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Treating perinatal opioid use disorder in rural settings: Challenges and opportunities

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ABSTRACT

Perinatal opioid use disorder (OUD) is a life-threatening condition that significantly impacts women in rural areas. Medication assisted treatment (MAT) is the recommended treatment but can be difficult to access. Pregnant women may initially present for treatment of OUD in the emergency department, on labor and delivery units, or in an office setting, each of which presents unique challenges. Initiation of MAT in the appropriate setting, based on accurate assessment of gestational age, is a centrally important component of care for perinatal OUD. However, initiating treatment may present challenges to providers who lack experience treating this disorder. Vermont and New Hampshire are predominantly rural states which have focused on expanding MAT access for pregnant women using two different approaches to integrating treatment with maternity care.

1. Introduction

Perinatal opioid use disorder (OUD) is a serious, life-threatening condition necessitating treatment. Pregnancy-associated mortality involving opioids more than doubled from 2007 to 2016, and overdose accounted for 10% of all pregnancy-associated deaths in the United States in 2016 (Gemmill et al., 2019). Maternal mortality is four times higher for women with identified OUD compared to the general obstetric population (Maeda et al., 2014). The current opioid epidemic has particularly affected women of reproductive age in rural areas (Kozhimannil et al., 2019).

Women face unique barriers to both requesting and receiving treatment for OUD. Guilt and shame, experienced by most patients with this diagnosis, are compounded due to pregnancy, and impact treatment initiation both positively and negatively. Women may also be reluctant to initiate treatment due to concerns that disclosing substance use will result in losing custody of existing children. Housing and food insecurity, transportation, and demands of childcare also pose barriers (Patrick et al., 2019).

The recommended standard treatment for opioid use disorder in pregnancy is medication assisted treatment (MAT), also known as medications for opioid use disorder (MOUD) (American College of Obstetricians and Gynecologists, 2017; Substance Abuse and Mental Health Services Administration, n.d.-a), as detoxification is associated with high rates of relapse (Terplan et al., 2018). Evidence supports use of either methadone or buprenorphine (with or without naloxone) (Substance Abuse and Mental Health Services Administration, n.d.-a; Gawronski et al., 2014). When choosing between opioid agonist medications, there are multiple factors to consider including the woman's preference, treatment availability, setting, potential medication interactions, and experience with past treatments. The Substance Abuse and Mental Health Services Administration (SAMHSA) and the Department of Health and Human Services' clinical guidance for treating pregnant and parenting women with opioid use disorder supports shared decision making among patients and providers when choosing to start methadone versus buprenorphine (Substance Abuse and Mental Health Services Administration, n.d.-b). There is some evidence that buprenorphine may result in less severe neonatal abstinence syndrome when compared to methadone (Jones et al., 2010). Emerging research confirms the safety of the combined buprenorphine/naloxone product in pregnancy, (Gawronski et al., 2014; Jumah et al., 2016; et al., 2017; Dooley, et al., 2016; et al., 2018) however, safety and efficacy data is lacking for the use of oral or injectable naltrexone in pregnancy (Jones & Terplan, 2018).

Rural areas are disproportionally affected by shortages in treatment capacity and access to Opioid Treatment Programs licensed to administer methadone (Johnson et al., 2018). Distance, lack of transportation, the financial burdens of travel, and the demands of daily dosing

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Table 1
Differential for symptoms of sympathetic overload in pregnancy.

Symptoms of sympathetic overload	Differential	Symptoms and findings to consider in differential	Helpful labs
Agitation Paranoia Hallucinations Tachycardia Hypertension Tachypnea Tremor Seizures	1. Opioid withdrawal 2. Alcohol withdrawal 3. Benzodiazepine withdrawal 4. Stimulant overdose 5. Hallucinogen intoxication 6. Anticholinergic syndrome 7. Serotonin syndrome 8. Thyrotoxicosis 9. Preeclampsia	Abdominal pain, nausea, diarrhea -Opioid withdrawal Diaphoresis -Opioid withdrawal -Alcohol withdrawal Nystagmus -Hallucinogens Mydriasis -Opioid withdrawal -Anticholinergic syndrome Urinary retention -Anticholinergic syndrome Tremor, seizures, hyperreflexia -Alcohol or benzodiazepine withdrawal -Synthetic cathinone effect -Preeclampsia -Thyrotoxicosis Muscle rigidity -Serotonin syndrome	Urine -Toxicology[a] -EtG/EtS[b] -Urine protein/creatinine ratio Serum -AST/ALT -CBC -Creatinine -TSH, FT4 -CDT/PEth[c]

[a] You may need to specify certain drugs separately from drug panel (e.g. fentanyl, benzodiazepine, buprenorphine, synthetic opioids.
[b] Alcohol biomarkers in urine: EtG: ethyl glucuronide; EtS: ethyl sulfate.
[c] Alcohol biomarkers in serum: CDT: carbohydrate deficient transferrin; PEth: phosphatidylethanol.

regimens are all barriers to participation in methadone treatment programs, especially for individuals who are employed (Sigmon, 2014). For these reasons, buprenorphine prescribed in the office setting is generally a more accessible treatment for patients living in rural areas and is therefore often preferred by patients as an initial approach. Physiologically, transition to methadone can be performed relatively easily if a patient does not do well with buprenorphine treatment (Substance Abuse and Mental Health Services Administration, n.d.-a).

Access to MAT during pregnancy is particularly challenging in rural areas due to limited access to medical and mental health care in general, fewer MAT prescribers, and concerns from non-specialists about safety of MAT during pregnancy (Sigmon, 2014; Patrick et al., 2018). Therefore, the engagement of rural healthcare providers is critical to fill treatment gaps for this population. We outline how rural healthcare providers may facilitate treatment engagement for the newly identified pregnant patient with OUD in a variety of clinical settings. We focus on treatment with buprenorphine due to its potential to fill urgent gaps in access to treatment in rural areas.

2. Initial presentation in the Emergency Department

All women of reproductive age presenting with suspected OUD should have a urine pregnancy test, and if negative, pregnancy intention should be explored and referrals for contraceptive management provided as needed. Pregnancy is unplanned in > 80% of women with OUD (Heil et al., 2011), and assessment of last menstrual period is often unreliable for dating the pregnancy. Ultrasound is the gold standard for gestational age assessment and should be performed at diagnosis of pregnancy complicated by OUD in any setting. Standard prenatal labs should be obtained, including testing for sexually transmitted disease, HIV, hepatitis B surface antigen, hepatitis C, and renal and hepatic function (Substance Abuse and Mental Health Services Administration, n.d.-a).

Establishing gestational age is critically important to determine the appropriate location for initiating MAT, and specifically the approach to fetal assessment (see below for further discussion of fetal monitoring related to withdrawal and buprenorphine induction). Initiation of MAT in the emergency room setting has been shown to be safe in the non-pregnant patient (D'Onofrio et al., 2017); however, no data are available in the pregnant patient. When a decision is made to initiate treatment for a pregnant woman, assessment of fetal status is recommended. Therefore, in the emergency setting, buprenorphine induction should only be performed early in gestation when fetal monitoring is not performed (< 23 weeks) and with a plan for careful obstetric follow-up. Induction of buprenorphine during pregnancy should start with the standard 2–4 mg dose, repeated after 1–2 h (The American society of addiction medicine practice guideline for the use of medications in the treatment of addiction involving opioid use, n.d.).

Nausea, vomiting, and abdominal pain can be symptoms of opioid withdrawal, and also of pregnancy in reproductive aged women. Pregnant women are particularly sensitive to dehydration and hypotension due to decreased peripheral vascular resistance, and plasma volume expansion and intravenous fluids should be provided liberally. Clonidine should be used cautiously as an adjunctive treatment for withdrawal in pregnancy as it may precipitate hypotension (Goodman et al., 2015). Prochlorperazine or promethazine should be considered for nausea and vomiting; although ondansetron is generally considered safe for women on buprenorphine, avoidance in the first trimester may be prudent (Huybrechts et al., 2018).

3. Initial presentation on labor and delivery

Women with opioid withdrawal in the second and third trimester may present for evaluation to labor and delivery. Obstetric providers should consider consulting emergency department colleagues for pregnant patients with acute intoxication or withdrawal, as they may have established protocols which can be utilized for assessment and treatment. Differential diagnosis of acute opioid withdrawal includes any disease with sympathetic overload, including thyrotoxicosis, preeclampsia, alcohol or benzodiazepine withdrawal, or stimulant use (See Table 1). As with any medical emergency in pregnancy, stabilization of maternal disease can stabilize fetal status. Short acting opioids may be

considered if acute opioid withdrawal is suspected and can be both diagnostic and therapeutic. Once OUD is established and maternal and fetal status stabilized, opioids should be withheld to allow the mild withdrawal required for buprenorphine induction to occur.

Opioid withdrawal may present coincident with labor, but can also be precipitated by administering nalbuphine or butorphanol, mixed opioid agonist-antagonist medications commonly used for labor analgesia to a patient who is opioid dependent. Acute withdrawal in the laboring patient can cause maternal and fetal tachycardia, both of which are reversible by administration of a full opioid agonist (ie: morphine). Regional analgesia/anesthesia provides effective pain control in labor for women with OUD; the possibility of untreated withdrawal symptoms should be considered in patients with persistent discomfort following effective neuraxial analgesia (Meyer et al., 2010).

Pregnant women admitted to the hospital in acute withdrawal may be initiated on a treatment medication for OUD. The treating provider is not required to have a Drug Addiction Treatment Act 2000 Waiver to prescribe buprenorphine to a pregnant woman in-patient setting, as opioid withdrawal constitutes a serious complication of pregnancy. Additionally, as clarified in 1306.07 (c), a practitioner may to continue to provide medication for OUD while treating a hospitalized patient for an applicable medical condition including pregnancy (21 CFR 1306.07 – Administering or Dispensing of Narcotic Drugs, n.d.; Special Circumstances for Providing Buprenorphine, n.d.). However, only a waivered provider may prescribe buprenorphine to a non-hospitalized patient. Therefore, any initiation of MAT medication in the hospital setting must have a clear plan for follow-up after discharge. Collaborative agreements should be developed to allow for continued treatment by community based providers following in-hospital initiation of MAT. Labor and delivery units should develop protocols for initiating treatment which include discharge plans; with obstetric provider training for MAT induction.

4. Initial presentation in prenatal or MAT provider's office

Universal screening for drug, tobacco, and alcohol use by maternity care providers, using validated instruments, is an essential first step to identify women in need of treatment (Reddy et al., 2017; Guidelines for the Identification and Management of Substance Use and Substance Use Disorders in Pregnancy, n.d.). The American College of Obstetricians and Gynecologists (ACOG) recommends against universal drug testing (urine toxicology) for pregnant women as a screening approach, as women may avoid prenatal care if this is required (Stone, 2015; Roberts & Pies, 2011). When women screen positive for OUD, prenatal care providers are ethically obligated to facilitate treatment whether through an integrated care model, where MAT is provided in the context of prenatal care, or via collaboration with local MAT providers.

In parallel, MAT providers should have the capability to perform urine pregnancy tests and refer for obstetric when indicated. Prescribers should routinely ask women of reproductive age about pregnancy intention, facilitate initiation of prenatal vitamins when pregnancy is desired, and refer women at risk of undesired pregnancy for initiation of contraception.

Because women with OUD may receive sporadic medical care, assessment of gestational age at initial presentation in any medical setting, is optimal. Accurate gestational age assessment is essential for appropriate obstetric care and first trimester ultrasound is the most accurate way to date a pregnancy when last menstrual period is not precisely known (Obstet. Gynecol., 2017a).

5. Fetal assessment during buprenorphine initiation

For women with pregnancies < 23 weeks of gestation, electronic fetal monitoring is not indicated as a method of assessing fetal status (Obstet. Gynecol., 2017b). However, it is prudent to confirm viability of the pregnancy prior to starting MAT. If the pregnancy is between 23 + 0 to 25 + 6 weeks gestational age by reliable dating (Roberts & Pies, 2011), obstetric providers and hospital protocols should be consulted regarding whether fetal monitoring is indicated. The mild withdrawal required for initiation appears to be safe with careful medical management (Terplan et al., 2018). Hospitalization with intermittent fetal monitoring for the 24–48 h of buprenorphine induction may be considered for pregnancies > 23 weeks gestational age although there is little data on the utility of fetal monitoring at any gestational age in settings of withdrawal or MAT induction (American College of Obstetricians and Gynecologists, 2017; Kampman & Jarvis, 2015).

6. Addressing comorbidities and social determinants of health

Pregnant women with OUD should be screened for tobacco, alcohol, cannabis, and other drug use, at initiation to care and periodically. Screening for intimate partner violence, food, transportation, and housing insecurity, sexually transmitted infections, hepatitis B, C, and HIV should also be performed initially and repeated close to delivery. Due to the high comorbidity of substance use and other mental health disorders, all women with OUD should be screened and treated for depression and anxiety, including PTSD (Benningfield et al., 2010). Because women tend to be motivated to be healthy and are more likely to have health insurance while pregnant, engaging women in care for medical and psychiatric comorbidities in the prenatal period is critical for their long term as well as perinatal health.

7. Perinatal OUD treatment models in rural settings

In rural areas, transportation and other barriers make co-location of services a practical approach. The integration of maternity care and MAT is associated with high rates of satisfaction for both pregnant women and providers, although data on perinatal outcomes, long term treatment success, and retention of child custody are sparse (Ordean et al., 2013). Below, we describe how two rural states, Vermont and New Hampshire, have approached expanding access to MAT in pregnancy from two different directions.

7.1. Vermont hub and spoke

Vermont was an “early adopter” of expanding MAT access through increasing the number of community-based buprenorphine providers, facilitating treatment throughout the state using a “hub and spoke” approach Initially, this community-based approach was not applied during pregnancy, and most pregnant women were treated with buprenorphine at a tertiary obstetric clinic (Meyer et al., 2015). This centralized model included co-located social work, counseling, MAT provision, and OB care with other integrated statewide supports (Collaborative Approach to the Treatment of Pregnant Women with Opioid Use Disorders, n.d.). Recently, Vermont has transitioned to community-based obstetric care for women with OUD within the Hub and Spoke model: “Hubs” still perform buprenorphine induction during pregnancy, and care for higher acuity patients, while “Spokes” provide office based care with integrated services on site for women with moderate risk pregnancies (Brooklyn & Sigmon, 2017). Pregnant women now may remain in their community for MAT, obstetric, and pediatric care by collaborating providers.

7.2. New Hampshire's iMAT-OB program

Treatment for pregnant women with OUD in New Hampshire has historically been provided by opioid treatment programs which dispense methadone, or a network of for-profit entities providing treatment with buprenorphine. Until recently, the vast majority of maternity care providers in New Hampshire did not provide treatment for OUD, and access to OUD treatment for pregnant women was very limited in

rural areas.

In 2018, the state of New Hampshire was awarded federal dollars to fund an integrated medication assisted treatment program (iMAT) at selected maternity care sites. Teams comprised of physicians, APRNs, and nurse midwives initiate and manage MAT with buprenorphine through at least three months postpartum, in collaboration with behavioral health clinicians, case managers, and peer recovery support. A "Q &A line" managed by the state's tertiary care center was also launched for provider-to-provider consultation on complex cases. In January 2019, another state-wide initiative designated seven New Hampshire hospitals as entry points for any individual seeking treatment, underscoring the need to develop maternity-focused treatment initiation protocols.

8. Discussion

Pregnant women with OUD may present for care urgently at a number of points in the medical system, and maternity care providers are frequently at the front line when a pregnant women discloses her need for treatment. It is critical that providers have a plan to initiate OUD treatment promptly as appropriate for gestational age, and symptom severity, regardless of the care setting where a woman present initially. Access to immediate treatment can be expanded through empowering and training practitioners in low volume obstetric services to initiate buprenorphine during pregnancy, and facilitate continued treatment through collaboration with community-based providers. This coordinated approach is critical to improve access to evidence-based care in the rural, under-resourced areas hardest hit by this epidemic.

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