

Treatment of Prescription Opioid Use Disorder in Pregnant Women

Constance Guille, M.D., M.S.C.R., Kelly S. Barth, D.O., Julio Mateus, M.D., Ph.D., Jenna L. McCauley, Ph.D., Kathleen T. Brady, M.D., Ph.D.

At the time of her initial presentation to a reproductive psychiatry clinic, “Ms. P” was 30 years old, divorced, and approximately 8 weeks pregnant with her fifth child. She was referred by her obstetrician regarding chronic use of prescription opioid pain medication. The patient had been in good health until 7 years earlier, when she was in a motor vehicle crash that fractured her coccyx and left her suffering from pelvic and neck pain. Her primary care physician prescribed hydrocodone for the pain. She was maintained on hydrocodone with dosage increases for 6 years until the previous year, when she was switched to oxycodone because of inadequate pain control with hydrocodone.

On presentation, Ms. P was taking 10 mg of oxycodone every 4 hours (60 mg total daily) as prescribed, and she reported inadequate pain control with a negative impact on her ability to work and care for her four children. She and the father of the baby expressed concern about the use of oxycodone during pregnancy. When she learned that she was pregnant, she stopped her oxycodone abruptly and experienced significant withdrawal symptoms. She then resumed her usual dosage and tried to cut down, but was unsuccessful. She endorsed a strong urge to use oxycodone but was requesting help in discontinuing the medication during pregnancy.

Ms. P reported that in the past 2 years she had frequently run out of oxycodone before the next refill because of increasing the dosage on her own. She denied ever obtaining oxycodone illegally and reported that she could generally find a physician to refill her oxycodone early and increase her dosage when requested. She reported that she was preoccupied with concerns about running out of oxycodone and that she spent a significant amount of time attending doctor’s appointments to acquire oxycodone, at the expense of time with her children and other activities. She had tried on three occasions to cut down or discontinue oxycodone, without success. Each month she became anxious and irritable because of fear of running out of oxycodone, which often resulted in arguments with

the father of the baby and being “very short” with her children. She reported significant strain on her relationship with her mother, who felt that she was a different person since starting prescription painkillers. Her mother currently refused to have a relationship with her if she continued to use prescription opioids. A review of the South Carolina State Prescription Drug Monitoring Program database indicated that the patient had four different providers of oxycodone in different medical practices, multiple early refills of medication, and an increasing dosage of oxycodone over time, but no overlapping prescriptions. The patient denied any use or abuse of alcohol, tobacco, illicit drugs, or other prescribed medications.

On the Brief Pain Inventory, Ms. P rated her average pain at 6/10 and her worst pain in the past 24 hours at 7/10 and indicated that her current dosage of oxycodone was providing 10% pain relief. She also indicated having significant impairment, rated at 7–10 out of 10, in seven domains of functioning, including general activity, walking, work, mood, enjoyment in life, relationships, and sleep. Her score on the Current Opioid Misuse Measure was 31 (highly suggestive of opioid misuse). Urine drug testing was negative for amphetamines, barbiturates, cocaine, marijuana, methadone, phencyclidine, and opioids, but a confirmatory test was positive for oxycodone.

Assessment of Pertinent and Challenging Clinical Issues

Ms. P’s presentation was consistent with an opioid use disorder of moderate severity, as evidenced by escalating opioid use, unsuccessful attempts to quit or cut down on opioid use, continued use of opioids despite persistent interpersonal problems, opioid cravings, and spending an excessive amount of time obtaining opioid medications.

The pharmacological treatment for prescription opioid use disorder in pregnancy is controversial. The standard of care for women with heroin use disorder in pregnancy, established more than 30 years ago, is treatment with opioid

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agonist therapies, such as methadone and buprenorphine, as opposed to medication-assisted withdrawal (1). One rationale for this approach is that a repeated cycle of withdrawal and relapse, which is often seen in opioid use disorders when individuals attempt to go “cold turkey,” would be worse for the developing fetus than a stable dosage of a prescribed opioid. However, with exposure throughout pregnancy to opioid maintenance medications, there is a 60%–80% incidence of neonatal abstinence syndrome (2), often requiring a stay in the neonatal intensive care unit. It is unclear, however, whether maintenance medications, as opposed to medication-assisted withdrawal, should be the standard of care for pregnant women with prescription opioid use disorder (3), and if not, how best to taper these medications.

Ms. P's case is further complicated by a chronic pain condition that could potentially worsen with the discontinuation of oxycodone and the progression of pregnancy. While there is evidence to support nonpharmacological (exercise, cognitive-behavioral therapy [CBT]) and nonopioid pharmacological treatments (acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs]) for musculoskeletal pain in nonpregnant populations, the effectiveness of these therapies in pregnancy is unknown. Furthermore, the use of NSAIDs during pregnancy carries significant risks, and patients frequently report a poor response to acetaminophen.

Treatment Plan and Course

Shared decision-making techniques were used to guide overall treatment choice and weekly medication management decisions. The clinician first provided information on available evidence related to medication-assisted withdrawal and opioid maintenance medications (methadone and buprenorphine) for pregnant women with opioid use disorder. The patient discussed her values and preferences, including her preference not to take maintenance medication because of difficulties with access, cost, and concern about potential harm to her unborn child. While she preferred to stop opioid medications, she felt that she needed treatment for her pain condition and identified pain as her greatest trigger for relapse to opioid use. The clinician and patient discussed evidence-based opioid alternative pain interventions, such as CBT for chronic pain (4), which has demonstrated a reduction in chronic pain severity and improvement in functioning among nonpregnant populations (5).

The patient, the father of the baby, the psychiatrist, and the obstetrician agreed that the patient's medications would be tapered slowly each week (6) in conjunction with CBT for chronic pain and routine obstetrics care. Opioid risk mitigation strategies such as a patient-physician agreement, weekly review of the Prescription Drug

Monitoring Program database, regular urine drug screens with confirmatory testing of prescribed opioids, and weekly monitoring of misuse behaviors and urges or craving to use opioids would be employed to monitor risk for or evidence of relapse to opioid use or other substances.

Treatment included a total of seven 60–90 minute weekly sessions of CBT for chronic pain and medication management. Each week, the provider assessed for symptoms of withdrawal (using the Clinical Opiate Withdrawal Scale) and pain level (using the Brief Pain Inventory), discussed the patient's readiness to adjust her medications, and arrived at a decision either to reduce or to continue the current opioid medication dosage. During the weekly CBT sessions, the father of the baby cared for the patient's children and was therefore unable to attend these appointments. However, at Ms. P's request, after each session, the patient, the father of the baby, and the provider discussed, in person or via speakerphone, the treatment plan for the following week. Ms. P felt that this made her more likely to adhere to the prescribed medication regimen, and strategies were discussed for how the father of the baby could support her in making positive changes.

After the initial assessment, the patient cut down her oxycodone dosage by 20 mg/day. Subsequently, on average, the dosage was decreased by 5–10 mg per week except during week 4, when the patient was experiencing significant pregnancy-related nausea (Figure 1). The small adjustments appeared to have subtle positive physiological and psychological effects, including increasing the patient's self-efficacy related to opioid cessation. During week 6, the patient decided to stop her oxycodone (which was then down to 5 mg b.i.d.) entirely; she experienced mild withdrawal symptoms that resolved within 24 hours. She stated that the medication was not helping her pain and was just preventing withdrawal, “So I figured I would just get it [withdrawal] over with.” At week 7, Ms. P rated her average pain at 5/10 and her worst pain in the past 24 hours at 6/10, and she indicated that her current treatment was providing 40% pain relief. She also indicated less functional impairment in each of the seven domains of functioning compared with before treatment. Her score on the Current Opioid Misuse Measure was now 7 (unlikely opioid misuse).

At that time, Ms. P felt that with the demands of child care, full-time employment, and regular obstetric appointments, the additional regular psychiatric appointments at a different location were no longer essential. She had completed the CBT for chronic pain protocol, and she felt confident that she would not use prescription opioids and could instead manage her pain with CBT tools. An appointment was made for 3 weeks later, which the patient did not attend.

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At 32 weeks of gestation, Ms. P called and left a message with her obstetrician indicating that her pelvic and neck pain was worsening and that she wanted to restart an opioid medication. The obstetrician contacted the psychiatrist to discuss a collaborative approach to her care. The obstetrician had continued to see the patient at regular obstetric appointments and felt that the described pain was consistent with the normal progression of pregnancy and did not warrant opioid therapy. Instead, he offered a referral to physical therapy, an abdominal belt, and an appointment with the psychiatrist to review CBT techniques and discuss other nonopioid pain management options. In a telephone call follow-up with the psychiatrist, Ms. P revealed several recent stressors: the father of the baby had recently relapsed to substance use, which had put a significant strain on their relationship, and she was finding that sitting at a desk for several hours each day was worsening her back and neck pain. The psychiatrist revisited the discussion about the use of buprenorphine to treat her opioid use disorder and its potential for pain relief; however, the patient again expressed a preference for abstaining from maintenance medication use. Over the course of three 45- to 60-minute telephone calls, the psychiatrist reviewed applicable CBT concepts with

the patient and worked with her to apply problem solving and stress management techniques.

Ms. P continued to attend routine obstetric appointments. She had a normal spontaneous vaginal delivery at 38 weeks' gestation. The newborn was healthy and without any evidence of neonatal abstinence syndrome during its hospital stay. The patient's urine drug screen on delivery was negative for all substances, including opioids, and confirmatory tests for oxycodone and hydrocodone were negative. Based on the Prescription Drug Monitoring Program database, the patient last received a controlled substance from her psychiatrist at approximately 14–15 weeks of gestation.

On discharge from the postpartum unit, Ms. P was given a prescription for oxycodone/acetaminophen, 5 mg/325 mg every 6 hours (a total of 20 tablets), and ibuprofen, 800 mg every 6 hours. She called the psychiatrist to discuss the use of the oxycodone/acetaminophen and pain management strategies. She opted to fill the prescription for ibuprofen, and she gave the oxycodone/acetaminophen prescription to her pharmacist to hold and not fill unless she called and requested it. After 1 month, the prescription was voided, and at 6 months postpartum, the patient continues not using controlled substances for her pain.

DISCUSSION

Epidemiology of Prescription Opioid Use Disorder in Pregnancy

The prevalence of prescription opioid use during pregnancy has increased significantly over the past decade, with 14%–22% of pregnant women filling an opioid medication prescription during pregnancy (7, 8). In the United States, the proportion of pregnant women filling opioid prescriptions varies by state, ranging from 9.5% to 41.6%, with southern states having the greatest number of women using opioids during pregnancy (8, 9). There is also variation based on insurance coverage, with 14.4% among those with private insurance to 21.6% among those with Medicaid filling prescriptions for opioid medications (7, 8).

Over the past decade, the overall prevalence of other substance use disorders in pregnancy has remained stable, with approximately 5% of women reporting drug use during pregnancy (10, 11). However, the proportion of pregnant women with prescription opioid use disorder has increased dramatically. In a review of 14 years of data from the Nationwide Inpatient Sample, which included data on 57 million pregnant women admitted to a hospital for delivery, the prevalence of opioid use disorder in this group was reported to have doubled between 1998 and 2011, from 0.17% to 0.39% (12). Similarly, nationwide data from the Treatment Episodes Data Set (13), which tracks admissions to 83% of U.S.

substance abuse treatment facilities, demonstrated that the proportion of pregnant women with prescription opioid use disorder increased from 2% in 1992 to 28% in 2012.

There are substantial maternal, fetal, and newborn risks associated with opioid use disorder during pregnancy. In addition to the same risk of unintentional overdose and death that is seen in the general population (14), opioid use disorder during pregnancy is associated with considerable obstetric morbidity and mortality (12). A recent systematic review evaluating potential fetal harms associated with prescription opioid use in pregnancy reported the possibility of poor fetal growth, birth defects, and preterm birth, but findings are inconsistent, and methodological limitations inherent to the study of medications in pregnancy hinder our ability to draw definitive conclusions (12, 15).

Neonatal abstinence syndrome, or newborn opioid withdrawal, is due to maternal opioid use during pregnancy. A large medical record review found that among newborns with neonatal abstinence syndrome, 65% had mothers who had at least one prescription for an opioid pain medication during the pregnancy (16). Neonatal abstinence syndrome is characterized by hyperirritability of the CNS and dysfunction of the gastrointestinal tract and respiratory system and can result in serious illness and even death if untreated (17). The incidence of neonatal abstinence syndrome has increased fivefold in the past decade. Currently a baby is born with

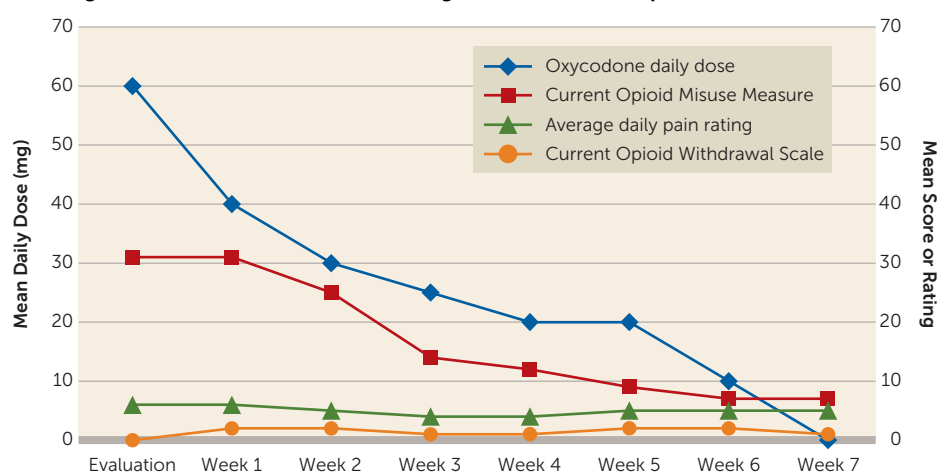
neonatal abstinence syndrome every 25 minutes in the United States, and the impact on newborn health and utilization of health care resources makes it a major public health concern (2, 16). On average, the cost of caring for a newborn with neonatal abstinence syndrome is \$65,000, compared with \$5,000 for a healthy newborn. Currently, Medicaid is covering 87% of the total cost of care of newborns with neonatal abstinence syndrome (2). Unfortunately, pregnant women with prescription opioid use disorder are often not aware of the risk and potential severity of neonatal abstinence syndrome.

Diagnosis and Treatment of Opioid Use Disorder

The diagnosis of an opioid use disorder during pregnancy is no different from diagnosis in nonpregnant populations (Figure 2). The standard of care for women with heroin use disorder in pregnancy is treatment with opioid agonist therapies such as methadone or buprenorphine, as opposed to medication-assisted withdrawal (1), and it is based on data collected prior to the prescription opioid epidemic. These data include retrospective chart reviews covering a total of 389 women withdrawn from methadone using different tapering strategies of varying duration (3–56 days) and in different treatment settings (e.g., outpatient, intensive outpatient, inpatient) (18–22). Rates of conversion to methadone maintenance following medication-assisted withdrawal or relapse to heroin use collectively ranged from 41% to 96%, with poor obstetric outcomes related to relapse to drug use (18, 22). One retrospective study comparing methadone maintenance to a 3- or 7-day methadone-assisted withdrawal (21) demonstrated that 52.2% of those completing methadone-assisted withdrawal eventually converted to methadone maintenance. Women on methadone maintenance stayed in treatment longer (a mean of 110 days compared with 20 days), attended more obstetrical visits (a mean of 8.3 compared with 2.3), and were more likely to deliver at the program hospital (21).

These data collectively demonstrate that pregnant women with heroin use disorder are at high risk of relapse to drug use if they undergo medication-assisted withdrawal and that agonist maintenance therapies, such as methadone and buprenorphine, should be the standard of care (1). Although there are obstetric and newborn risks associated with maintenance medications (23), heroin relapse places women at high risk of infectious diseases, exposure to violence, legal problems, and poor obstetric outcomes. Thus, experts conclude

FIGURE 1. Oxycodone Dosage, Opioid Withdrawal Symptoms, and Self-Reported Opioid Misuse and Pain During Evaluation and Treatment of a Pregnant Patient With Opioid Use Disorder



that the risks associated with relapse to heroin use far outweigh those associated with maintenance medications (1).

It is unclear, however, whether this rationale applies to the treatment of pregnant women with prescription opioid use disorder. The few studies that have compared demographic and drug use characteristics of adults in the general population with prescription opioid use disorder and those with heroin use disorder have demonstrated differences (24, 25). Those with prescription opioid use disorder are more likely to be white, receive legal income, use private insurance, and have greater family and social supports (24, 26). For women, these characteristics have been associated with higher rates of addiction treatment retention and completion (27, 28). Notably, individuals with prescription opioid use disorder are less likely than those with heroin use disorder to use nonopioid illicit drugs or to inject drugs (24–26, 29). Therefore, it is unlikely that pregnant women with prescription opioid use disorder have the risks that are associated with nonopioid illicit drug use, and their fetuses are not at risk for the dramatic cycles of high-level opioid exposure and withdrawal seen with intravenous heroin use. High-risk behaviors and legal consequences associated with heroin use are also not as common in prescription opioid use disorder. The 2013 National Survey on Drug Use and Health demonstrated that 50.5% of people who misused prescription opioids got them from a friend or relative for free, and 22.1% got them from a doctor (30). Recent data also suggest that prescription opioids can be successfully withdrawn during pregnancy without an increased risk of poor obstetric outcomes (6). Furthermore, newborn outcomes, including neonatal abstinence syndrome, appear to be improved among women who undergo medication-assisted withdrawal (3, 6, 31–33). At present, however, it remains unclear whether pregnant women with prescription opioid use disorder who undergo medication-assisted withdrawal are at high risk of relapse to prescription opioid use or other drug use.

Since the start of the prescription opioid epidemic, there have been several published studies covering a total of 613 pregnant

FIGURE 2. DSM-5 Criteria for Opioid Use Disorder^a

- A. A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:
1. Opioids are often taken in larger amounts or over a longer period than was intended.
 2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
 3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
 4. Craving, or a strong desire or urge to use opioids.
 5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
 6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
 7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
 8. Recurrent opioid use in situations in which it is physically hazardous.
 9. Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
 10. Tolerance, as defined by either of the following:
 - a. A need for markedly increased amounts of opioids to achieve intoxication or desired effect.
 - b. A markedly diminished effect with continued use of the same amount of an opioid.
- Note:** This criterion is not considered to be met for those taking opioids solely under appropriate medical supervision.
11. Withdrawal, as manifested by either of the following:
 - a. The characteristic opioid withdrawal syndrome.
 - b. Opioids (or a closely related substance) are taken to relieve or avoid withdrawal symptoms.

Note: This criterion is not considered to be met for those individuals taking opioids solely under appropriate medical supervision.

^a Reprinted from American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, Washington, DC, American Psychiatric Association, 2013, p. 541. Copyright 2013, American Psychiatric Association. Used with permission.

women, primarily with prescription opioid use disorder, who attempted medication-assisted withdrawal (3, 6, 31–33). A small study comparing opioid-assisted withdrawal (N=8) to methadone (N=12) or buprenorphine (N=5) in a comprehensive outpatient treatment program found no differences in maternal obstetric outcomes or urine drug screens between groups (3).

Cohort studies conducted in Norway (31) and Canada (32) reviewed the maternal and newborn outcomes of opioid-dependent women participating in outpatient opioid maintenance programs who lowered their medication dosage during pregnancy. A range of 40%–80% of pregnant women with opioid use disorder were able to reduce their maintenance opioid medication, and 2%–10% were able to stop opioid medication completely during pregnancy. At the time of

delivery, 50%–100% were successful at using only the reduced medication and had favorable newborn outcomes.

In a retrospective cohort study (33) of 95 pregnant women undergoing inpatient opioid detoxification, 56% (53/95) were successful with opioid cessation. Those who were successful in stopping had longer inpatient detoxification admissions (median stay, 25 days compared with 15 days) and were more likely to complete the entire detoxification program compared with women who were not successful (33). Most recently, Bell et al. (6) reported finding no increased risk of poor obstetric outcomes in 301 pregnant women with opioid use disorder who stopped drug use during pregnancy, even with vastly different withdrawal protocols, including abrupt cessation with symptomatic treatment (108 incarcerated women), a 5- to 10-day inpatient buprenorphine-assisted withdrawal protocol (100 women), and a 6- to 12-week outpatient buprenorphine-assisted withdrawal protocol (93 women). Groups differed in risk of relapse, with the greatest risk among those who had little or no outpatient care after inpatient detoxification (77%). The rate of relapse to prescription opioid use was 17.2% for women who completed an inpatient taper followed by discharge to a group home and 17.4% for women who completed an outpatient taper with intensive outpatient follow-up care (6).

Taken together, these data demonstrate that women can reduce or discontinue their use of prescription opioid medications during pregnancy with a low risk of poor obstetric and newborn outcomes and a low risk of relapse to drug use for those who receive longer and more intensive follow-up care (6, 33). Overall, these data are reassuring, given the limited access and suboptimal adherence to methadone and buprenorphine maintenance treatments (34), as well as the common patient preference for discontinuing opioid medications during pregnancy (21). However, the characteristics of optimal care for pregnant women with prescription opioid use disorder who choose medication-assisted withdrawal are largely unknown, and further research in this area is greatly needed.

CONCLUSIONS

The case presented here highlights the clinical challenges of treating prescription opioid use disorder during pregnancy. The standard of care for the treatment of heroin use disorder is clear, as the risks associated with relapse to heroin or intravenous drug use far outweigh the risks associated with opioid maintenance medications such as methadone and buprenorphine. This rationale, however, may not apply to pregnant women with prescription opioid use disorder. Increasing data suggest that the maternal and fetal risks associated with carefully monitored tapering or discontinuation of opioid medications are low and that these approaches may help support patient preference and may be beneficial to the newborn. However, an integrated team approach that includes mental health specialists who can provide psychological and pharmacological treatments, as

well as continued follow-up care to address pain and ongoing stressors, is critical to continued abstinence from opioids and the health of the mother and newborn. Pregnancy may represent an ideal time for this type of more intensive intervention, as all pregnant women are afforded health insurance, and they are often motivated to engage in positive health behaviors to invest in their newborn's health and future (35). Moreover, providing women with appropriate treatment and follow-up care could result in substantial cost savings by preventing or reducing rates and severity of neonatal abstinence syndrome. Further research is needed to determine tapering and follow-up regimens that enhance the success of medication-assisted withdrawal and reduce the risk of relapse. Further research is also needed to identify the demographic, psychiatric, and psychosocial factors that increase the likelihood of unsuccessful medication-assisted withdrawal, as well as factors that protect individuals from relapse, in an effort to minimize the potential risks associated with relapse and ensure that our limited substance abuse treatment resources are allocated to those women at highest risk of relapse to drug use during pregnancy.

AUTHOR AND ARTICLE INFORMATION

From the Department of Psychiatry and Behavioral Sciences and the Department of Obstetrics and Gynecology, Medical University of South Carolina, Charleston; and the Ralph H. Johnson VA Medical Center, Charleston.

Address correspondence to Dr. Guille (guille@musc.edu).

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