BUPRENORPHINE

for Opioid Use Disorder

Module 4: Special Populations

Pregnancy and Breastfeeding Women

- Opioid misuse during pregnancy carries the risks of overdose, pregnancy termination, and other health consequences.[1,2] These risks must be weighed against the risks of using medication for the treatment of Opioid Use Disorder (OUD) in pregnancy. Opioid Agonist Treatment (OAT) is recommended over abstinence-based treatments or withdrawal management in pregnant women who are physically dependent on opioids.[3]
- Methadone has historically been considered the "gold standard" for treatment of OUD in pregnant women,[2] however, recent data have supported that buprenorphine is a reasonable alternative.[4,5] It may be associated with a shorter length of stay and less medication treatment for Neonatal Abstinence Syndrome (NAS) in neonates with buprenorphine treated mothers, compared to that seen with methadone treatment.[6]
- Human data on use of buprenorphine in pregnancy is limited; however, available data do not indicate increased risk of malformations due to buprenorphine exposure.[5,6]
- While previously it was common practice to use the monoproduct in pregnant patients, many providers now use the combination buprenorphine/naloxone product for all patients, including pregnant women.[7]
- Close collaboration with an obstetrician, and incorporating psychosocial treatment into the care plan is recommended when treating pregnant women for OUD.[4]

Breastfeeding

- Buprenorphine passes into breast milk, but exposure to the infant is minimal (less than 1% of the weight-adjusted maternal dose).[7,12,13]
- Encouraging breastfeeding during buprenorphine treatment is recommended.[4,11-12] Breastfeeding increases mother-infant bonding, encourages active maternal participation in the management of the infant, and may decrease incidence or likelihood of complications from NAS.[10,14]
- Circumstances in which extra precautions are warranted in breastfeeding include HIV-positive mothers and mothers using alcohol or other substances which could be excreted in breast milk.[4]

Pregnancy and Breastfeeding Women

Neonatal Abstinence Syndrome (NAS)

A common complication in neonates born to women treated with buprenorphine during pregnancy.

- Findings strongly suggest **no deleterious effects of buprenorphine relative to methadone, or of treatment for NAS severity relative to not-treated for NAS on growth, cognitive development, language abilities, sensory processing, and temperament.** Moreover, findings suggest that prenatal opioid agonist exposure is not deleterious to normal physical and mental development.[9]
- Prevalence: 22-67% of infants born to treated mothers.[10]

- Clinical Course: Generally appears within the first 2 days of life, peaks within 3 or 4 days, and lasts for 5 to 7 days.[3] It may persist for up to 28 days or more.[10]
- Symptoms: tremors, irritability, diarrhea, poor feeding, and distinct, excessive, high-pitched crying. Tremors, hypertonia, myoclonic jerks, temperature instability, and seizures can occur.[10]
- Treatment: supportive care and non-pharmacologic treatment is recommended as first-line treatment for mild NAS, but management with pharmacologic treatment is sometimes required.[10]
- It is recommended that communication with a pediatrician and/or a neonatologist occurs before delivery to assure that a plan is in place for handling NAS.
- **Studies show that allowing mothers to room with their infants leads to shorter hospitalizations, since breastfeeding, holding and swaddling are all therapeutic interventions.[11] Neonatal intensive care is generally not required if clinicians are experienced with treatment of NAS. Therefore, transfer of the infant to a NICU should be discouraged unless clinically indicated. Hospitals will need to have a protocol in place for treating NAS with opioid medications (e.g. methadone, buprenorphine, morphine).**
- While pharmacokinetic studies of pregnancy-induced changes are limited, data suggest that pregnancy may impact buprenorphine metabolism and excretion, and buprenorphine dosing may need to be adjusted (typically increased) during the later stages of pregnancy.[12]

Patients with Pain

Common therapeutic challenges encountered:

- Patients with chronic painful conditions may present seeking treatment for OUD.
- Patients may develop acute or chronic painful conditions which require treatment while maintained on buprenorphine treatment for OUD.

Patients with comorbid OUD and severe chronic pain requiring treatment with opioids may benefit from switching to buprenorphine treatment:[18]

- Patients treated with long-term high doses of prescription opioids can develop heightened pain sensitivity, which may improve when switched to buprenorphine treatment.[19,20]
- Should be collaboratively managed with a pain treatment specialist where possible.[3,4]

If appropriate, non-pharmacologic or non-opioid-based medication treatments based on etiology of pain should be considered first-line treatment in patients with OUD.[3,4]

If patients maintained on buprenorphine for OUD require treatment for acute pain:

- Temporarily increasing buprenorphine dosing and dividing the dose may be effective for **mild-to-moderate** pain, but may not provide sufficient analgesia for moderate-to-severe pain.[3]
- **For moderate-to-severe acute pain,** two approaches to consider are:[3]
  - Continue buprenorphine treatment and use full agonist opioids for added pain relief. Higher-than-usual doses of opioids or use of agents with relatively high binding affinities (such as fentanyl, hydromorphone, and morphine) may be needed to overcome buprenorphine blockade.
  - Discontinue buprenorphine temporarily and use full agonist opioids to treat pain and prevent withdrawal. This approach avoids the blockade effect of buprenorphine on the muopioid receptors but leaves the patient vulnerable to relapse.
- For **perioperative pain management,** most patients can continue use of buprenorphine throughout the operative period. Regional anesthesia, non-opioid pain management, or full agonist opioids can be used to manage postoperative pain.[3] Alternatively, temporary discontinuation of buprenorphine 24-36 hours before dosing of the analgesic can be considered, ideally after consultation with the attending surgeon and anesthesiologist.[4]
- Re-induction of buprenorphine after temporary discontinuation should be attempted carefully, with consideration given to the half-life of the opioid analgesic used, in order to avoid precipitated withdrawal.
- Pregnant women on buprenorphine can continue buprenorphine through their labor; labor pain can be managed with epidural analgesia, intravenous opioids or spinal analgesia.[3,21-23]

Adolescents

- Patients younger than 18 years of age are at particularly high risk for serious complications of addiction (e.g., overdose deaths, suicide, HIV, other infectious diseases).[3]
- Buprenorphine is indicated only for the treatment of patients who are aged 16 years and older, however some evidence supports off-label treatment of OUD with buprenorphine in younger adolescents.[3,4,24,25]
- Clinicians should be aware of legal and ethical considerations unique to adolescents.
- Involving and obtaining consent from the parents and guardians of minors seeking treatment for OUD is currently required under NY Mental Hygiene Law 22.11, unless provider determines that seeking such involvement and consent would have a detrimental effect on the course of the treatment.
- Adolescents may benefit from treatment in specialized facilities that provide multidimensional services specific to teens.[4]
- **All patients, including adolescents, have a high relapse rate if buprenorphine is used only for detox and may benefit from longer term maintenance treatment with buprenorphine in order to maintain sobriety.[24]**

People Who Inject Drugs

- People who inject drugs are at elevated risk of overdose, as well as hepatitis C, HIV, skin infections, abscesses, and infections of the heart.[25]
- **Harm reduction, including needle/syringe programs and OAT, is an evidence-based approach to treatment and care for people who inject drugs.[27]**
- Other components of a comprehensive care plan for people who inject drugs may include HIV testing and counseling, behavioral interventions, prevention and management of viral hepatitis, sexual and reproductive health interventions, and provision of naloxone and training on overdose prevention.[27]

Comorbid Conditions

Co-occurring Psychiatric Disorders

- Lifetime prevalence of comorbid psychiatric illness in patients seeking treatment for OUD is **nearly 50%.**[27]
- Psychiatrically stable patients can be readily accepted into treatment and stabilized on buprenorphine.[3,4]
- Patients with comorbid psychiatric disorders should be assessed for stability prior to treatment initiation.
- Clinicians should consider:
  - Is the patient actively suicidal or homicidal?
  - Has he or she recently attempted suicide or homicide?
  - Do current emotional, behavioral, or cognitive conditions complicate treatment?
- Substance use and addiction can mimic, exacerbate, or precipitate psychiatric symptoms and disorders. Care should be taken to differentiate substance-induced psychiatric disorders from underlying psychiatric comorbidities.
- Referral to psychiatric treatment services or other psychosocial support should be facilitated as appropriate.[3]
- Clinicians must be aware of medications which may interact with buprenorphine (i.e. benzodiazepines). See Module 2 for more information regarding medications which may interact with buprenorphine.

HIV and Hepatitis C

- Patients presenting for OUD treatment should be screened for Hepatitis C Virus (HCV) and HIV, which are disproportionately common among patients with OUD.[3,29]
- **Buprenorphine treatment may improve compliance with, and outcomes for, antiviral treatments for HCV[30] and highly active antiretroviral therapies (HAART) for HIV.[3,31]**
- Several drug interactions must be considered in patients receiving antiviral treatments, including non-nucleoside reverse transcriptase inhibitors, protease inhibitors, cobicistat, and direct-acting antivirals for HCV,[3,31] which may induce, inhibit, or compete for metabolism with buprenorphine via Cyp3A4. (See Module 2 for more information.)
- When starting any of the above medications for a patient maintained on buprenorphine, counsel patients on potential drug interactions and the possibility for withdrawal or excess sedation from buprenorphine. In patients maintained on these medications who are starting buprenorphine, providers should be cautioned that a lower or higher dose of buprenorphine may be required for desired effect. Patients should be closely monitored, especially in the first 1-2 weeks after making these medication changes.
- Mild elevations in liver enzymes have been noted in patients with hepatitis who received long-term buprenorphine.[32,33]

Incarcerated Patients and Patients Recently Released from Incarceration

- Pharmacotherapy with buprenorphine for OUD is effective in this population, increases rates of engagement with community treatment upon release[15,16] and is recommended for incarcerated individuals and parolees regardless of the length of their sentenced term.[2]
- Individuals that are recently released from incarceration are at an increased risk of experiencing an opioid overdose compared to the general population.[17]
- Most jails and prisons do not offer treatment with OAT to incarcerated patients due to preference for abstinence-based treatments and concerns about diversion/misuse.[17]
- Community providers may encounter patients recently released from incarceration with a history of OUD. Providers should consider initiating treatment both to those who have relapsed, and those who are felt to be at risk of relapse.
- Physicians should be prepared to determine, verify, and explain a treatment regimen (e.g., to parole and probation officers), document the patient's adherence, and to interact with the legal system, employers, and others.

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