 mM/l		
Oliguria (diuresis <500 ml $24h^{-1}$)		
Excessive volume requirement		
Inappropriate fear or restlessness		
Coagulopathy (detected clinically or by VET)		

BP, blood pressure; bpm, beat per minute; Hb, haemoglobin; PPH, postpartum haemorrhage; VET, viscoelastic testing.

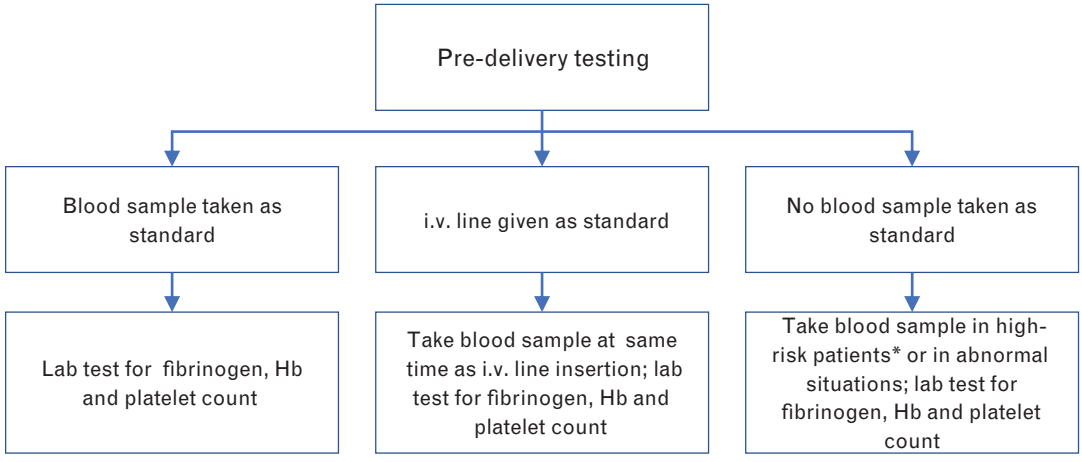
Assessment of postpartum haemorrhage-associated coagulopathy

Early recognition of coagulopathy is crucial for successful patient management. Haemostatic changes during PPH are not well defined and differ from other types of bleeding such as in trauma. For example, prothrombin time and activated partial thromboplastin time (aPTT) in pregnant women were found to remain mostly normal despite large blood loss of up to 5000 ml.[31,32,42] The results from standard laboratory tests (SLTs) to assess coagulation during PPH (*e.g.* partial thromboplastin, aPTT, Clauss fibrinogen) often take about 60 min to become available and so provide historical information, but coagulation in patients with PPH may be dynamic and unstable. Moreover, the Clauss fibrinogen test is a predictive marker of PPH progression whilst PT and aPTT are less useful.[31,43] In severe bleeding, like PPH, fibrinogen reaches critically low plasma concentrations at an earlier stage compared to other coagulation factors.[44,45] Viscoelastic tests (VETs), such as thromboelastometry (ROTEM, Clotpro) and thrombelastography (TEG), provide dynamic information on the speed of coagulation initiation, kinetics of clot growth, clot strength, and breakdown of the clot.[46] There is evidence showing that TEG and ROTEM FIBTEM assays correlate moderately well with fibrinogen levels assessed by the Clauss method during PPH and can be used as surrogate measurements to identify hypofibrinogenaemia.[47–49] Their main advantage is that they can identify clinically significant low fibrinogen levels more rapidly than SLTs, with the results available in 10 min. Both TEG and FIBTEM amplitude at 5 min (A5) can reliably detect fibrinogen levels ≤ 2 g l^{-1} and thus provide very fast and useful information about coagulation impairment.[48,49] However, VET is more expensive than SLTs and not available in all hospitals.

Fibrinogen as a predictive marker of severe postpartum haemorrhage

Normal levels of fibrinogen at delivery range from 3.5 to 6.5 g l^{-1} which is significantly higher than in nonpregnant women (2.0–4.5 g l^{-1}).[14] In PPH, like in other types of massive haemorrhage, fibrinogen plasma levels fall below the normal range for pregnancy sooner than other coagulation factors and decrease proportionately with blood loss.[30,42] Clinically significant low fibrinogen levels during delivery or early postpartum, i.e. below 2 g l^{-1}, were found to be a good predictive marker of progression to severe PPH.[31,32,43] The exact threshold for intervention to replace fibrinogen is still unclear, although a fibrinogen level above 2 g l^{-1} appears to be adequate for haemostasis during PPH.[45] The importance of monitoring fibrinogen levels during delivery is therefore obvious; however, the benefit of measuring predelivery fibrinogen is not clear.[50,51] Lower antepartum levels of fibrinogen have been identified in women who later developed severe PPH and bleeding complications, but the differences may not be large enough to establish clinically meaningful threshold values.[50] In contrast, another study found antepartum fibrinogen levels to be a poor predictor of PPH.[52] A blood sample is normally taken at 32–38 weeks' gestation, but this timepoint is likely be too early to provide meaningful results as fibrinogen may still be increasing as part of the normal haemostatic process. Evidence that low fibrinogen is predictive of PPH may be too weak to justify routine testing of all patients; moreover, it would increase the medicalisation of delivery and the costs may

Fig. 2 Suggested decision tree for pre-delivery laboratory blood testing.



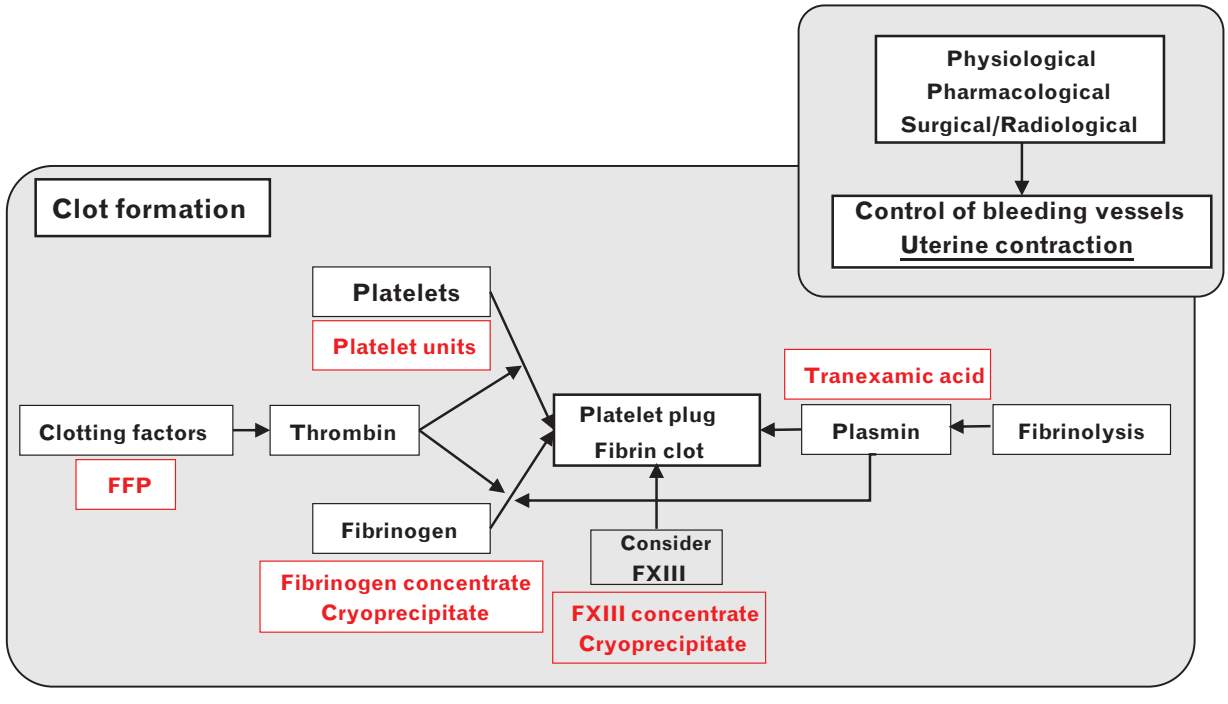
*As defined in the text for women with increased risk due to accumulation of risk factors, such as previous severe PPH, known coagulopathy, invasive placenta or suspected placental abruption or sepsis. Hb, haemoglobin; i.v., intravenous.

be prohibitive in many hospitals. Lower fibrinogen levels before birth do not necessarily require treatment, although inherited hypo- or dysfibrinogenaemia would require specialist multidisciplinary management. If the patient is otherwise well, treatment may not be necessary, but it should alert staff to be highly vigilant and ensure the team is prepared for abnormal or prolonged bleeding. A fibrinogen level should be measured if placental abruption is suspected and replacement therapy may be needed. A decision tree with suggestions for testing close to delivery is shown in Figure 2.

Haemostatic support in postpartum haemorrhage

In most cases of PPH, bleeding is initially controlled by timely obstetric measures including administration of uterotonic drugs, bimanual uterine compression, removal of retained placenta and intrauterine balloon

Fig. 3 Summary of haemostatic intervention strategies for obstetric bleeding.



Clot stability is affected by different factors (black text) and the main goals of haemostatic management (red text) are to treat hyperfibrinolysis and to restore clot formation. FFP, fresh frozen plasma; FXIII, factor XIII.

tamponade, and surgical suturing of any lacerations, in parallel with resuscitation and treatment of anaemia and coagulopathy.[8] For the purpose of this review, we will focus mainly on haemostatic support of abnormal coagulation. Treatment of coagulopathy should be considered early and simultaneously with the other strategies, especially in aetiologies with a higher risk of coagulopathy such as abruption or AFE. The main goals of haemostatic management are to treat hyperfibrinolysis and to restore clot formation. In the case of PPH this includes the use of antifibrinolytics like tranexamic acid (TXA), and agents that act on the coagulation cascade, such as coagulation factor concentrates, fresh frozen plasma (FFP) and platelets as highlighted in Figure 3.

Tranexamic acid

TXA is an antifibrinolytic agent that reduces bleeding by inhibiting plasminogen from interacting with fibrin, thus reducing plasmin activation, and so reduces clot breakdown.[53] The WOMAN trial showed that administration of TXA within 3 h of delivery to women with established PPH decreased maternal mortality secondary to bleeding and reduced the need for laparotomy to control haemorrhage.[54] However, there is limited evidence for prophylaxis with TXA.[55] The TRAAP trials showed a mild reduction of the incidence of PPH after prophylactic administration of TXA.[56,57] The first TRAAP trial showed that among women delivering vaginally the prophylactic use of TXA did not decrease the rate of PPH when defined as a measured blood loss of at least 500 ml; however, TXA administration decreased blood loss of more than 500 ml as estimated by the clinician and the use of other uterotonic drugs.[57] The most recent TRAAP2 trial showed that, in cases of caesarean delivery, prophylactic oxytocin and TXA administration reduced the incidence of PPH, although the secondary haemorrhage-associated clinical outcomes (i.e., blood loss, blood transfusion or use of additional uterotonics) remained unchanged.[56]

Clotting factor supplementation

Restoration and maintenance of clot strength can be supported by administering coagulation factors. Fibrinogen is the first factor to fall to critical levels and can be replaced via FFP, fibrinogen concentrate or cryoprecipitate depending on availability. FFP has a fibrinogen level of approximately 2 g l^{-1}; therefore, infusion of FFP during PPH can further reduce fibrinogen concentration by dilution if the plasma concentration of the patient is above 2 g l^{-1}.[58] If the plasma fibrinogen concentration is lower than 2 g l^{-1} substitution through cryoprecipitate or fibrinogen concentrate is needed.[58] Advantages of fibrinogen concentrate include easy administration, convenient storage, standardised fibrinogen content, and low risk of complications such as transfusion-transmitted infection and transfusion-related acute lung injury.[59] In comparison, cryoprecipitate contains additional coagulation factors, such as FVIII, VWF and FXIII; however, it requires thawing prior to administration which can delay the treatment.[60] Similar to FFP, cryoprecipitate needs to be administered in larger volumes in comparison with fibrinogen concentrate to restore fibrinogen levels.[59] Currently there is no evidence that either fibrinogen concentrate or cryoprecipitate is a more effective treatment in patients with fibrinogen plasma level above 2 g l^{-1}. A systematic review of fibrinogen replacement therapies in PPH showed that there is insufficient evidence that early and systematic administration of fibrinogen concentrate improves the clinical outcomes in PPH.[61] The FIB-PPH trial found no evidence to support preemptive, empirical treatment with fibrinogen concentrate in patients with severe PPH probably because most patients had normal fibrinogen levels at the time of the intervention.[33] Similarly, the results of the OBS2 trial have shown that fibrinogen concentrate treatment provided no benefit in clinical outcomes for FIBTEM A5 >12 mm or fibrinogen concentration greater than 2 g l^{-1}. It is important to note that the study was underpowered for lower fibrinogen levels, therefore an effect below these levels cannot be excluded.[45] Recently published results of the FIDEL trial confirmed that early and systematic treatment with fibrinogen concentrate did treat hypofibrinogenaemia but did not reduce the blood loss and transfusion requirements.[62] A recent cluster-randomised pilot study (ACROBAT) evaluated the feasibility of early cryoprecipitate administration in PPH.[63] Preliminary clinical outcomes showed that cryoprecipitate administration at any time-point was accompanied by reductions in red blood cell (RBC) transfusions, surgery, and intensive care unit admission.[64] Another recent retrospective study suggested higher transfusion requirements in the cryoprecipitate treated group *vs.* control group.[65] However, less fluids were administered in the cryoprecipitate group.[65] Overall, further studies are needed to assess not only the clinical efficacy but also the optimal dosing of early fibrinogen replacement therapy in PPH.[61]

Other factor concentrates such as prothrombin complex concentrate (PCC, concentrate of human-derived vitamin K-dependent clotting factors II, VII, IX, X) or recombinant activated FVII (rFVIIa) concentrate have been occasionally used off-label in PPH treatment. Currently administration of PCC is not substantiated by any clinical trials, therefore its use is generally not recommended.[30,39] rFVIIa was approved by the European Medicines Agency (EMA) in May 2022 for treatment of severe PPH unresponsive to treatment with uterotonics, based on a recent study showing a 40% relative risk reduction in women who received a single dose of rFVIIa compared to standard of care.[66]

Goal-directed treatment of postpartum haemorrhage

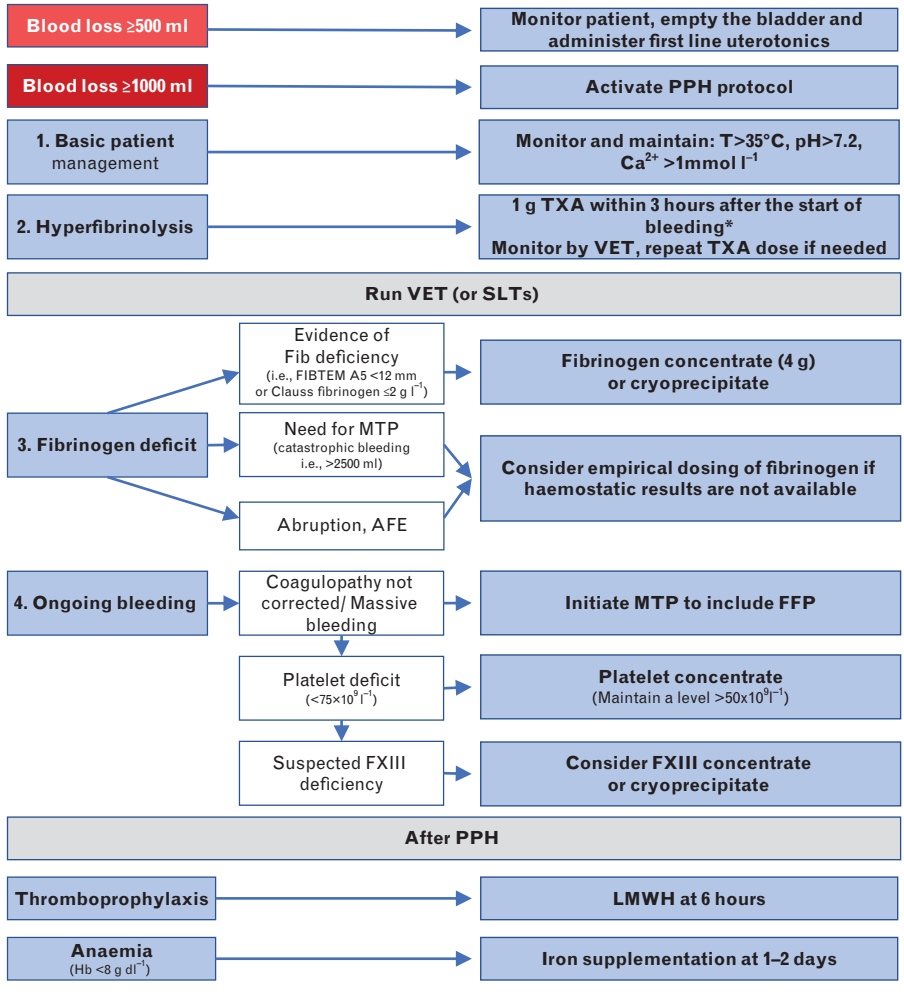
The use of algorithms or massive haemorrhage protocols for the management of PPH can help reduce overall transfusion requirements and haemorrhage-associated

morbidity.[67,68] A countrywide implementation of standardised PPH management that included measured blood loss and goal directed fibrinogen replacement guided by VET was associated with an increase in the number of identified bleeds of >1000 ml, likely due to better recognition of PPH, but a decrease in the number of massive bleeds ≥2500 ml. Use of blood products such as FFP and RBCs had also decreased.[69] Many guidelines recommend empirical blood product treatment with fixed ratios of FFP, RBCs and platelets especially in the absence of haemostatic testing. But many of these protocols are based on data from massive bleeding in trauma patients and their suitability for obstetric patients is not clear. Moreover, empirical transfusion packages in many cases will lead to over-transfusion of plasma products and platelets. In contrast, point-of-care (POC) testing, such as VET like TEG and ROTEM, provides rapid coagulation assessment and can guide the goal-directed treatment to correct fibrinogen levels which may improve outcomes of PPH.[32] Comparative studies showed that POC-guided therapy in women with PPH resulted in less blood product replacement and improved patient outcomes compared to those without guided therapy.[45,69–71]

Suggested treatment algorithm

A suggested haemostatic treatment algorithm is presented in Figure 4. Initiation of haemostatic treatment is guided by the volume of blood loss. Blood loss equal or greater than 500 ml should trigger infusion of TXA and close monitoring of the patient, including initial SLTs (Clauss fibrinogen) or VET (ROTEM/TEG). The algorithm starts with a reminder regarding basic patient management, including monitoring and maintaining body temperature, acid-base status and calcium levels. The recommended first-line treatment is 1 g of TXA, which should be administered as soon as abnormal

Fig. 4 Suggested haemostatic treatment algorithm in PPH.



*Caution is needed in patients receiving more than 2 g day^{-1} due to potential renal and epileptogenic effects of TXA. AFE, amniotic fluid embolus; F, factor; FFP, fresh frozen plasma; FIBTEM, fibrinogen thromboelastometry; Fib, fibrinogen; Hb, haemoglobin; LMWH, low-molecular-weight heparin; MTP, massive transfusion protocol; PPH, postpartum haemorrhage; SLTs, standard laboratory tests; TXA, tranexamic acid; VET, viscoelastic testing.

bleeding is recognised and at the latest before 3 h after bleeding onset.[54] Hyperfibrinolysis is difficult to measure and VET are insensitive measures that only detect gross abnormalities; therefore TXA should be considered in all patients with PPH as a simple way to reduce fibrinolysis (taking into account their overall haemodynamic state).[72] Caution is needed in patients receiving high doses (more than 2 g day^{-1}) due to potential renal or epileptogenic effects of TXA[73], particularly in patients with preeclampsia.[74] Fibrinogen concentrate should generally only be given when there is evidence of fibrinogen deficiency (i.e., FIBTEM A5 <12 mm or Clauss fibrinogen levels $\leq$2 g l^{-1}) to allow goal-directed therapy. The recommended starting dose is 4 g which in an average woman should lead to an increase in fibrinogen plasma levels of about 1 g l^{-1}. If VET is not available, standard Clauss fibrinogen should be still performed, but in case of catastrophic bleeding or in suspected AFE or abruption, empirical fibrinogen replacement can be considered on a case-by-case basis by treating clinicians. There is currently no evidence supporting empirical dosing of fibrinogen concentrate based on blood loss only as previous randomised trials did not find any significant improvement in blood loss or transfusion needs.[33,62]

If bleeding continues or coagulopathy has not been fully corrected after fibrinogen concentrate, or in cases of massive bleeding, FFP should be used as part of a massive transfusion protocol. Moreover, if the platelet count is low, platelet concentrate should be considered to maintain platelet count above 50×10^9 l^{-1}. The consensus recommendation is to transfuse platelets at 75×10^9 l^{-1} to maintain this level.[39] In very rare cases if the bleeding continues, some clinicians suggest that administration of FXIII concentrate may be considered. FXIII is known to crosslink and thus stabilise fibrin contributing to the overall clot strength. A recent study showed that at the onset of labour women with a subsequent PPH had slightly but significantly lower FXIII activity than women without PPH.[75] Several recent studies suggested that FXIII deficiency might be detected in the FIBTEM profile, although none of these studies were related to obstetric haemorrhage.[76,77] Alternatively, cryoprecipitate could be administered as it contains not only fibrinogen but also high concentrations of FXIII. However, cryoprecipitate is not available in all countries. Thrombin generation normally remains high in PPH, so PCC or FVIIa concentrate are generally not considered useful for haemostatic intervention. As mentioned above, the EMA has recently supported extension of the rFVIIa (NovoSeven) license for use in PPH when uterotonics fail to control bleeding. However, the authors advocate that rFVIIa should be seen as a last-line tool in the treatment of PPH and further studies are needed to determine its exact role and safety. Thromboprophylactic treatment with low molecular weight heparin (6 h after bleeding has stopped) is recommended after PPH >1000 ml and/or transfusion. Iron supplementation should be considered after the PPH (1–2 days after bleeding) to help treat the associated anaemia.

In summary, the key difference in this suggested algorithm in comparison with most PPH guidelines is the proposed use of fibrinogen replacement with fibrinogen concentrate or cryoprecipitate and not FFP as the first-line treatment for fibrinogen deficiency as they represent a more concentrated source of fibrinogen to rapidly restore haemostasis.

Organisational management

It is key to remember that organisational factors are equally as important as clinical aspects in the treatment of PPH.[78] Each institution must promote a complete and reliable clinical record of each case in order to allow for audits and benchmarking between institutions. PPH management should include simulation multidisciplinary staff training to ensure implementation of protocols/checklists. Simulation training has been shown to significantly increase staff knowledge.[79] Debriefing sessions for all the members of the multidisciplinary team involved in the case of severe PPH provide not only further training opportunities but also space for discussion about the procedures to further improve the treatment.

Conclusion

Early recognition and prompt obstetric treatment are essential to avoid development of coagulopathy and severe PPH as well as the associated maternal morbidity. Suggested recommendations include consensus PPH definition for use in clinical practice for prompt recognition of PPH and recommendations for management during bleeding. Standardised algorithms or massive haemorrhage protocols should be developed to reduce the risk of morbidity/mortality and improve overall clinical outcomes. Where available, VET should be used to guide goal-directed haemostatic treatment in PPH. Organisational factors are equally important as clinical interventions in the treatment of PPH and have the potential to improve patient outcomes.

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