



Jaimey M. Pauli, MD

Dr. Pauli is Associate Professor and Attending Perinatologist, Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Penn State Health, Milton S. Hershey Medical Center, Hershey, Pennsylvania.

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A maternal-fetal medicine physician tackles 3 high-priority obstetric topics: managing opioid use disorders in pregnant women, protocols for postpartum hemorrhage, and new carrier screening recommendations

The past year brought new information and guidance from the American College of Obstetricians and Gynecologists (ACOG) on many relevant obstetric topics, making it difficult to choose just a few for this Update. Opioid use in pregnancy was an obvious choice given the national media attention and the potential opportunity for intervention in pregnancy for both the mother and the

fetus/newborn. Postpartum hemorrhage, an “oldie but goodie,” was chosen for several reasons: It got a new definition, a new focus on multidisciplinary care, and an exciting novel tool for the treatment toolbox. Finally, given the rapidly changing technology, new screening recommendations, and the complexity of counseling, carrier screening was chosen as a genetic hot topic for this year.

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Opioids, obstetrics, and opportunities

Reddy UM, Davis JM, Ren Z, Greene MF; Opioid Use in Pregnancy, Neonatal Abstinence Syndrome, and Childhood Outcomes Workshop Invited Speakers. Opioid use in pregnancy, neonatal abstinence syndrome, and childhood outcomes: Executive summary of a joint workshop. Obstet Gynecol. 2017;130(1):10-28.

ACOG Committee on Obstetric Practice. ACOG committee opinion No. 711: Opioid use and opioid use disorder in pregnancy. Obstet Gynecol. 2017;130(2):e81-e94.

The term “opioid epidemic” is omnipresent in both the lay media and the medical literature. In the past decade, the United States has had a huge increase in the number of opioid prescriptions, the rate of admissions and deaths due to prescription opioid misuse and abuse, and an increased

rate of heroin use attributed to prior prescription opioid use.

Obstetrics is unique in that opioid use and abuse disorders affect 2 patients simultaneously (the mother and fetus), and the treatment options are somewhat at odds in that they need to balance a stable maternal status and intrauterine environment with the risk of neonatal abstinence syndrome (NAS). Additionally, pregnancy is an opportunity for a woman with opioid use disorder to have access to medical care (possibly for the first time) leading to the diagnosis and treatment of her disease. As the clinicians on the front line, obstetricians therefore require education and guidance on best practice for management of opioid use in pregnancy.

In 2017, Reddy and colleagues, as part of

a joint workshop on opioid use in pregnancy, and a committee opinion from ACOG provided the following recommendations.

Screening

Universally screen for substance use, starting at the first prenatal visit; this is recommended over risk factor-based screening.

Use a validated screening tool. A tool such as a questionnaire is recommended as the first-line screening test (for example, the 4Ps screen, the National Institute on Drug Abuse Quick Screen, and the CRAFFT Screening Interview).

Do not universally screen urine and hair for drugs. This type of screening has many limitations, such as the limited number of substances tested, false-positive results, and inaccurate determination of the frequency or timing of drug use. Information regarding the consequences of the test must be provided, and patient consent must be obtained prior to performing the test.

Treatment

Use medication-assisted treatment with buprenorphine or methadone, which is preferred to medically supervised withdrawal. Medication-assisted treatment prevents withdrawal symptoms and cravings, decreases the risk of relapse, improves compliance with prenatal care and addiction treatment programs, and leads to better obstetric outcomes (higher birth weight, lower rate of preterm birth, lower perinatal mortality).

Know that buprenorphine has several advantages over methadone, including the convenience of an outpatient prescription, a lower risk of overdose, and improved neonatal outcomes (higher birth weight, lower doses of morphine to treat NAS, shorter treatment duration).

Prioritize methadone as the preferred option for pregnant women who are already receiving methadone treatment (changing to buprenorphine may precipitate withdrawal), those with a long-standing history of or multi-substance abuse, and those who have failed other treatment programs.

Prenatal care

Screen for comorbid conditions such as sexually transmitted infections, other medications or substance use, social conditions, and mental health disorders.

Perform ultrasonography serially to monitor fetal growth because of the increased risk of fetal growth restriction.

Consult with anesthesiology for pain control recommendations for labor and delivery and with neonatology/pediatrics for NAS counseling.

Intrapartum/postpartum care

Recognize heightened pain. Women with opioid use disorder have increased sensitivity to painful stimuli.

Continue the maintenance dose of methadone or buprenorphine throughout hospitalization, with short-acting opioids added for a brief period for postoperative pain.

Prioritize regional anesthesia for pain control in labor or for cesarean delivery.

Consider alternative therapies such as regional blocks, nonopioid medications (nonsteroidal anti-inflammatory drugs, acetaminophen), or relaxation/mindfulness training.

Avoid mixed antagonist and agonist narcotics (butorphanol, nalbuphine, pentazocine) as they may cause acute withdrawal.

Encourage breastfeeding to decrease the severity of NAS and maternal stress and increase maternal-child bonding and maternal confidence.

Offer contraceptive counseling and services immediately postpartum in the hospital, with strong consideration for long-acting reversible contraception.

Opioid prescribing practices

Opioids are prescribed in excess post-cesarean delivery. Several recent studies have demonstrated that most women are prescribed opioids post-cesarean delivery in excess of the amount they use (median 30–40 tablets prescribed, median 20 tablets used).^{1,2} The leftover opioid medication

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Medication-assisted treatment prevents withdrawal symptoms and cravings, decreases relapse risk, improves compliance, and leads to better obstetric outcomes

usually is not discarded and therefore is at risk for diversion or misuse. A small subset of patients will use all the opioids prescribed and feel as though they have not received enough medication.

Prescribe post-cesarean delivery opioids more appropriately by considering individual inpatient opioid requirements or a shared decision-making model.³

Prioritize acetaminophen and ibuprofen during breastfeeding. In a recent editorial in OBG MANAGEMENT, Robert L. Barbieri, MD, recommended that whenever possible, acetaminophen and ibuprofen should be

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Universal screening for substance use should be performed in all pregnant women, and clinicians should offer medication-assisted treatment in conjunction with prenatal care and other supportive services as the standard therapy for opioid use disorder. More selective, patient-specific opioid prescribing practices should be applied in the obstetric population.

the first-line treatment for breastfeeding women, and narcotics that are metabolized by CYP2D6 should be avoided to reduce the risk to the newborn.⁴

Postpartum hemorrhage: New definitions and new strategies for stemming the flow

ACOG Committee on Practice Bulletins—Obstetrics. ACOG practice bulletin No. 183: Postpartum hemorrhage. Obstet Gynecol. 2017;130(4):e168–e186.

From the very first sentence of the new ACOG practice bulletin, postpartum hemorrhage (PPH) is redefined as “cumulative blood loss greater than or equal to 1,000 mL or blood loss accompanied by signs or symptoms of hypovolemia within 24 hours after the birth process (includes intrapartum loss) regardless of route of delivery.” Although this does not seem to be a huge change from the traditional teaching of a 500-mL blood loss at vaginal delivery and a 1,000-mL loss at cesarean delivery, it reflects a shift in focus from simply responding to a certain amount of bleeding to using a multidisciplinary action plan for treating this leading cause of maternal mortality worldwide.

Focus on developing a PPH action plan

As part of the shift toward a multidisciplinary

action plan for PPH, all obstetric team members should be aware of the following:

- For most postpartum women, by the time they begin to show signs of hemodynamic compromise, the amount of blood loss approaches 25% of their total blood volume (1,500 mL). Lactic acidosis, systemic inflammation, and a consumptive coagulopathy result.
- Risk stratification prior to delivery, recognition and identification of the source of bleeding, and aggressive early resuscitation to prevent hypovolemia are paramount. Experience gleaned from trauma massive transfusion protocols suggests that judicious transfusion of packed red blood cells, fresh frozen plasma, and platelets in a 1:1:1 ratio is appropriate for obstetric patients. Additionally, patients with low fibrinogen levels should be treated with cryoprecipitate.
- The use of fixed transfusion ratios and standardized protocols for recognition and management of PPH has been demonstrated to increase earlier intervention

FAST TRACK

ACOG’s new PPH definition reflects a shift in focus from simply responding to a certain amount of bleeding to using a multidisciplinary action plan for treatment

TABLE Facts about tranexamic acid

- The dose is 1 g IV; it may be repeated once in 24 hours
- Half-life is 2 hours
- Clearance is renal—so do *not* use in patients with renal impairment
- Antifibrinolytic activity usually lasts 7 to 8 hours
- Tranexamic acid is contraindicated in patients with a history of thromboembolism in pregnancy
- The drug is believed to be compatible with breastfeeding

and resolution of hemorrhage at an earlier stage, although the maternal outcomes results have been mixed.

- Multidisciplinary team drills and simulation exercises also should be considered to help solidify training of an institution's teams responsible for PPH response.

Novel management option: Tranexamic acid

In addition to these strategies, there is a new recommendation for managing refractory PPH: tranexamic acid, which works by binding to lysine receptors on plasminogen and plasmin, inhibiting plasmin-mediated fibrin degradation.⁵ Previously, tranexamic acid was known to be effective in trauma, heart

surgery, and in patients with thrombophilias. Pacheco and colleagues recently demonstrated reduced mortality from obstetric bleeding if tranexamic acid was given within 3 hours of delivery, without increased thrombotic complications.⁵ ACOG recommends its use if initial medical therapy fails, while the World Health Organization strongly recommends that tranexamic acid be part of a standard PPH package for all cases of PPH (TABLE).⁶

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Postpartum hemorrhage requires early, aggressive, and multidisciplinary coordination to ensure that 1) patients at risk for hemorrhage are identified for preventive measures; 2) existing hemorrhage is recognized and quickly treated, first with noninvasive methods and then with more definitive surgical treatments; and 3) blood product replacement follows an evidence-based standardized protocol. Tranexamic acid is recommended as an adjunct treatment for PPH (of any cause) and should be used within 3 hours of delivery.

FAST TRACK

Tranexamic acid was shown to reduce mortality from obstetric bleeding when given within 3 hours of delivery

Carrier screening—choose something

ACOG Committee on Genetics. Committee opinion No. 690: Carrier screening in the age of genomic medicine. Obstet Gynecol. 2017;129(3):e35–e40.

ACOG Committee on Genetics. Committee opinion No. 691: Carrier screening for genetic conditions. Obstet Gynecol. 2017;129(3):e41–e55.

Ideally, carrier screening should be offered prior to pregnancy to fully inform couples of their reproductive risks and options for pregnancy. If not performed in the preconception period, carrier screening should be offered to all pregnant women. If a patient chooses screening and screens positive for a particular disorder, her reproductive partner should then

be offered screening so that the risk of having an affected child can be determined.

New ACOG guidance on prepregnancy and prenatal screening

Carrier screening recommendations have evolved as the technology available has expanded. All 3 of the following strategies now are considered “acceptable” according to 2 recently published ACOG committee opinions.

Traditional ethnic-specific carrier screening, previously ACOG’s sole recommendation, involves offering specific genetic

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WHAT THIS EVIDENCE MEANS FOR PRACTICE

All pregnant patients or patients considering pregnancy should be offered carrier screening as standard reproductive care, including screening for cystic fibrosis, hemoglobinopathies, and spinal muscular atrophy. Ethnic, panethnic, or expanded carrier screening (and patient-requested specific screening) all are acceptable options, and a standard screening and counseling protocol should be determined by the ObGyn or practice.

screening to patients from populations with a high prevalence for certain conditions. One such example is Tay-Sachs disease screening in Ashkenazi Jewish patients.

Panethnic screening, which takes into account mixed or uncertain backgrounds, involves screening for a certain panel of disorders and is available to all patients regardless of their background (for example, cystic fibrosis screening offered to all pregnant patients).

Expanded carrier screening is when a large number of disorders can be screened for simultaneously for a lower cost than previous testing strategies. Expanded carrier screening panels vary in number and which conditions are tested by the laboratory. An ideal expanded carrier screening panel has been debated in the literature but not agreed on.⁷

ObGyns and practices therefore are encouraged to develop a standard counseling and screening protocol to offer to all their patients while being flexible to make available any patient-requested screening that is outside their protocol. Pretest and posttest counseling, including a thorough family history, is essential (as with any genetic testing) and should include residual risk after testing, potential need for specific familial mutation

testing instead of general carrier screening, and issues with consanguinity.

Three essential screens

Regardless of the screening strategy chosen from the above options, 3 screening tests should be offered to all pregnant women or couples considering pregnancy (either individually or in the context of an expanded screening panel):

- **Cystic fibrosis.** At the least, a panel of the 23 most common mutations should be used. More expanded panels, which include hundreds of mutations, increase detection in non-Caucasian populations and for milder forms of the disease or infertility-related mutations.
- **Hemoglobinopathies (sickle cell, α - and β -thalassemia).** Complete blood count and red blood indices are recommended for all, with hemoglobin electrophoresis recommended for patients of African, Middle Eastern, Mediterranean, or West Indian descent or if mean corpuscular volume is low.
- **Spinal muscular atrophy (SMA).** The most recent addition to ACOG's recommendations for general carrier screening due to the relatively high carrier frequency (1-in-40 to 1-in-60) and the severity of the disease, SMA causes degeneration of the spinal cord neurons, skeletal muscular atrophy, and overall weakness. Screening is via polymerase chain reaction for *SMN1* copy number: 2 copies are normal, and 1 copy indicates a carrier of the *SMN1* deletion. About 3% to 4% of patients will screen negative but still will be "carriers" due to having 2 copies of the *SMN1* gene on 1 chromosome and no copies on the other chromosome. ●

FAST TRACK

All pregnant women should be offered screening for cystic fibrosis, hemoglobinopathies, and spinal muscular atrophy

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