Introduction

More than 140,000 women give birth in Pennsylvania each year. The significant physical changes of pregnancy can cause pain for these women during pregnancy, after delivery or even while breastfeeding. Pregnant patients also can experience pain from other causes during this critical time in their lives.

This guideline addresses the use of opioids for the treatment of pain in pregnant patients, during and immediately following delivery, and while breastfeeding. Separate guidelines will address the treatment of substance use disorder during pregnancy.

This guideline is intended to help healthcare providers improve patient outcomes when caring for these patients, which includes avoiding the potential adverse outcomes associated with the use of opioids to treat pain. This guideline is intended to supplement and not replace the individual provider’s clinical judgment.
Providers should review associated Pennsylvania state guidelines related to the use of opioids in different patient populations. Those guidelines contain important information that may be relevant to this patient population.

Prescription opioid abuse has become an issue of national importance, as drug overdose is the leading cause of accidental death in adults living in America. Most of these deaths involve the use of prescription drugs. To help stem this epidemic, there has been a call for more judicious prescribing on the part of physicians and other healthcare providers.

Opioid prescriptions for women have been on the rise. The Centers for Disease Control and Prevention (CDC) found nearly a third of women of reproductive age had an opioid prescription filled in every year from 2008 – 2012. Of the 1.1 million pregnant women enrolled in Medicaid nationally, nearly 23 percent filled an opioid prescription during their pregnancy in 2007, up from nearly 19 percent in 2000.

Chronic opioid use during pregnancy is associated with an increased risk of early delivery and low birth weight infants.** While chronic opioid administration can lower patient-reported pain intensity in some patients experiencing chronic pain, the impact of chronic opioids on pain intensity is modest and diminishes over time. Providers should use caution when considering chronic opioids in women of childbearing age, and should use extreme caution when considering chronic opioids during pregnancy.

In addition to the recommendations included in the previously-published Pennsylvania Prescribing Guidelines for Obstetrics and Gynecology, these guidelines suggest that healthcare providers incorporate the following key practices into their care of patients who are pregnant or breastfeeding. These guidelines also outline key practices for treatment of pain during delivery for patients who are undergoing treatment for opioid-use disorder.

1. **Patient screening for substance-use disorder:**
   
a) All pregnant and post-partum patients should receive a brief screening for substance-use disorder, and when indicated should be referred to appropriate treatment at the intensity and duration of care as indicated by the individualized assessment.

b) The use of validated screening tools (such as the NIDA Drug Use Screening Tool: Quick Screen, or the Brief Screener for Alcohol, Tobacco, and other Drugs (BSTAD)) may facilitate patient assessment for substance use disorder and risk for aberrant drug-related behavior.

c) Screening for maternal substance use disorder should be completed by providers involved in the care of both mother and infant.

   i. A clinician may refer the patient to their insurance carrier or the Department of Drug and Alcohol Programs Get Help Line at 1-800-662-4357 (HELP) or www/DDAP.PA.GOV

d) Screening may include a review of the patient’s data included in the Pennsylvania Prescription Drug Monitoring Program (PDMP).

2. **The use of opioids for the treatment of pain in women of childbearing age:**
   
a) Clinicians should consider the risk of pregnancy when prescribing opioids to women of childbearing age and should consider pregnancy testing as a part of ongoing monitoring for these patients.

b) Women of childbearing age should be informed of the risk of harm associated with the use of opioids during pregnancy. Information
regarding this risk should be included in the opioid agreement.

c) Women of childbearing age receiving chronic opioids should use an effective form of birth control and should be advised to inform their prescribing physician if they decide to try to or become pregnant.

3. The use of opioids for the treatment of pain during pregnancy:

a) Proper pain control should be provided to pregnant patients experiencing acute pain during pregnancy. A guiding principle in the care of the pregnant patient is to minimize the use of all medications unless the potential benefit clearly outweighs the risk of harm to both mother and fetus. Therefore, it is important to use non-pharmacologic therapies whenever possible. These non-pharmacologic therapies should continue to be used in combination with medication management when medication is required.

b) When considering medication management for acute pain during pregnancy, non-opioid analgesics such as acetaminophen should be used first, and opioids should be considered when acetaminophen is not effective as the sole analgesic.

i. Even when opioids are required, acetaminophen should be continued on a scheduled basis, as acetaminophen has an opioid-sparing effect and will allow for the use of the lowest effective opioid dose. However, care should be taken to avoid the use of total acetaminophen doses greater than 3,000 mg a day from all sources of acetaminophen.

ii. Non-steroidal anti-inflammatory drugs (NSAIDs) use during the first and third trimester may be associated with increased risk of fetal harm. All NSAIDs, including over-the-counter NSAIDs, should only be used by pregnant patients on the advice of their physicians. In the second trimester, NSAIDs such as ibuprofen and indomethacin, may be considered for short courses, no more than 48 hours.

c) When opioids are considered for the control of acute pain in pregnant patients, the risks of such medications should be reviewed with the patient. These risks may include preterm delivery, low birth weight and neonatal abstinence syndrome (NAS). It is important to note that while there is a modest increased risk of birth defects compared to baseline risk, the absolute risk remains low.

d) When opioids are required, a short course of immediate-release, as-needed opioids should be administered. Every effort should be made to avoid escalating opioid doses as well as the continuation of opioids beyond two weeks duration. Acute administration of opioids should never transition to chronic opioid administration without careful consideration.

e) Clinicians are advised to avoid the use of chronic opioids whenever possible during pregnancy. The initiation of chronic opioid therapy should only be done following careful consideration of the risks of harm to the patient and fetus and the potential benefits. When chronic opioids are administered during pregnancy, consultation with a high-risk obstetrics specialist as well as a pain specialist should be considered. NAS is a condition that occurs in newborn infants who were exposed to chronic opioids during pregnancy. These infants can demonstrate a wide variety of symptoms from feeding difficulties to seizures. Providers should discuss NAS condition with
patients prior to delivery and be prepared to monitor for and treat this condition if it occurs.

f) As in non-pregnant patients, pregnant patients who are given prescriptions for opioids should be educated about ways to avoid diversion of the medication to others. These medications should be stored in a secure location, taken as prescribed, and never shared with others. Unused medication should be properly disposed. This information is especially important in patients who have older children in the home, as 68 percent of the people aged 12 or older who used opioids for non-medical purposes reported that they obtained the opioid from a friend or relative.

4. The use of opioids for the treatment of pain during and following delivery:

a) There are several possible sources of pain when patients give birth that must be managed appropriately to promote postpartum recovery. Unrelieved pain can negatively impact a patient’s ability to care for herself and her infant, breastfeed and may contribute to depression. When considering postpartum analgesia, the clinician should consider methods that provide adequate pain relief with the least maternal side effects including limiting as much as possible the impact on a woman’s ability to care for her newborn.

b) Proper pain control should be provided to women experiencing acute pain following delivery. A vast majority of pain does not require pharmacologic therapies. Non-pharmacologic therapies, such as cold, heat and sitz baths, are often sufficient for the relief of mild pain in postpartum women.

c) If pain medications are indicated, use the safest drug available as a first-line agent. NSAIDs or acetaminophen are often sufficient analgesia for women experiencing mild to moderate pain.

d) If opioids are deemed necessary, providers should use the lowest potency available, for the shortest duration of time. Long-acting or extended release tablets should not be necessary. Neuraxial morphine or PCA morphine/hydromorphone/fentanyl can be used for the first 24 hours. Intravenous hydromorphone and fentanyl can be used for an additional 24 hours as needed in breastfeeding women. Short acting opioids can be used on a PRN basis and should not be needed post-discharge for routine vaginal delivery. In the event of cesarean delivery or severe perineal trauma, oral opioids may need to be used for three to five days.

e) Consider multimodal approach to pain management. The concurrent use of scheduled dosing of NSAIDs and acetaminophen in combination with short acting opioids on an as needed basis have repeatedly demonstrated reduced overall opioid consumption.

5. The use of opioids for the treatment of pain in women who are breastfeeding:

a) In the case of the breastfeeding patients, the choice of analgesic should be influenced by the individual drug’s ability to transfer into breast milk and cause adverse effects on the neonate. The American Academy of Pediatrics advises clinicians to use the most comprehensive and current database of drugs that effect infants and/or lactation. This information is available at LactMed (http://toxnet.nlm.nih.gov).

b) Drugs that have high lipid solubility, low protein binding, low molecular weight and that are unionized are easily secreted into breast milk. Opioids are excreted into breast milk. Breast milk concentrations of codeine and morphine
are equal to or somewhat greater than maternal plasma concentrations. Therefore, breastfeeding infants will be exposed to the opioids consumed by their mothers.

a) Early breastfeeding by patients who have received medications during delivery pose little risk to the infant.

b) Breast milk is synthesized and secreted during and immediately after breastfeeding. It is recommended that medications be taken after breastfeeding, to maximize the time between taking the medication and breast feeding, and thus minimizing drug transfer through breast milk.

c) When considering medication management for acute pain in patients who are breastfeeding, non-opioid analgesics such as acetaminophen should be used first. Opioids should only be considered when acetaminophen is not effective as the sole analgesic. If opioids are required, acetaminophen should be continued and monitored to avoid daily doses above 3,000 mg.

d) Non-steroidal anti-inflammatory drugs (NSAIDs) are effective for the treatment of several pain conditions and are opioid-sparing when used in combination with opioids. Several acute pain guidelines suggest that NSAIDs be used for the treatment of acute pain unless contra-indicated.

i. In general, short-term maternal use of several NSAIDs are considered low risk to the breastfed infant.

ii. Ibuprofen 400 mg every 6 hours is detectable in breast milk at the lower limit of quantification, and the relative infant dose is less than 1 percent of the maternal dose, even after repeated maternal dosing. Similar low infant dosing is observed following the administration of indomethacin and diclofenac.

iii. Maternal use of aspirin should be avoided, as aspirin persists in maternal milk for up to 24 hours, and neonatal metabolism is slow. Even after a single maternal dose of aspirin, the infant is exposed to 9-21 percent of the maternal dose once lactation is fully established.

iv. It is important to note that ketorolac contains a black box warning stating that ketorolac is contraindicated in nursing mothers because of the potential adverse effects of prostaglandin-inhibiting drugs on neonates.

e) When short-term use of opioids is required in breast-feeding mothers, providers should consider the use of short-acting opioids such as hydromorphone.

i. Intrathecal and epidural analgesia using low doses of morphine or fentanyl are generally considered safe in breastfeeding women, as the amount of opioid delivered to the infant via breast milk is minimal.

ii. Short-term (i.e., 24 hours) use of intravenous opioids such as fentanyl or hydromorphone delivered via patient-controlled analgesia is generally considered safe.

iii. When opioids are required, a short course of immediate-release, as-needed opioids should be administered. Every effort should be made to avoid escalating opioid doses and the continuation of opioids beyond five days. Acute administration of opioids should never transition to chronic opioid administration without careful consideration of the significant risks associated with

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chronic use of opioids, balanced against the potential benefits of chronic opioid therapy.

iv. Codeine is metabolized into morphine, and both codeine and morphine is passed into the infant through breast milk. Codeine metabolism is highly variable, and individuals who are “high metabolizers” of codeine have been identified. Unfortunately, there has also been a report of an infant death associated with morphine overdose in a mother consuming codeine while breastfeeding. While limited use of codeine is likely to be safe in breastfeeding mothers, chronic use should be avoided.

v. Oxycodone administration has been reported to be associated with a high risk of neonate sedation, which may be due to variable metabolism of oxycodone to oxymorphone, which is an active metabolite, more potent than oxycodone. Some authors have advised against the use of oxycodone in breastfeeding mothers, especially within two months of delivery.

vi. Meperidine undergoes hepatic metabolism to normeperidine. Normeperidine causes central nervous system activation, and higher doses can cause tremors, myoclonus, and seizures. Normeperidine has a long half-life, and can accumulate quickly in patients who are female, obese, hypovolemic, or have renal function compromise. Normeperidine can pass into the breast milk, and the half-life of normeperidine is markedly prolonged in newborns. Therefore, repeated use of meperidine should be avoided.

f) Breastfeeding should be encouraged in the opioid-dependent mother maintained on buprenorphine or methadone if she is not using illicit drugs. Providers should refer to existing guidelines and consult with a substance abuse treatment provider.

6. The treatment of pain during pregnancy, labor and delivery, and postpartum in patients receiving medication-assisted treatment for opioid use disorder:

a) It is important to note that outcomes for mothers and infants are significantly improved in those women who are undergoing active treatment for their substance use disorder during pregnancy. Participation in medication assisted treatment (MAT) is associated with significantly improved outcomes compared with no treatment.

i. Medically-supervised withdrawal is NOT recommended. Pregnant patients with opioid use disorder should not be encouraged to withdraw from pharmacotherapy during their pregnancy or shortly after their delivery.

ii. Attempts to criminalize opioid-use disorder in pregnancy should be avoided, as this may deter the patient from obtaining adequate prenatal care for themselves and the fetus.

b) Providers are encouraged to review existing guidelines and consult with an addiction medicine specialist.

c) Opioid prescribing by the obstetric team should be carefully coordinated with the MAT treatment team and be for the shortest duration possible.

d) In general, buprenorphine or methadone should be continued on their current dose during pregnancy, delivery, and immediately postpartum.

i. The use of multi-modal analgesia is important in patients on MAT who are
experiencing pain. This includes the use of scheduled NSAIDs and acetaminophen as discussed earlier. In addition, these patients may benefit significantly from the use of regional anesthesia and analgesic techniques, when possible.

ii. Patients receiving buprenorphine or methadone may report poorly-controlled pain following a painful procedure. Patients who are opioid tolerant often report increased pain, and systemic opioids may not be effective. Aggressive opioid dosing to address pain complaints may lead to significant patient harm. Early consultation to a pain specialist should be considered.

iii. Buprenorphine is a partial opioid agonist-antagonist that binds tightly to the opioid receptor. While some women may report analgesia with the use of supplemental opioids in addition to the prescribed buprenorphine, many will not. Unfortunately, aggressive opioid administration in these patients may lead to rapid onset of potentially serious opioid-induced adverse effects. Careful monitoring for sedation and adequacy of ventilation should be considered when high doses of systemic opioids are administered.

iv. Patients receiving methadone may have higher opioid requirements when systemic opioids are used following surgery. Supplemental opioids should be used for the shortest duration possible, and discharge medications should be carefully coordinated the MAT team.

Resources:


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