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A Multidisciplinary Approach to the Treatment of Co-occurring Opioid Use Disorder and Posttraumatic Stress Disorder in Pregnancy: A Case Report

Daisy J. Goodman, CNM, DNP, MPH[1], **Catherine U. Milliken, LICSW, MLADC, LCS**[2], **Regan N. Theiler, MD, PhD**[1], **Benjamin R. Nordstrom, MD, PhD**[2], and **Sarah C. Akerman, MD**[2]

Daisy J. Goodman: daisy.j.goodman@hitchcock.org; Catherine U. Milliken: catherine.u.milliken@dartmouth.edu; Regan N. Theiler: regan.n.theiler@hitchcock.org; Benjamin R. Nordstrom: benjamin.r.nordstrom@dartmouth.edu; Sarah C. Akerman: sarah.c.akerman@dartmouth.edu

[1]Department of Obstetrics and Gynecology, Dartmouth-Hitchcock Medical Center and Geisel School of Medicine, Lebanon, NH

[2]Department of Psychiatry, Geisel School of Medicine at Dartmouth, Lebanon, NH

Abstract

Perinatal opioid use disorders negatively impact maternal and neonatal outcomes and are a public health problem of increasing severity. More than half of women with a substance use disorder have a history of posttraumatic stress disorder that, if not adequately addressed, can impede substance use disorder treatment. This case report describes complexities in the treatment of a pregnant woman with opioid use disorder and posttraumatic stress disorder and reviews the psychotherapeutic and pharmacologic approaches available to treat these co-occurring disorders in pregnancy. This case demonstrates the importance of early screening and intervention for co-occurring posttraumatic stress disorder in pregnant women who use substances, in a closely coordinated, multidisciplinary approach to improve outcomes for women and their infants.

Keywords

pregnancy; opioid; PTSD; methadone; buprenorphine; perinatal; multidisciplinary

Case Presentation

KL is a 20-year-old Caucasian woman who presented to the Emergency Department with complaints of opioid withdrawal. She discovered she was pregnant by home pregnancy test a month earlier, but had not yet sought care. She moved back to the area the previous day after leaving a physically abusive relationship, was without transportation, and was homeless and temporarily staying with a friend.

Corresponding Author: Sarah C. Akerman, Department of Psychiatry, Geisel School of Medicine at Dartmouth, Lebanon, NH, sarah.c.akerman@dartmouth.edu, phone: 603-653-1860, fax: 603-448-5335.

Note: The patient described in this case is fictitious, but her presentation, clinical course and outcome are based on a composite of patient experiences from the authors' clinical practice.

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KL disclosed using Suboxone (buprenorphine/naloxone) 8 mg daily, supplied by her boyfriend, since learning she was pregnant. Her last use of illicit Suboxone was 2 days prior. In the year prior to this, she used up to 100mg of oxycodone by nasal insufflation (snorting) daily. She reported that her opioid use began when she was prescribed narcotics for tooth pain and found quickly that she liked the way they made her feel, including decreasing her persistent hypervigilance and insomnia. She transitioned herself to illicit Suboxone after learning she was pregnant, at the advice of a friend, and said that Suboxone helps her “to feel normal”. She also disclosed cannabis use 3-4× per week, for anxiety and pregnancy-related nausea, and smoking 20 tobacco cigarettes daily. This is her second pregnancy. Her past medical history was significant for a recent pregnancy loss at 12 weeks after her boyfriend pushed her down a flight of stairs, childhood sexual trauma, and untreated posttraumatic stress disorder (PTSD).

KL's vital signs in the Emergency Department were: temperature 98.9°F, pulse 80, respiratory rate 18, blood pressure 96/58. The fetal heartbeat was reassuring at 160 bpm. She measured about 16 weeks pregnant. A voluntary urine drug screen was positive for cannabis and buprenorphine, consistent with her self report of recent use. She was visibly anxious on exam and exhibited signs of moderate opioid withdrawal on the Clinical Opiate Withdrawal Scale (COWS) including restlessness, dilated pupils and diaphoresis (excessive perspiration). She reported myalgia (muscle pain), diarrhea, and difficulty sleeping.

The earliest available appointment for the following week was made at an outpatient addiction treatment program because inpatient substance use disorder treatment was not readily available. Clonidine 0.1 mg every four hours and promethazine 25 mg three times daily were prescribed for symptom relief. KL was counseled about the potential effects of continued substance use and withdrawal on the pregnancy and instructed to call if she experienced abdominal pain, cramping, or bleeding. She was discharged to the care of her friend.

Early the following morning, KL called the hospital reporting weakness, syncope (fainting), and loss of vision. She was instructed to present to the emergency department immediately and not to drive. She arrived by ambulance, profoundly hypotensive (blood pressure 70/38, pulse 50), weak, pale, and diaphoretic (sweaty). She was placed on cardiorespiratory monitoring, treated aggressively with intravenous fluids, oxygen, and other supportive measures. After 12 hours, her blood pressure improved to 90/48 and she was no longer bradycardic (having a slow heartbeat). When she began to feel better, she disclosed that she took three additional clonidine tablets the previous evening to attempt to alleviate nightmares and associated anxiety. KL was seen by a consulting psychiatrist and found to exhibit symptoms consistent with posttraumatic stress disorder (PTSD), but did not meet requirements for inpatient psychiatric hospitalization. Bedside ultrasound revealed a viable intrauterine pregnancy at 17 weeks. Once stable medically, she was discharged with instructions to discontinue clonidine and follow up with the outpatient addiction treatment program as planned.

When seen the following week at the outpatient addiction treatment program, KL enrolled in the medical center's comprehensive perinatal addiction treatment program, which included

weekly group and individual counseling. She disclosed that she continued to use illicit Suboxone and cannabis and no other substances (consistent with her urine drug screen that day), so was not currently experiencing opioid withdrawal symptoms. She elected to begin medication-assisted treatment and was started as an outpatient on buprenorphine for her opioid use disorder. KL received a full psychiatric evaluation and was diagnosed with PTSD as well as tobacco use disorder. She elected to begin sertraline for PTSD, received smoking cessation counseling, and declined a prescription for nicotine replacement gum, preferring to try to reduce smoking without it.

KL attended treatment weekly for the remainder of her pregnancy, including regular attendance at group counseling sessions and kept all appointments for medication management. Over the course of her pregnancy, her buprenorphine dose was gradually increased from 8 mg to 16 mg to achieve symptom control. Cigarette use was assessed during medication follow up visit and she was counseled using the “5 A's” technique (ask, advise, assess, assist, arrange). Sertraline was titrated to 100 mg daily and PTSD symptoms improved. With counseling from her providers, she was able to taper her cigarette use to 5 cigarettes daily, but was unable to stop completely. After meeting with the domestic violence advocate, she had no further contact with the father of her pregnancy. KL received support from the program's social worker and was able to move into subsidized housing during the third trimester of her pregnancy.

KL received regular prenatal care from the nurse midwife who was co-located at the addiction treatment program each week. Her symptoms of nausea were controlled with promethazine and she discontinued cannabis use. KL had a normal pregnancy course and delivered a healthy 3000 gm (∼6 lbs, 10 oz) infant at 39 weeks. Her infant required treatment for neonatal abstinence syndrome (withdrawal syndrome observed in babies exposed to opioids in utero) from postnatal days 4-6 and was discharged on day 8. KL stayed with him for the duration of his hospitalization, and breastfed successfully with the support of nurses and certified lactation consultants experienced with the management of breastfeeding in the context of neonatal abstinence. Postpartum, she was transitioned from buprenorphine monotherapy to combination buprenorphine-naloxone and continued in the treatment program.

In the discussion below, we review existing evidence supporting components of care for pregnant women with opioid use disorder and co-occurring posttraumatic stress disorder. These include the prenatal treatment of opioid physiologic dependence and/or withdrawal; psychotherapeutic approaches commonly used during pregnancy; and the benefits and risks of pharmacologic approaches for treating opioid use disorder and comorbid PTSD. Finally, we call for a collaborative approach across disciplines to provide access to comprehensive treatment.

Literature Review and Discussion

Opioid Use Disorders in Pregnancy

The prevalence of opioid use disorders among pregnant women has increased more than fourfold since 2002 (Patrick et al., 2012). In addition to the risk of infectious disease, death

from overdose, and drug-related violence, pregnant women who continue to use drugs also face increased rates of placental abruption, intrauterine fetal demise, preterm delivery, and a higher likelihood of having a low birth weight baby (Goler, Armstrong, Taillac, & Osejo, 2008). Neonatal abstinence syndrome, a withdrawal syndrome observed in babies exposed to opioids in utero, can lead to autonomic dysfunction, gastrointestinal abnormalities, and central nervous system hyperirritability in newborns (Goler et al., 2008). Infants with neonatal abstinence syndrome often require prolonged hospitalization at a mean fivefold increase in hospital expenditures (Patrick et al., 2012).

Maternal treatment of opioid use disorders improves maternal and neonatal outcomes (Kaltenbach, Berghella, & Finnegan, 1998). Both the World Health Organization (WHO) and the American College of Obstetricians and Gynecologists (ACOG) endorse a treatment model involving close collaboration across disciplines (ACOG Committee on Health Care for Underserved Women and American Society of Addiction Medicine, 2012; WHO, 2013), because “Services for pregnant and breastfeeding women with substance use disorders should have a level of comprehensiveness that matches the complexity and multifaceted nature of substance use disorders and their antecedents”(WHO, 2013, p. XI) . The limited data available about perinatal opioid use disorder treatment suggests that outcomes are best when women are cared for within multidisciplinary programs designed to provide obstetric care and the treatment of substance use and psychiatric disorders (Ashley, Marsden, & Brady, 2003; Goler et al., 2008; Goler et al., 2012). In the following sections we review available treatments for pregnant women with co-occurring opioid use disorder and PTSD and the benefits of offering treatment in a multidisciplinary environment.

Management of Opioid Withdrawal in Pregnancy—A pregnant woman with an opioid use disorder may be in opioid withdrawal at the time of first point of contact with the healthcare system. Opioid withdrawal during pregnancy is associated with abdominal pain, uterine contractions, non-reassuring fetal heart patterns, and reduced placental function (Kaltenbach et al., 1998). Detoxification from opioids is generally not recommended during pregnancy, both due to potential neonatal risks and the high likelihood of maternal relapse to illicit opioid use following detoxification (Jones et al., 2014; Jones, O'Grady, Malfi, & Tuten, 2008). Medication-assisted treatment with buprenorphine or methadone is the recommended treatment to manage opioid withdrawal in pregnancy, and to maintain treatment gains (ACOG Committee on Health Care for Underserved Women and American Society of Addiction Medicine, 2012) . Optimally, initiation of medication-assisted treatment should occur at the time that the patient presents for care, to avoid risks posed by the continuing cycle of withdrawal and subsequent illicit use. However, when pregnant patients present in acute withdrawal in the emergency or outpatient obstetric setting, immediate access to a facility and provider able to prescribe medication-assisted treatment may not be possible. In these cases, the use of a medication such as clonidine, an alpha-2-adrenergic agonist, is an option to alleviate withdrawal symptoms (Gowing, Farrell, Ali, & White, 2014). However to our knowledge this medication has not been studied in the treatment of withdrawal in pregnancy and may lead to side effects such as hypotension in pregnancy (Maina et al., 2014), particularly if misused as occurred in the case described above. In general, short-term medication treatments for opioid withdrawal pose a significant

risk of relapse to illicit opioid use once the course is complete (Dunn, Sigmon, Strain, Heil, & Higgins, 2011), making maintenance treatment preferable.

Medication Assisted Treatment in Pregnancy

Methadone: Methadone maintenance therapy has been the standard treatment of perinatal opioid use disorder for over forty years. A long acting mu-receptor agonist with maximum efficacy at about 3 hours post administration, methadone effectively decreases illicit drug use by decreasing craving and withdrawal symptoms. Methadone is dispensed in federally-licensed methadone clinics as a directly observed therapy (Jones, Finnegan, & Kaltenbach, 2012; Mattick, Kimber, Breen, & Davoli, 2008)..

Methadone crosses the placenta readily, with approximately 31% reaching the fetus at term (de Castro et al., 2011; Nanovskaya, Nekhayeva, Hankins, & Ahmed, 2008). Common side effects of methadone during pregnancy include sedation at peak serum concentrations, nausea and constipation, and reduction in fetal heart rate variability (Jansson, DiPietro, & Elko, 2005). Less common adverse effects include cardiac QT prolongation, especially at doses higher than 100mg/day, somnolence, and respiratory depression. Life threatening interactions can occur with benzodiazepines or alcohol, and with other medications prolonging the QT interval such as ondansetron. Drug interactions are also possible with certain antidepressants, antifungals, and antiretrovirals (Bruce, Altice, Gourevitch, & Friedland, 2006). The most common neonatal effect of in utero methadone exposure is neonatal abstinence syndrome (as seen in the case described here). A significant proportion of prenatally exposed infants will require pharmacologic treatment and prolonged hospitalization. The long-term prognosis for these infants appears reassuring as long as a supportive environment is provided (Hudak & Tan, 2012).

In clinical practice, wide variation exists in methadone doses prescribed during pregnancy, ranging from 20 mg/day to well over 200 mg/day. High-dose methadone (> 100 mg/day) may be more successful in reducing illicit use than doses under 100 mg/day in some pregnant women and does not appear to increase the severity of neonatal abstinence syndrome (McCarthy, Leamon, Parr, & Anania, 2005). Dose increases and/or divided dosing may be required with advancing gestation to achieve symptom control (McCarthy, Leamon, Willits, & Salo, 2015). A desire to reduce fetal exposure must be balanced by the central importance of treatment efficacy. In the postpartum period, the methadone dose may need to be decreased to avoid maternal sedation, which can lead to infant falls or other injuries. In the absence of concurrent illicit drug use, maternal treatment with methadone is compatible with breastfeeding (Bernshaw, 2002).

Buprenorphine: Buprenorphine has been approved in the United States for the treatment of opioid use disorder since 2002. Buprenorphine acts as a partial agonist with high receptor affinity at the mu-receptor, and as an antagonist at the kappa receptor. This partial agonist activity creates a “ceiling effect” for buprenorphine with regard to respiratory depression and other opioid effects, giving the drug a more favorable safety profile than methadone (Center for Substance Abuse Treatment, 2005).

Buprenorphine has poor absorption into the system when given orally, so it is administered via sublingual tablets (Subutex®) or combined with naloxone as sublingual tablets or film (Suboxone®). Sublingually, buprenorphine is rapidly effective with a half-life of 37 hours (Elkader & Sproule, 2005). In non-pregnant patients, peak buprenorphine withdrawal symptoms occur around 4 days after discontinuation (Kosten & O'Connor, 2003). Commonly reported side effects to buprenorphine include nausea and constipation; serious adverse effects include the potential for life threatening interaction with benzodiazepines or alcohol (Elkader & Sproule, 2005). QT prolongation has not been identified in the literature, although it remains a theoretical concern.

While methadone is still considered the standard of care for the treatment of opioid use disorder in pregnancy, antepartum buprenorphine treatment is generally accepted and is endorsed as an alternative to methadone by the American College of Obstetricians and Gynecologists (ACOG Committee on Health Care for Underserved Women and American Society of Addiction Medicine, 2012). Buprenorphine may be prescribed through office-based programs by physicians, including obstetricians, who complete an 8-hour training course and apply for prescribing authority (i.e., the “X” number) through the Drug Enforcement Agency.

Because of its high receptor affinity, buprenorphine effectively treats symptoms of opioid withdrawal. However, the same receptor affinity allows buprenorphine to displace full agonists at mu-receptor sites, potentially precipitating withdrawal if initiated while full agonists remain in the system (Center for Substance Abuse Treatment, 2005). This risk of precipitated withdrawal complicates the process of inducting pregnant patients onto buprenorphine and can cause fetal distress (Jones et al., 2014), so must be undertaken under close supervision.

Little data exists on the optimal buprenorphine dose range in pregnancy. Doses from 2mg to 32 mg/day have been used in some clinical trials and treatment settings (Jones et al., 2010). Placental analysis indicates that buprenorphine is metabolized by the placenta, and less than 10% of maternal buprenorphine is transferred to the fetus (Nanovskaya, Deshmukh, Brooks, & Ahmed, 2002). Dose increases may be required to achieve symptom control with advancing gestation (Concheiro et al., 2010).

In a multi-center, randomized, placebo-controlled trial comparing methadone to buprenorphine in the treatment of pregnant women with opioid dependence, buprenorphine appeared equivalent in safety and efficacy to methadone (Jones et al., 2010). Although the proportion of neonates requiring treatment for neonatal abstinence syndrome did not differ significantly, infants exposed to buprenorphine required lower methadone treatment doses over a significantly shorter period of time, resulting in a 43% reduction in hospital length of stay (Jones et al., 2012; Jones et al., 2010). Given the reassuring data on perinatal outcomes, buprenorphine has recently been endorsed as an alternative to methadone maintenance during pregnancy by the American College of Obstetricians and Gynecologists (ACOG Committee on Health Care for Underserved Women and American Society of Addiction Medicine, 2012). Treatment with buprenorphine is compatible with breastfeeding (Hudak &

Tan, 2012). In the case described above, treatment with buprenorphine in the context of a comprehensive outpatient program proved to be an effective approach for KL.

Psychotherapeutic Approaches to Treat Substance Use Disorders in Pregnancy—Psychotherapeutic treatment should always be offered in conjunction with medications for the treatment of opioid use disorders in pregnancy. However, the optimal approach is unclear. Methodological issues including small sample size, confounding, problems with randomization, inconsistency in outcome measures, and unblinded observation complicate most research comparing psychotherapeutic approaches in pregnancy. The broad categories of treatment approaches are described below.

Outpatient Interventions

Motivational Enhancement Therapy: Is based on principles of motivational psychology, designed to be non-confrontational and produce rapid internally motivated change. Motivational enhancement therapy strategies give women the power to choose and be heard by evoking and selectively reinforcing self-motivational statements, a powerful technique for women with a history of trauma and abuse. This treatment approach also helps women progress through the stages of change and is most effective in moving from preparation to action and post relapse to re-engage women in treatment. This therapeutic strategy has been studied in relationship to prenatal alcohol use. A pilot study comparing written education vs. a one-hour motivational enhancement therapy intervention for pregnant drinkers (N=42) found that 81% showed a significant reduction in alcohol consumption and peak intoxication levels at 2 months. Women who reported the highest blood alcohol concentration levels showed a significantly greater reduction in their BACs at follow-up when assigned to the intervention group (Handmaker, Miller, & Manicke, 1999).

Twelve Step Facilitation: Is a manualized approach based on the 12 Steps of Alcoholics Anonymous, which include a commitment to abstinence from alcohol or other substances and regular meeting attendance. However, this approach has not been widely tested in pregnant women and was found not to be superior to other evidence-based outpatient treatment approaches in one study of pregnant women with cocaine dependence (Burns et al., 2013).

Cognitive Behavioral Therapy: Is a therapeutic approach which assists clients in identifying maladaptive behaviors, links emotional distress to unhelpful coping behaviors, and reinforces healthy coping behaviors. Although cognitive behavioral therapy has not been well tested in pregnant women with substance use disorders, it has been utilized successfully with other female populations and pregnant women with depression (Sockol, 2015) and is widely used in clinical practice. A study by Cohen and colleagues comparing cognitive behavioral approaches to a no-treatment control condition found that this type of therapy alleviated PTSD symptoms and decreased alcohol use for women with complex trauma histories and substance use disorders (Cohen & Hien, 2006). A meta-analysis of studies using cognitive behavioral therapies specifically for the treatment of substance use disorders showed small to medium effects on drug use. The authors pointed out that in the included studies, agonist treatments (i.e., buprenorphine or methadone) were more effective than

therapy for opioid use disorders, but did not comment on the potential benefit of combining the two approaches (Hofmann, Asnaani, Vonk, Sawyer, & Fang, 2012).

Contingency Management: Is an approach based on operant conditioning principles, using reinforcement such as cash or vouchers to motivate abstinence, treatment attendance, or other healthy behaviors. While typically used as an adjunct to treatment, contingency management has been shown to improve access and retention in treatment with pregnant women with substance use disorders in a limited number of studies (Akerman et al., 2015; Jones, Haug, Silverman, Stitzer, & Svikis, 2001).

Intensive Outpatient Treatment: Offers a higher level of care than traditional outpatient programs. Intensive outpatient services are multidimensional and can vary in intensity and duration, usually involving 9-15 hours of treatment per week. One study indicated that rates of treatment completion were higher for postpartum women with cocaine use disorder who participated in an intensive outpatient program (45%) versus women in traditional outpatient treatment (21%) (Strantz & Welch, 1995).

Residential and Inpatient Interventions: Comprehensive, residential level treatment of substance use disorders in pregnant and postpartum women is associated with lower infant morbidity and mortality compared with an untreated comparison group (Conners, Grant, Crone, & Whiteside-Mansell, 2006; Greenfield et al., 2004). Other positive outcomes of residential treatment include abstaining from substances, avoiding criminal justice system involvement, having a non-using partner, making employment gains, improving mental health, and retaining or obtaining child custody (Porowski, Burgdorf, & Herrell, 2004). Gender specific services which allow young children to reside with their mother during treatment have been shown to increase self-esteem, improve parenting attitudes and decrease depressive symptoms (McComish et al., 2003). Unfortunately, access to residential treatment allowing children is extremely limited. In the case presented above, residential treatment could have addressed KL's problem of homelessness and encouraged the developmental of parenting skills in a supervised environment.

Substance Treatment Services in Non-Traditional Settings: Home based interventions for perinatal substance users demonstrate positive long-term outcomes following treatment completion, including high rates of abstinence and low rates of subsequent unplanned pregnancies. These programs utilize an advocacy approach and staff with similar backgrounds to participants, decreasing loss of child custody, reducing drug use, and increasing treatment participation(Grant, Ernst, Pagalilauan, & Streissguth, 2003; Jansson, Svikis, & Beilenson, 2003).

Posttraumatic stress and substance use disorders in the context of pregnancy

The link between posttraumatic stress disorder (PTSD) and substance use in women is well established (Kessler, 1995; Lisa M. Najavits, Weiss, & Shaw, 1997). However, this association has not been well studied during pregnancy. A very limited amount of data is available, yet the findings are consistent with what is observed for non-pregnant women. For example, Jones and colleagues (Jones, Svikis, Rosado, Tuten, & Kulstad, 2004) found the

prevalence of PTSD among women with substance use disorders to be as high as 62%, compared to 12% among pregnant women without substance use disorders (Jones et al., 2004; Morland et al., 2007) Conversely, pregnant women who are diagnosed with PTSD are more than twice as likely to use substances as those without trauma history (Morland et al., 2007; Rogal et al., 2007). Psychiatric comorbidity appears to complicate the treatment of substance use disorders during pregnancy, as is also the case for non-pregnant women (Benningfield et al., 2010).

Untreated PTSD is associated with unplanned pregnancy and other high-risk behaviors in women (Orsillo, Raja, & Hammond, 2002). Symptomatic PTSD is also associated with pregnancy complications. These include hyperemesis (persistent severe vomiting), low birth weight (Seng, Low, Sperlich, Ronis, & Liberzon, 2011), preterm birth (Seng et al., 2011; Yonkers et al., 2014), poor nutrition or excessive weight gain, higher rates of smoking, drug and alcohol use, and depression; all of which are independently associated with poor perinatal outcomes (Bell & Seng, 2013; Udechuku, Nguyen, Hill, & Szego, 2010). In one small study, women diagnosed with concurrent PTSD and major depression were four times more likely to deliver prematurely than those who did not have these comorbidities (Yonkers et al., 2014). Unfortunately, women with symptomatic PTSD are less likely to seek prenatal care, to attend prenatal visits consistently, or to report a feeling of alliance with their maternity provider (Bell & Seng, 2013; Morland et al., 2007).

Pharmacologic treatment of PTSD during pregnancy—Current evidence supports the effectiveness of pharmacologic treatment in conjunction with psychotherapeutic treatment for PTSD. Detailed guidelines, as well as prescriber-level synopses are available from the National Center for PTSD at http://www.healthquality.va.gov/guidelines/MH/ptsd/ and http://www.ptsd.va.gov/professional/treatment/overview/clinicians-guide-to-medications-for-ptsd.asp. Unfortunately, there is little data or guidance for clinicians available regarding pharmacotherapies to treat PTSD during pregnancy. Current recommendations include the use of selective serotonin reuptake inhibitors (SSRIs) as a first line treatment for PTSD in the general population (Jeffreys, 2015). While not studied specifically in the treatment of PSTD in pregnancy, SSRIs have been evaluated through observational studies; they are commonly used to treat depression and anxiety disorders in pregnancy, and are considered appropriate choices if there are clear benefits of treatment (Steiner, 2012a; Udechuku et al., 2010).

Most observational studies have found that SSRI exposure is associated with an increased likelihood of preterm delivery, a small difference in mean birth weight, and transitory neonatal adaptation problems (Oberlander et al., 2004; Ray & Stowe, 2014; Steiner, 2012b; Udechuku et al., 2010). About 30% of newborns exposed to SSRIs in the third trimester experience transitory adaptation problems after birth (Diav-Citrin & Ornoy, 2012) with symptoms ranging from mild (tremor, irritability, poor feeding) to more severe, including seizures, respiratory symptoms, temperature dysregulation or hypo- or hypertonia. These symptoms generally resolve within a few days without long-term effects. Of all the SSRIs, only paroxetine has been consistently linked to congenital anomalies and should therefore be avoided during pregnancy (Diav-Citrin & Ornoy, 2012; Udechuku et al., 2010). Sertraline and fluoxetine are associated with less severe symptoms than newer agents such as the

serotonin norepinephrine reuptake inhibitors (Udechuku et al., 2010). Although a link has been proposed between late trimester prenatal SSRI exposure and persistent pulmonary hypertension of the newborn, the evidence for this association is inconsistent (Udechuku et al., 2010).

Effect sizes in studies evaluating SSRIs in pregnancy are inconsistent, making it difficult to quantify the risk of treatment compared to non-treatment, especially because untreated psychiatric disease itself is strongly associated with increased risk of preterm birth and low birth weight. Given the well-documented adverse perinatal effects of untreated psychiatric disease, there is consensus among both obstetrical and psychiatric providers that the benefits of treating significant psychiatric symptoms in women outweigh the risks presented by SSRI exposure (Na, 2008). Clinicians should engage in shared decision making with pregnant women regarding the use of SSRIs, in particular sertraline and fluoxetine, for treating symptomatic PTSD (Diav-Citrin & Ornoy, 2012; Ray & Stowe, 2014; Steiner, 2012b).

Sertraline has been studied in the largest number of mother–infant dyads, and drug levels are nearly undetectable in most breastfed infants, making it the medication of choice (Weissman et al., 2004). The majority of women treated with fluoxetine breastfeed without incident, although several case reports involving colic, prolonged crying, vomiting, tremor, and other symptoms have been reported, and recent data suggest that fluoxetine may reduce weight gain in some breastfed infants. In a recent review of antidepressant safety in breastfed infants, 22% of breastfeeding infants exposed to fluoxetine had breast milk levels above 10% of average maternal serum concentrations, making fluoxetine less preferred for breastfeeding mothers (Weissman et al., 2004).

After carefully reviewing the risks and benefits with her provider team, the woman in our case, KL, chose to begin sertraline during pregnancy, achieved symptom reduction, and continued this medication into the postpartum period. Guidance regarding patients who fail these first line treatments is not clear. Anticonvulsants and antipsychotics, which can be used when first line treatments fail in the general population, can present significant reproductive risks (Na, 2008). Although often used to treat anxiety disorders in women, benzodiazepines are neither an evidence-based therapy for PTSD nor considered safe in pregnancy (Jeffreys, 2015).

Psychotherapeutic Treatment of PTSD in Pregnancy—The recognition of labor and delivery as triggering experiences for women with pre-existing trauma histories, and the burden of postpartum PTSD following difficult childbirth are emerging areas of study (Beck, 2004; Simkin, 2011). However, very little research has been done on the treatment of PTSD during the perinatal period.

Psychotherapeutic approaches for treating PTSD in women in general significantly improve symptoms, compared to no treatment or to placement on a waiting list (Classen, Koopman, Nevillmanning, & Spiegel, 2001; Cloitre, Koenen, Cohen, & Han, 2002; Feske, 2008; Ford, Steinberg, & Zhang, 2011; Hinton, Hofmann, Rivera, Otto, & Pollack, 2011; Johnson, Zlotnick, & Perez, 2011; McDonagh et al., 2005; McHugo & Fallot, 2011; Schnurr et al., 2007). Studies of men and mixed gender samples have shown significant promise for

cognitive behavioral therapies, including those which include re-exposure to traumatic memory in a therapeutic context, an approach known as prolonged exposure. However attrition rates as high as 41%were evident among women participating in these trials (McDonagh et al., 2005; Schnurr et al., 2007). Exposure-based therapies are believed to be safe during pregnancy, however more research is needed (Arch, Dimidjian, & Chessick, 2012)

Meta-analyses of studies testing cognitive behavioral approaches for perinatal mood disorders found that both prenatal and postpartum depression respond better to a combination of cognitive behavioral therapy and antidepressant medication than to medication alone, however, these studies did not address comorbid PTSD (Hofmann et al., 2012). Cognitive behavioral therapies have also demonstrated effectiveness in treating non-pregnant women dually diagnosed with PTSD and substance use disorders (Cohen & Hien, 2006; L. M. Najavits, Weiss, & Liese, 1996).

A number of treatment programs have been developed which focus specifically on the relationship between trauma and substance use, although data describing their efficacy is limited. *Beyond Trauma* and *Healing Trauma* emphasize the relational model as central to understanding women in recovery (Covington, Burke, Keaton, & Norcott, 2008). *Trauma, Recovery & Empowerment* acknowledges that current problematic behaviors and symptoms may have originated as legitimate and even courageous attempts to cope with or defend against trauma (Harris & Anglin, 1998). *ATRIUM* (Addictions and Trauma Recovery Model) combines four basic principles of trauma recovery: recognizing and reinforcing resilience, achieving abstinence from addiction, recognizing and healing the wounds of non-protection, and creating a sacred connection to the world beyond the self with a sense of social purpose (Miller, 2002). *Seeking Safety* focuses on eliminating substance use, reducing PTSD symptoms and increasing safety from HIV risk, domestic violence and self-harm (Brown et al., 2007; L. M. Najavits et al., 1996; Lisa M. Najavits, Gallop, & Weiss, 2006; Lisa M. Najavits et al., 1997). *Seeking Safety* has been tested primarily in women, but with mixed results (Brown et al., 2007; McHugo & Fallot, 2011; Lisa M. Najavits et al., 2006). The Boston Consortium Model utilizes service-system integration strategies and skill-building group modules (Amaro et al., 2005). The Triad Women's Project addresses mental health, substance abuse, & trauma with an emphasis on skills building (Salasin, 2005). More research is needed to determine the efficacy of these treatment approaches specifically for pregnant women.

Multidisciplinary Treatment Approach in Perinatal Substance Use Disorders

To address the complex problem of perinatal substance use disorders, the U.S. Centers for Disease Control and Prevention recommends a multidisciplinary approach incorporating maternity care, addiction treatment, behavioral health, health promotion, and education (Jones et al., 2014). Despite this recommendation, only 12% of addiction treatment programs in the U.S. have services specifically for pregnant or postpartum women (SAMHSA, 2014).

A few novel programs have incorporated outpatient treatment for substance use disorders into obstetric and gynecology settings to enhance access, retention, and communication

among providers. These programs report improved perinatal outcomes and increased satisfaction with care (Goler et al., 2008; Lefebvre et al., 2010). A review of 38 studies of substance abuse treatment for women also found positive treatment outcomes associated with collaborative, multidisciplinary programs, which provided services including child care, prenatal care, mental health treatment, women-only admissions and a comprehensive treatment approach (Ashley et al., 2003).

Providing integrated care for pregnant women with comorbid opioid use disorder and PTSD requires coordination across a variety of systems, with collaboration among a multi-disciplinary, interprofessional team, which includes at minimum obstetrics, addiction psychiatry, and pediatrics. Beyond collaboration, co-location of services should be attempted, as attendance significantly decreases when referrals are made offsite (Batki, Gruber, Bradley, Bradley, & Delucchi, 2002; Umbricht-Schneiter, Ginn, Pabst, & Bigelow, 1994)

In our clinical case, KL self-identified as an opioid user and was able to participate in a collaborative perinatal addiction treatment program, receiving comprehensive outpatient care at a single location. There she received medication-assisted treatment for her opioid use disorder, psychiatric care, and trauma-informed substance use disorder treatment in conjunction with on-site obstetrical care and social work services. Close coordination with the inpatient pediatric service ensured that she was informed about neonatal abstinence and emotionally prepared to remain in the hospital with her newborn and participate fully in his care.

Conclusion

Posttraumatic stress disorder is strongly associated with substance use disorders among pregnant women, and the co-occurrence of these disorders can lead to poor obstetrical outcomes. As our clinical case demonstrates, integrating obstetrical, psychiatric, and addiction treatment services can provide women the support they need to facilitate retention in treatment and support a healthy pregnancy.

Perinatal treatment programs should incorporate psychiatric evaluation and treatment with a special awareness of trauma history. Although pregnancy is a time of high motivation for recovery, it is not known if the physiologic and psychological changes that may occur during pregnancy change the efficacy of established therapies for non-pregnant women. Research is urgently needed to explore psychotherapeutic and pharmacologic treatment approaches for pregnant women with co-occurring opioid use disorder and PTSD. Providers working with pregnant women with substance use disorders must work together across disciplines to overcome barriers and ensure access to comprehensive care. The development of strong consultative relationships, along with protocols for shared management, can help solve the critical problem of access to timely and effective treatment for pregnant women with co-occurring disorders.

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