Hemodynamic and Hemostatic Resuscitation for Obstetric Hemorrhage

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Definitions: postpartum hemorrhage (PPH) — loss of >500 mL of blood after vaginal birth or > 1 L after cesarean delivery; clinically significant hemorrhage — persistent bleeding of >1 L despite use of first-line uterotonics and uterine massage; severe maternal morbidity from hemorrhage — requirement for ≥4 U of red blood cells (RBCs) or whole blood, or admission to intensive care unit (ICU)

Epidemiology of PPH: incidence — occurs in 3% of women; 3% receive blood transfusion during hospitalization for delivery; 3% of that 3% (1 in 1250 women) experience major morbidity related to PPH, such as massive transfusion of blood (>10 U), admission to ICU, or hysterectomy; 1 in 35,000 women has hemorrhage-related cardiac arrest or dies; morbidity and mortality — survival 50% after cardiac arrest due to PPH; PPH among leading causes of maternal death, maternal cardiac arrest, and lawsuits against anesthesiologists; improving systems — many reviews report that lack of timely diagnosis, transfusion, and reoperation often reflect poor communication among team members; improving treatment of PPH offers greatest number of opportunities to prevent deaths; resources include toolkit from California Maternal Quality Care Collaborative (CMQCC) and hemorrhage bundle from National Partnership for Maternal Safety (NPMS)

Risk-stratified preparation of blood products: recommended by CMQCC, NPMS, and other organizations; risk factors should be evaluated in antenatal period, at time of admission, and again before transfer to operating room; low risk — in lowest-risk women, drawing clot adequate; type and screen takes twice as long for Rh-negative women; 57% of Rh-negative women may have positive screen; with tests required to identify antibody, evaluation may require ≥4 hr; high risk — crossmatched blood should be prepared for patients with ≥10% risk for transfusion, including women with abnormal placentation, anemia, thrombocytopenia, bleeding on admission, coagulopathy, fetal demise, abruptio, or risk for uterine rupture; patients undergoing trial of labor after cesarean delivery need targeted assessment of hemorrhagic risk; prolonged procedures may be needed to find compatible blood products for women with antibodies other than anti-D, history of difficult crossmatch, autoimmune hemolytic anemia, or sickle cell disease (SCD); patients with SCD often have antibodies to minor antigens and severe delayed hemolytic reactions due to fragility of RBCs

Transfusion reactions: immediate — related to blood groups A and B; polysaccharide antigens found on surfaces of RBCs, bacteria, and plant seeds; exposure via microbiome of gut common; most antibodies IgM and complement-fixing; membrane attack complex punches pores in membranes of RBCs, which leads to acute massive hemolysis within 6 hr of transfusion; delayed — related to minor membrane-bound antigens in patients with previous exposure to allogeneic blood from transfusion, transplantation, or pregnancy; most antibodies IgG; antibodies crosslink to bind cytotoxic monocytes and T helper cells, which leads to erythropagocytosis in reticuloendothelial system; develops in 3 to 14 days; signs include decreased hemoglobin, fever, jaundice, and hemoglobinuria

Emergent transfusion: if crossmatched blood not ready, O-negative blood and AB plasma may be given

Abnormal placenta: minority of women with abnormal placentation need transfusion of >10 U; maternal age, depth of invasion, and other clinical variables do not predict transfusion; 4 to 20 U of each blood product should be available, depending on individual’s risk and capacity of institution to prepare and deliver blood products; if blood bank slow, obstetrician should set up 20 U of each product

Recommendations for all births (ie, stage 0 PPH): include quantification of blood loss, monitoring of vital signs, fundal height, and uterine tone, and active management of third stage; Association of Women’s Health, Obstetric and Neonatal Nurses (AWHONN) and NPMS encourage quantification rather than estimation of blood loss; 1 mL of blood weighs 1 g; blood from suction canisters, drapes, absorptive materials used to wipe blood from floor, underpads, and laparotomy sponges should be weighed; dry weights of pads and sponges and weight of other fluids subtracted to estimate blood loss; changes in vital signs may identify concealed (eg, retroperitoneal) bleeding

Maternal early warning criteria: multidisciplinary committee reviewed early warning systems; labor and delivery units report difficulty getting physician to bedside; if patient reaches predefined warning thresholds, evaluating clinician should be available promptly (within >15 min) to help initiate diagnostic and therapeutic interventions; health care team should follow trends in baseline maternal heart rate (HR) and intervene if necessary

Active management of third stage with oxytocin (Pitocin): 350 mU bolus adequate for preventing atony; as infusion, 300 mU/min or 18 U/hr sufficient to establish uterine tone; stage I hemorrhage (>500 mL of bleeding after vaginal birth or >1 L

Educational Objectives

The goals of this program are to improve diagnosis and treatment of postpartum hemorrhage. After hearing and assimilating this program, the clinician will be better able to:

1. Identify women at risk for major postpartum hemorrhage (PPH).
2. Compare the pathophysiology of immediate and delayed transfusion reactions.
3. Appropriately apply contemporary transfusion practices to the obstetric setting.
4. Participate in efforts to increase preparedness for obstetric hemorrhages.
5. Use thromboelastography to monitor coagulation in patients with PPH.

Faculty Disclosure

In adherence to ACCME Standards for Commercial Support, Audio Digest requires all faculty and members of the planning committee to disclose relevant financial relationships within the past 12 months that might create any personal conflicts of interest. Any identified conflicts were resolved to ensure that this educational activity promotes quality in health care and not a proprietary business or commercial interest. For this program, members of the faculty and planning committee reported nothing to disclose. In her lecture, Dr. Mhyre presents information that is related to the off-label or investigational use of a therapy, product, or device.
after cesarean delivery) requires bedside interventions to control bleeding and escalation of uterotonics; recommended intravenous dose of oxytocin 40 to 80 U/L; however, obstetrician should think in terms of infusion rates; oxytocin first-line uterotonic for prophylaxis and treatment; side effects—increase significantly when infusion rate increased; decrease in mean arterial pressure (MAP) of 30 mm Hg observed after 5-U bolus of oxytocin; decrease in MAP of 10 mm Hg observed after infusion of 5 U over 5 min (this leads to decreased coronary perfusion, changes in ST segment, and troponin leak); infusion rate—delivery by infusion pump reduces side effect of chest pain; infusion should be started at 18 U/hr, increased to 36 U/hr if tone not established promptly, and increased to 60 U/hr if bleeding persists; if ineffective, secondary uterotonics should be used rather than higher doses of oxytocin.

Other uterotonics: methylergonovine (Methergine) preferred agent; although drug produces hypertension, this side effect therapeutic when patient hemorrhaging; when mouth dry, buccal or sublingual misoprostol not well absorbed

Delays in treatment: observational study of 4500 women with stage I hemorrhage assessed optimal time frames for performing specific interventions to prevent severe hemorrhage; oxytocin should be given within 10 min; manual examination of uterine cavity should be performed within 20 min; anesthesiologist and obstetrician should be notified within 10 min; anesthesiologist can provide venous access, fluid resuscitation, and analgesia for bedside maneuvers, administer oxytocin and secondary uterotonics, and prepare for possible surgery.

Stage II hemorrhage: declared when bleeding continues despite initial management with bedside interventions and uterotonics; team should be mobilized, patient moved to operating room, and clinical laboratory tests ordered; system of simultaneous paging may be used to bring key personnel to bedside; hemorrhage cart—should be in visible location near obstetric operating suite; drawers should be labeled; laboratory assessment—includes platelets, hematocrit, prothrombin time (PT), International Normalized Ratio, and fibrinogen; fibrinogen—most accurate predictor of subsequent severe blood loss; during pregnancy, normal fibrinogen 4 to 6 g/L; fibrinogen level ≥2 g/L protective against hemorrhage; level ≤2 g/L pathognomonic for subsequent severe hemorrhage; resuscitation guidelines recommend maintaining fibrinogen level at ≥1 g/L, but 2 g/L better target for obstetric patients; testing fibrinogen takes 1 hr, so test not useful in real time; however, results of assay that uses rotational thromboelastometry to measure firmness of clot (rot-ema) available in 10 min; test result correlates with fibrinogen level and predicts subsequent severe hemorrhage.

Transfusion thresholds: when nadir of hematocrit <20%, blood flow to microvasculature compromised; adequate volume and RBCs required for circulation and oxygenation; when acute normovolemic hemodilution induced before elective surgery, good perfusion may be maintained at lower hematocrit levels; however, in dynamic setting in which bleeding uncontrolled, hematocrit less useful than other measures of hemodynamic instability, such as ST changes; transfusion often initiated when bleeding ongoing after giving 2 L of crystalloid; other useful parameters include lactate and base excess; in obstetric setting, mixed venous oxygen saturation and extraction ratios unavailable, so anesthesiologist should look over drape to evaluate surgical situation.

Stage III hemorrhage: refers to continued bleeding after loss of 1500 mL of blood; stage III considered massive hemorrhage

Stage IV hemorrhage: refers to cardiovascular collapse with hypovolemic shock; may occur with amniotic fluid embolism (AFE); requires mobilization of other institutional resources; when venous collapse occurs, intraosseous needle may be inserted in proximal humerus to administer drugs or ≤125 mL of fluid or blood products; other maneuvers include elevation of legs, manual compression of aorta, permissive hypotension, and shock garments; obstetrician should know technique for performing firm manual compression of aorta, which may be maintained for 50 min; Teflon pledgetsed sutures helpful for friable tissue

Massive transfusion: goal-directed transfusion—gold standard; reasonable transfusion goals include hematocrit >21%, PT and partial thromboplastin time ≤1.5 times upper limit of normal, platelet count >50,000/mm³, and fibrinogen >2 g/L; goal-directed therapy possible when resuscitation began at onset of stage II hemorrhage, laboratory results available within 30 min, and rate of bleeding <3 U/hr; under other circumstances, fixed-ratio transfusion recommended; fixed-ratio transfusion—high ratio of plasma to RBCs improves 24-hr survival; older literature criticized because of survival bias (ie, patients who survived long enough to be treated with fresh frozen plasma more likely to survive); some trauma centers and emergency teams in field now stock thawed plasma; first 3 hr most crucial period of time for giving plasma; plasma deficits—low plasma deficit defined by difference of ≤2 U (RBC units minus plasma units); high plasma deficit means ≥6-U difference; low plasma deficit improves survival; literature on survival and plasma deficit applies to patients receiving ≥10 U of blood, but most obstetric hemorrhages do not fall into this category; massive transfusion protocol with fixed ratios not required unless surgical control of hemorrhage fails

Evidence for fixed ratios: benefit—ongoing trial evaluating mortality in 680 trauma victims randomized to different transfusion ratios; few data in obstetric patients; however, observational study of 142 women found association between low transfusion ratio and decreased need for invasive procedures; harm—1:1 transfusion ratio confers no survival benefit in patients receiving fewer than 6 to 9 U; multidonor components (eg, platelets, cryoprecipitate) may precipitate alloimmunization against minor antigens; inflammatory mediators in plasma may cause transfusion-related acute lung injury and acute respiratory distress syndrome; plasma should be avoided in patients who require transfusion of <6 U; transfusion-related immunomodulation may induce tolerance to cancers; concentration of citrate in plasma 7-fold higher than that in RBCs and platelets; citrate toxicity manifested as hypocalcemia and hypomagnesemia; rapid transfusion associated with hyperkalemia; management—serial measurements of electrolytes and infusion of calcium chloride required for patients receiving >1 U of plasma in 15 min

Protocols: Stanford protocol provides massive transfusion pack of 6 U RBCs, 4 U plasma, and 5-pack of platelets; 5-pack of platelets contains same concentration of hemostatic mediators as 1 U of plasma; selection of subsequent blood products based on serial laboratory analyses; major obstetric hemorrhages are uncommon, so institutional protocol for transfusion should be used; however, protocols may be adapted for obstetric unit

Viscoelastic monitoring: rapid turnaround of laboratory tests facilitates decisions about transfusion; thromboelastography—allows images of coagulation profiles to be displayed in real time on bedside monitor; to perform test, place 340 μL of blood in cup; add tissue factor and platelet inhibitor (to remove effects of intrinsic and extrinsic pathways and platelets, and isolate final common pathway); test assesses action of thrombin and crosslinking of fibrin, and provides indirect measure of function of fibrinogen

Tranexamic acid: indications—antifibrinolytic recommended by World Health Organization for continued bleeding after administration of uterotonics; dose 1 g over 1 min, repeated once after 30 min; drug may confer small benefit as prophylactic agent in patients undergoing elective cesarean delivery, but most important role treatment of uncontrolled hemorrhage; studies—in randomized trial including 20,000 patients with trauma, tranexamic acid associated with small but significant decrease in mortality (from 16% to 14.5%); thromboembolic complications not increased; ongoing World Maternal Antifibrinolytic Trial studying tranexamic acid

Cryoprecipitate: most concentrated form of fibrinogen; used during fixed-ratio transfusion when more fibrinogen needed; useful when limited volume desirable, as in patients with
transfusion-associated circulatory overload; standard dose 2 g; used off-label for PPH

**Other techniques:** cell salvage — in >650 published cases, no evidence links cell salvage with AFE; hemofiltration may be helpful in AFE; factor VIIa — used off-label; therapy of last resort because of association with thromboembolic complications (eg, myocardial infarction, stroke); other agents — no data available on use of other coagulation factors in obstetric patients

**Improving systems:** NPMs recommends multidisciplinary review of patients receiving ≥4 U of RBCs; Council on Patient Safety in Women’s Health Care sponsors series of free webinars on topics related to PPH

**Questions and Answers**

**Respiratory rate and oxygen saturation:** respiratory rate of 30 breaths per minute too high to provide early warning; pulse oximetry not useful because patients receive supplemental oxygen; saturation of 95% on room air adequate; patients with increasing oxygen requirement need evaluation

**Cell saver:** less cost-effective in low-risk populations; team should be trained in its use before emergency arises

**Fibrinogen levels:** in nontrauma hospitals without rapid turnaround of fibrinogen levels, physician should transfuse based on fixed ratios and ask laboratory to report fibrinogen level within 1 hr

**Heart rate:** epidural analgesia could affect sympathetic system and lower heart rate; not all patients with hemorrhage have tachycardia; assessing level of block helpful

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POSTPARTUM HEMORRHAGE

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1. Postpartum hemorrhage (PPH) after cesarean delivery is defined as:
   (A) Loss of >1 L of blood
   (B) Loss of >1500 mL of blood
   (C) Inadequate response to uterotonics and uterine massage
   (D) Requirement for administration of red blood cells

2. An obstetric patient with which of the following does not require crossmatched blood upon admission to the labor unit?
   (A) Placenta accreta
   (B) Anemia
   (C) Thrombocytopenia
   (D) Rh-negative blood type

3. Immediate transfusion reactions are associated with which of the following?
   1. IgM antibodies
   2. IgG antibodies
   3. Membrane attack complex
   4. Development of fever and jaundice over 3 days
   5. Previous exposure to allogeneic blood
   (A) 1,3
   (B) 1,4,5
   (C) 2,3
   (D) 2,4,5

4. Select the true statement about transfusion needs of women with abnormal placentation.
   (A) Transfusion of >10 U is required in a majority of cases
   (B) Maternal age is a predictor of need for transfusion
   (C) Depth of invasion is a predictor of need for transfusion
   (D) None of the above

5. A patient with PPH does not respond to infusion of oxytocin at 36 U/hr. Which of the following should the obstetrician do next?
   (A) Increase the infusion to 60 U/hr
   (B) Administer tranexamic acid
   (C) Administer methylergonovine
   (D) Administer misoprostol

6. In a patient with stage I PPH, the anesthesiologist should be notified within no more than:
   (A) 10 min
   (B) 15 min
   (C) 20 min
   (D) 30 min

7. Which of the following is the most accurate predictor of severe blood loss during delivery?
   (A) Platelet count
   (B) International Normalized Ratio
   (C) Fibrinogen
   (D) Thrombin

8. When massive transfusion is indicated, the gold standard for determining which blood products should be used is which of the following?
   (A) Fixed-ratio transfusion
   (B) Assessment of plasma deficit
   (C) Goal-directed transfusion

9. Viscoelastic monitoring is used to rapidly assess the function of:
   (A) Platelets
   (B) Fibrinogen
   (C) Intrinsic pathway
   (D) Extrinsic pathway

10. Which of the following statements about cryoprecipitate is incorrect?
    (A) Most concentrated form of fibrinogen
    (B) Used during fixed-ratio transfusion when more fibrinogen is needed
    (C) Useful in patients with transfusion-associated circulatory overload
    (D) Approved for use in patients with PPH

Answers to Audio Digest Obstetrics/Gynecology Volume 62, Issue 06: 1-D, 2-C, 3-B, 4-B, 5-B, 6-C, 7-D, 8-A, 9-B, 10-B