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Haemostatic support in postpartum haemorrhage: A review of the literature and expert opinion

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Postpartum hemorrhage (PPH) is still the main universal cause of death associated to pregnancy, as well as the cause for one quarter of maternal deaths, most of them in countries with low resources, but also in first-world countries.

In case of abnormal puerperal bleeding, typically obstetrics, resuscitation, and coagulopathy treatment measures are simultaneously implemented. An early diagnosis of coagulopathy is essential, since it contributes to the progression toward massive hemorrhage.

The first barrier in the PPH scenario is precisely its definition, since there are no universal criteria. It is based on the bleeding volume, which is hart to monitor and can lead to delays in the treatment.

A multidisciplinary approach should be considered to define PPH, taking into account vital signs, clinical symptoms, and changes in coagulation and in the hemodynamic situation.

Furthermore, standardized treatment algorithms and massive hemorrhage protocols should be developed in order to minimize the morbidity and mortality risk and to improve the progression of PPH cases.

Several pregnancy-specific factors are involved in the pathophysiology of PPH. Uterine blood flow is increased, and it reaches up to 10% of cardiac output, thus furthering the risk of massive hemorrhage after delivery.

In contrast, other changes during pregnancy are aimed at favoring hemostasis.

Specifically, factor VIII and factor von Willebrand and fibrinogen are increased, whereas anticoagulant factors and the fibrinolysis rate are reduced.

Risk factors for PPH include antepartum hemorrhage, induction of labor, instrumental deliveries, and C-sections, chorioamnionitis, fetal macrosomia, polyhydramnios, maternal anemia, thrombocytopenia, hypofibrinogenemia, maternal obesity, multifetal pregnancies, prolonged labor, placental abnormalities, and advanced maternal age.

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Hereditary hemostatic disorders and a previous history of PPH also increase the risk of PPH.

The causes of PPH are typically described as the "4 Ts":

Tone (uterine atony)

Trauma (lacerations, hematomas, uterine inversion, or rupture)

Tissue (retention of placental fragments, invasive placenta)

Thrombin (hereditary bleeding disorders)

Uterine atony occurs in most cases of PPH.

Early coagulopathy is not usual in PPH, but if diagnosis is delayed or if the bleeding volume is underestimated, the onset of coagulopathy seemingly happens earlier, as well as in cases of abruptio placenta and amniotic fluid embolism.

The definition of PPH changes in different countries and different management guides, so reaching a consensus would seem difficult. Furthermore, it is traditionally based on the volume of blood loss, estimated either visually or by weighing gynecological pads, as well as measuring hemoglobin. None of these methods has proven superior to the others, but clearly a visual estimation usually underestimates the losses. Therefore, ideally individual tolerance concepts should be associated to the bleeding, since a pregnant woman can lose over 1000 ml of blood without showing any clinical signs, since her blood volume is increased during pregnancy. Tachycardia is usually the earliest sign of excessive bleeding.

The lack of immediate availability to perform a lab test or a blood gas test in some delivery rooms delays de identification of PPH.

The definition of PPH should be multidisciplinary, comprising vital signs, clinical symptoms, coagulation status, and bleeding rate.

The proposed definition for PPH is an accumulated blood loss over 1000 ml, or any loss associated to shock or tissue hypoperfusion clinical and/or analytical data within 24 hours of birth.

Viscoelastic tests (VETs) are the suggested method for the early identification of coagulopathy, since they are quick and because of the evidence of moderate correlation with fibrinogen levels measured by the Clauss method. However, VETs are more expensive than standard lab tests, and they are not available at all hospitals.

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Low levels of fibrinogen (< 2 grams/liter) during labor or early puerperium are a good predictor of severe PPH progression, although the exact threshold for the replacement of this factor is not clear.

The importance of monitoring fibrinogen levels during labor seems obvious, but this is not the case for antepartum monitoring, on which literature is inconsistent.

In most PPH cases, the first therapeutic maneuvers are obstetric, through the administration of uterotonics, uterine manual compression measures, removal of placental remnants, tear suture, or insertion of intrauterine balloon tamponade.

Treating the coagulopathy should be considered at an early stage and concurrently with the strategies mentioned. Prohemostatic strategies in PPH include tranexamic acid, replacing coagulation factors using factor concentrates or frozen fresh plasma and platelets.

Tranexamic acid (TXA) proved effective to reduce mortality due to puerperal bleeding in the WOMAN trial, although the benefit of its prophylactic use during vaginal delivery could not be ascertained in the TRAAP trial. The TRAAP2 trail provided evidence of a bleeding reduction with the prophylactic use of oxytocin and TXA in C-section births.

Fibrinogen must be supplemented and restored to plasma levels over 2 grams/liter through the administration of concentrates of this factor or with cryoprecipitate in PPH cases. However, there is not enough evidence to support a systematic early administration of fibrinogen to improve the evolution of PPH (studies FIB-PPH, OBS, and FIDEL).

The use of cryoprecipitate at early stages of PPH was studied in the ACROBAT trial, with promising preliminary results.

The use of prothrombin complex concentrate and recombinant activated factor VII is not backed by any clinical trial, and so it is not recommended on a general basis.

Procedure algorithms can reduce transfusion requirements and morbidity associated to PPH. Hemostatic therapy is proposed, guided by the bleeding volume, administering TXA (1 gram, within 3 hours of birth), if this is > 500 ml, and establishing a strict monitoring plus a lab test or VET.

A fibrinogen concentrate will be administered if there is evidence of a deficiency (FIBTEM < 12 mm or Clauss < 2 gr/l), with a recommended starting dose of 4 grams.

The platelet count should stay above 50,000, and the consensus recommends the transfusion of platelets at levels of 75,000. In the rare cases of persistent bleeding, the use of factor XIII concentrate is proposed to stabilize the fibrin mesh.

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As a last resort, recombinant activated factor VII may be administered, although its safety and efficacy have not been ascertained.

As with the procedure algorithm, the proposal is for every institution to promote training through PPH case simulation, as well as to record and review PPH cases in order to determine aspects to improve.