Bleeding news

Patient blood management to minimize transfusions during the postpartum period

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Postpartum hemorrhage (PPH) is still the most common cause of maternal mortality and accounts for 27% of postpartum deaths every year worldwide.

Early detection and the right treatment are crucial to reduce morbimortality associated to this condition.

A distinction can be made between primary PPH when bleeding occurs within 24 hours after the delivery, and secondary PPH when bleeding occurs after 24 hours to 12 weeks after delivery.

Early detection of PPH can be complex because the clinical signs are often latent and it is not always easy to quantify blood losses in this scenario. Therefore, bearing in mind risk factors associated with PPH speeds up management.

Risk factors for postpartum hemorrhage
Previous retained placenta or postpartum hemorrhage
Maternal hemoglobin level below 8.5 g/dL at onset of labor
BMI greater than 35 kg/m^2
Grand multiparity (parity 4 or more)
Antepartum hemorrhage
Overdistention of the uterus (e.g., multiple pregnancy, polyhydramnios or macrosomia)
Existing uterine abnormalities
Low-lying placenta
Induction
Prolonged first, second or third stage of labor
Oxytocin use
Precipitate labor
Operative birth or cesarean section

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Even though transfusion is an essential tool in the management of PPH, regardless of its etiology, excessive or unnecessary transfusion leads to unwanted effects. This is why the concept of Patient Blood Management (PBM), with its three pillars, can be applied to postpartum hemorrhage in the following way:

1st pillar: prenatal anemia prediction and correction.

40% of pregnant women suffer from anemia caused by an iron deficiency, and so anemia screening in all pregnant women and oral or parenteral iron supplementation correspond to the first pillar of PBM in this patient group. Moreover, in cases not responding to parenteral iron therapy, the use of erythropoiesis-stimulating agents may be considered. Red blood cell transfusion should be reserved to hemoglobin values under 6 mg/dL.

2nd pillar: hemorrhage prevention and reduction during delivery.

During the third phase of delivery, some known instrumental maneuvers may be used to prevent PPH, such as umbilical cord traction or uterine massage.

Furthermore, uterotonic drugs are universally used—uterine atony is still the most prevalent cause of PPH,—such as oxytocine, ergometrine, misoprostol or—the most expensive alternative,—carbetocin.

Tranexamic acid given within three hours of the bleeding has shown a high therapeutic efficacy to control the bleeding (0.5-1 gram intravenous dose).

Intrauterine tamponade with Bakri balloon, therapeutic angiography, or compressive vascular suture are instrumental alternatives in this 2nd pillar.

As a last resort, hysterectomy may be considered.

The optimal time for transfusion in PPH is not well defined, but if justified by the clinical situation, massive hemorrhage protocols should be activated.

It is fundamental to remember that fluid replacement and transfusion should be performed with a fluid heater.

Acidosis correction and early administration of fibrinogen are additional treatment measures.

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3rd pillar: limiting the use of transfusions and optimizing postpartum anemia treatment.

In the postpartum period, the most frequent causes of hemorrhage are the retention of placenta remains and endometritis. Both conditions have specific treatments in gynecological protocols.

Approximately 50% of pregnant women present postpartum anemia (not uniformly defined as Hb <10 gr/dL 24 hours after delivery, < 11 g/dL in the week after or <12 g/dL after 8 weeks).

Oral iron supplementation is recommended in the puerperal period, and parenteral supplementation in

cases of moderate or severe anemia.

Red blood transfusion should be restricted to cases where Hb is below 6 g/dL, or values of 7-9 gr/dL together with anemia symptoms.

In conclusion, puerperal hemorrhage is a condition for which PBM philosophy is fully fitting, leading to a more responsible management of this patient group and avoiding excessive or unnecessary transfusions, as well as the collateral damages it entails.

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Examining Bleeding Risk, Transfusion-related Complications, and Strategies to Reduce Transfusions in Lung Transplantation

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The authors present a review of bleeding and transfusion implications in lung transplantation. A patient undergoing a lung transplantation presents a higher morbidity and mortality, compared to other solid organ transplants. Thus, although results have significantly improved in the last decade, survival after 5 years barely exceeds 50%. One of the factors that may potentially be involved is blood transfusion, given that, in other scenarios, both anemia and transfusion have been linked to worse results.

Transfusion, both for the donor and the recipient, has been associated with a worse prognosis in lung transplantation. It has been described that transfusion to the donor patient complicates the study of further compatibility and increases the chances of rejection by the recipient. If transfusion is required, the authors recommend the use of leukoreduced blood products. In the same way, transfusion during surgery has been associated with a higher incidence of primary graft dysfunction, although clinically, it is hard to distinguish this condition from other transfusion-related pulmonary injuries, such as TACO (due to volume overload) or TRALI (immune)—with a higher incidence of chronic rejection or mortality.

From the pre-operative study of candidate patients to transplantation, the existence of a coagulopathy is ruled out, with special consideration to certain situations, such as acquired vitamin K deficiency in final stages of cystic fibrosis; the Hermansky-Pudlak syndrome, combining plateletopathy and interstitial pulmonary disease; or pulmonary hypertension, which may go together with acquired von Willebrand factor deficiency and/or acquired platelet deficiency due to the use of inhaled pulmonary vasodilators. Anemia is also included in the pre-operative study, although the indication of intravenous iron or erythropoietin is still controversial in the lung transplant scenario.

The risk of bleeding during lung transplant is multifactorial. On top of factors common to other scenarios (age, kidney disease, chronic treatment with antiaggregant or anticoagulant drugs, anemia), a higher need for transfusions has been described in patients with cystic fibrosis or pulmonary fibrosis, possibly due to the need for intraoperative circulatory support (ECMO) or the existence of previous thoracic surgery.

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All in all, in case of bleeding, in lung transplant, as well as in other scenarios, a PBM strategy should be followed, reflected in an objective-guided multidisciplinary protocol, which has shown to decrease transfusions, morbidity, and costs. In this context, the authors recommend the use of blood recovery devices, provided that the patient does not present an active infection. All this notwithstanding, when the time comes, the decision to transfuse a patient in a lung transplant must consider other factors beyond a hemoglobin value (considering 7 g/dl as a restrictive threshold and 10 g/dl as a liberal one), providing an estimate of oxygen transport and consumption, tissue perfusion, or pace of bleeding. In these situations, the management of the coagulopathy based on a factor concentrate or blood products varies between regions, according to costs and availability, and no specific recommendation can be established. The use of fibrinolytic drugs is not standardized either—aprotinin is approved and its used is recommended in lung transplant in Europe.

In conclusion, as patients undergo successive lung transplantations, they get increasingly clinically complex. In these cases, reducing the bleeding, and thus transfusion, leads to better results. Therefore, further studies are required on the optimization of the donor and recipient, surgical techniques, more precise laboratory techniques, and the optimization of hemostasis.

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Patient blood management guideline for adults with critical bleeding.

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In this edition of ***bleeding news*** we discuss the latest **Australian guidelines** on PBM in adult patients with critical hemorrhage.

To assess the quality of the evidence, the authors used the GRADE system—Grading of Recommendations, Assessment, Development and Evaluation,— and, to draft the guidelines, they used AGREE—Appraisal of Guidelines for Research and Evaluation.

The accuracy with which they have assessed the quality of the evidence is remarkable, leading in some cases to different recommendation degrees to American, European, or Spanish guidelines.

RECOMMENDATIONS:

1. In the case of **patients with critical bleeding**, institutions should have a multidisciplinary **MTP** (Strong Recommendation). All international guidelines, including the Spanish ones (HEMOMAS II), agree with this degree of recommendation.

2. In **patients with critical bleeding** requiring the activation of MTPs, the early and frequent measurement of the following parameters is recommended: **temperature, pH, ionic Ca, Hb, PLQ, TP, INR, rTTPA, and fibrinogen** (Strong Recommendation). All international guidelines, as well as HEMOMAS II, agree with this degree of recommendation.

3. In **patients with critical bleeding**, high transfusion ratios of **pRBC:FFP:PLT** may be beneficial, although there is not enough evidence to recommend 1:1:1 ratios over 2:1:1 ratios (Weak Recommendation). Most international guidelines, including HEMOMAS II, agree with this degree of recommendation.

    a. Monitoring **fibrinogen levels** is also required, either through viscoelastic tests or conventional coagulation tests. On this issue, HEMOMAS II recommends the use of viscoelastic tests over conventional tests to guide the administration of fibrinogen in traumatic critical bleeding.

4. In **patients with critical bleeding**, the administration of at least 1 unit of FFP for each 2 pRBCs is recommended, and at least one PLT pool for each 8 pRBCs administered (Weak Recommendation). Most international guidelines, including HEMOMAS II, make no reference to these ratios, but to the ones recommended in the previous section.

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a. Supplementing **fibrinogen with 3-4 grams** whenever necessary.

b. **PCC, 25-50 UI/Kg,** to revert the effect of warfarin.

5. In **patients with critical bleeding,** it is suggested over routine use of **recombinant factor VII** (Weak Recommendation). In HEMOMAS this was considered as a Moderate Recommendation.

6. In **trauma** patients with critical bleeding, early use of **tranexamic acid** is recommended as part of MTPs (Weak Recommendation). Most international guidelines, including HEMOMAS II, consider this as a Strong Recommendation. Australian authors considered that the decrease in mortality due to the administration of tranexamic acid is too low to be appointed a Strong Recommendation, taking into account the low mortality rate of critical hemorrhages caused by trauma in Australia.

   a. There is not enough data to recommend the administration of **tranexamic acid** in gastrointestinal bleeding.

7. In **obstetric** patients with critical bleeding, early administration of **tranexamic acid** should be considered within MTPs (Weak Recommendation). HEMOMAS II did not include recommendations on obstetric bleeding, but half of the international guidelines recommend with a higher degree the administration of tranexamic acid.

8. The use of **viscoelastic tests** may be beneficial in patients with critical bleeding, but they reckoned there was not enough evidence to recommend them. Anyway, they do mention that, if they are used, it should be within an algorithm and an MTP. In trauma critical hemorrhage, most international guidelines, including HEMOMAS II, increase the degree of recommendation of viscoelastic tests to guide transfusion within MTP algorithms.

In conclusion, many international guidelines have been published with the goal of optimizing the prognosis of patients with critical hemorrhage, but choosing the appropriate guideline will very important depending on the mechanism causing the hemorrhage and the geographical area where we are working.

Abbreviations. PBM: Patient Blood Management. MTP: Massive Transfusion Protocol. Hb: Hemoglobin. PLT: Platelets. PT: Prothrombin Time. INR: International Normalized Ratio. APTTR: Activated Partial Thromboplastin Time Ratio pRBCs: Packed Red Blood Cells. FFP: Fresh Frozen Plasma. PCC: Prothrombin Complex Concentrate