

BLOOD PRODUCT REPLACEMENT: OBSTETRIC HEMORRHAGE

BLOOD PRODUCT REPLACEMENT

PACKED RED BLOOD CELLS (PRBCS)

The majority of protocols recommended four-six units of PRBCs be prepared and available and the patient's hematocrit be maintained minimally at 21-24% (hemoglobin 7-8g/dL).^{1,5,7,9,14} Ideally, the use of a single unit of PRBCs should increase the hematocrit by approximately 3-4% (1g/dL increase in hemoglobin) in a 70 kg patient.¹⁵ However, the expected increase in hematocrit may be slightly less in patients at term due to expanded blood volume during pregnancy. As noted elsewhere in this toolkit, any patient with continued bleeding after initial measures have failed (Stage 2) should be transfused with multiple units of PRBCs based on clinical signs and response to treatments. If these are not readily available, consideration should be given for the use of emergency released

uncross-matched group O negative blood while the blood bank is completing the patient's type, antibody screen and crossmatch. Note: For women with a negative antibody screen, virtually all type compatible units will also be crossmatch compatible. Consistent with recommendations from this toolkit, for any patient that reaches Stage 3, a massive OB hemorrhage pack, which includes 3 to 6 units of PRBCs as pre-arranged with the blood bank for massive transfusion protocol, should be prepared and transfused based on vital signs and blood loss. Good communication with the laboratory regarding the urgency of the situation is essential.

FRESH FROZEN PLASMA (FFP)

Fresh frozen plasma contains nearly all coagulation factors and can be used up to 24 hours after thawing and up to 5 days if relabeled as "thawed plasma." The type of plasma that is available can vary from institution to institution. Concomitant use of FFP and PRBCs is recommended during massive hemorrhage. Other acceptable choices for plasma include FP24, which is plasma that has been frozen within 24 hours of collection (instead of 8 hours as in FFP), and liquid (never frozen) plasma. FP24 is used virtually the same as FFP and can be stored up to 5 days if labeled "thawed" as well. Liquid plasma must be collected in a closed system and may contain cellular elements increasing the risk for CMV and therefore, perhaps a less desirable choice in this setting.

After the first two units of PRBC's, early transfusion with FFP is correlated with improved survival from hemorrhage after trauma. There is ongoing debate as to the optimal ratio but most protocols recommend ratios between 1:1 and 1:2 (FFP:RBC) for initial resuscitation. Similar recommendations have been established at centers with existing massive OB hemorrhage protocols with the goal of maintaining the INR at < 1.5-1.7.^{1,5,9,16,17} If diffuse bleeding is noted, or there is laboratory evidence of DIC and the patient's blood type is unknown, AB plasma is recommended. AB plasma is often in short supply. If AB plasma were not available, 2-3 units of mismatched plasma is usually well tolerated by adults while patient type is completed.¹⁸ FFP usually requires 20-30 minutes to thaw and may not be available immediately.

PLATELETS

All protocols in our review recommended transfusion of a single donor apheresis unit or a pool of 6 whole blood-derived platelets when platelet levels varied between are below 100K during Stage 3.^{6,8,9} Platelet pheresis units are the standard equivalent of 5-6 units of whole blood-derived pooled platelets and may increase the platelet count in a 70 kg patient by approximately 40-50,000/uL¹⁵

In the face of massive maternal hemorrhage, platelet transfusions should maintain platelet count between 50,000-100,000/uL. However, platelet counts should be used only as a guide and should be interpreted in conjunction with the patient's clinical condition.

These recommendations are consistent with those of the American Society of Anesthesiologists Task Force on Perioperative Blood Loss.¹⁹ Some protocols have suggested higher platelet counts for initiating transfusion and maintaining appropriate platelet levels. These suggestions are based on the assumption that unless bleeding and DIC have been controlled, the patient will experience ongoing platelet loss.^{2,5} Platelets do not require crossmatching and are not always type specific. Rh negative platelets (at least those from whole blood) are preferentially given to patients with an Rh negative blood type because of the small risk of sensitization to the D-antigen. However, a dose of Rh-Immune Globulin may be given and is protective if Rh negative platelets are unavailable. As a general rule, apheresis platelets rarely are significantly contaminated with red cells and therefore the observed seroconversion rate following Rh (D) + units in Rh (D) negative patients is vanishingly low if only receiving apheresis platelets.^{20,21}

CRYOPRECIPITATE AND FIBRINOGEN

In the face of hypofibrinogenemia (fibrinogen levels < 100-125 mg/dL and ongoing bleeding), fibrinogen should be used in addition to FFP. Transfusion recommendations were based on maintaining a fibrinogen concentration above 100 mg/dL. Cryoprecipitate released from the Blood Bank is often in pools of 4-10 units. Each unit provides \geq 150 mg of fibrinogen for a total of at least 1500 mg in a pool of 10 units in a total volume of approximately 80-100 cc. A pooled "ten-unit" pack would be expected to increase the fibrinogen level of a 70 kg patient by approximately 75 mg/dL. It is worth noting that a 10-unit pool represents 10 separate donor exposures. Improved manufacturing techniques are making smaller pools with equivalent fibrinogen dose common. This reduces the donor exposure risk, where available. If continued bleeding and hypofibrinogenemia is present, additional units of cryoprecipitate should be used. In the presence of severe abruptio or amniotic fluid embolism the initial request for blood products should include cryoprecipitate as both of these conditions are associated with significant fibrinogen depletion.

CALCIUM

Hypocalcemia is one of the most clinically significant electrolyte disturbances noted in massive transfusion. Both PRBCs and FFP contain the anticoagulant citrate, which binds calcium. Although this can be cleared in a short amount of time by the liver in optimal conditions, hepatic function may be impaired by significant hypotension, hypothermia, preexisting liver disease, or may be overwhelmed by the rate of blood product transfusion and dilution. Calcium is necessary for adequate clotting and myocardial contraction. Ionized calcium should be frequently monitored and replaced to keep levels within a normal physiologic range.

COAGULOPATHY, ACIDOSIS & TEMPERATURE

The coagulopathy frequently associated with massive hemorrhage may be further exacerbated by hypothermia and acidosis. Worsening acidosis often results from hypoperfusion of multiple organs and an increase in lactate levels. Activity of clotting factors is significantly reduced (> 50% reduction) at a pH of 7.0, compared to a pH of 7.4 and electrolytes are frequently abnormal.²²

Hypothermia associated with the infusion of cold fluids (including blood products) is the main cause of heat loss during massive transfusion. In trauma patients, each 1°C drop in temperature is associated with a 10% drop in clotting factor activity, and a core temperature below 33°C is associated with a > 50% reduction in normal factor activity.²² Acidosis and hypothermia are associated with increased morbidity and mortality in trauma patients. During massive transfusion resuscitation, the patient's arterial blood gas, electrolytes, and core temperature should be monitored to guide clinical management, all transfused fluids should be warmed, and direct warming of the patient should be initiated as needed to maintain eutherma.

RECOMBINANT FACTOR VIIa

Factor VII is a vitamin K-dependent serine protease with a pivotal role in coagulation. After reconstitution with sterile water, each vial contains approximately 0.6 mg/mL (600 µg/mL). Its approved indication for use is in patients with hemophilia A and B. The role of rFVIIa in primary postpartum hemorrhage is controversial.²³⁻²⁵ It has been reported (anecdotally) to significantly improve hemostasis in hemorrhaging obstetrical patients, but may also result in life-threatening thrombosis.²⁶ The committee reviewed the literature and it appears that the use of Factor VII in obstetrical patients continues to be very rare and other specialty areas seem to be moving away from their use of the medication. We therefore cannot recommend its usage but recognize that in patients where all other efforts fail this may be a last ditch option (see editorial in *Annals of Internal Medicine*).²⁷ Continued concern over the medication causing venous thrombosis prevents recommending usage outside this narrow range of patients.^{28,29} If rFVIIa is to be used, treatment should be provided in consultation with a local and/or regional expert in the area of massive hemorrhage, such as a hematologist, transfusion medicine specialist, or trauma surgeon. There is not a consensus on dosing recommendations in obstetrical hemorrhage patients.

SUMMARY

During obstetrical hemorrhage, the primary goals are to provide adequate and early blood product replacement and to either prevent or correct DIC. The literature and protocols reviewed provided remarkable consensus related to therapy in the setting of massive obstetrical hemorrhage.

RECOMMENDATIONS

For transfusion in the setting of massive obstetrical hemorrhage, use a ratio of PRBCs to FFP to platelets that is 4-6 units PRBC: 4 units FFP: 1 unit apheresis platelets.

STAT LABS

If bleeding exceeds expected volume for routine delivery and there is no response to initial therapy, request stat laboratory analysis for the following:

1. CBC with platelets
2. PT(INR) /PTT
3. Fibrinogen and ionized calcium

Repeat labs 1-3 every 30 minutes until patient is stable.

PBRCs

1. Initial request: 3-6 units of RBCs
2. O-negative or type-specific blood initially until cross match units are released

FFP

1. Initial goal of RBCs to FFP ratio should be 3:2
2. Infuse FFP to maintain INR < 1.5-1.7

PLATELETS

1. Prefer single donor apheresis platelet
2. Infuse to maintain platelet count > 50,000-100,000/uL in the face of ongoing hemorrhage

CRYOPRECIPITATE

1. Initial request: 6-10 units cryoprecipitate if fibrinogen is less than 100 mg/dL
2. Initial request: 10 units cryoprecipitate if severe abruption or amniotic fluid embolism is suspected (in some institutions one adult dose may contain fewer units with equivalent amount of fibrinogen)
3. Additional units to maintain fibrinogen concentration \geq 100-125 mg/dL

TRANEXAMIC ACID:

Currently under investigation³¹

RECOMBINANT ACTIVATED FACTOR VII (rFVIIA)

Not universally recommended

EDUCATIONAL TOOLS, SUPPORT DOCUMENTS

TABLE 1: Adverse Reactions to Transfusions (See Table 1 below)

EVIDENCE GRADING

Level of Evidence: II-3 C: Evidence obtained from multiple time series with or without intervention. Well-done QI studies with statistical process control analyses (or the like) fall into this category. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence. Recommendations based primarily on consensus and expert opinion.