

PERSPECTIVE

Opioid use disorder during pregnancy in Tennessee: expediency vs. science

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Abstract

Methadone and buprenorphine are highly effective and commonly prescribed for the treatment of opioid use disorder. Both medications are also efficacious for the treatment of pregnant women with this disorder. In one third of states, however, Medicaid reimbursement will cover the cost of buprenorphine, but not methadone, to treat opioid use disorder in pregnant women. This commentary will explore the clinical and policy rational and consequences of this policy, with the opinion that this approach is guided by political expediency rather than sound clinical research. The commentary will focus on the pharmacological management of prescription opioid dependence during pregnancy in Tennessee, one of the states that restrict Medicaid coverage of pregnant women to buprenorphine. Tennessee is also relevant in that this state ranks second nationally in the rate of prescriptions written for opioid pain relievers; in contrast to injection opioid use in urban populations, opioid addiction in rural and southeastern regions of the US is characterized by use of non-injection prescription opioids. Until recently, most research-based recommendations for the management of opioid use disorder during pregnancy have derived from studies of women using opioids intravenously. The lack of research in non-injection opioid-using pregnant women may partially explain why policy rather than scientific evidence guides Medicaid reimbursement. It is hoped that future research in pregnant women addicted to prescription opioids will clarify which opioid addicted pregnant women have better outcomes with buprenorphine or methadone treatment and these findings, in turn, will inform Medicaid reimbursement.

Keywords

Buprenorphine, methadone, opioid use disorder, pregnancy, policy

History

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A growing public health concern

Opioid use disorder in pregnancy is of mounting public health concern in our country, complicating an estimated 54 000 pregnancies annually (1). A wide range of consequences of opioid exposure during pregnancy for mother, fetus, and the neonate have been described and questions persist as to whether adverse effects continue into infant development and beyond (2). Neonatal abstinence syndrome (NAS) is a postnatal withdrawal syndrome, first described in heroin-exposed newborns; more recently, other factors than opioid exposure have also been implicated in this clinical syndrome (3). NAS presents with an array of clinical signs, including feeding difficulty, autonomic dysfunction, and behavioral distress. NAS has become widely recognized as a major healthcare expenditure associated with opioid use disorder during pregnancy and accordingly has been identified as an important focus for prevention efforts (4). The incidence of

NAS increased substantially in the United States between 2000 and 2009 (3). This increase has been striking in Tennessee, where 29% of pregnant women enrolled in Medicaid (TennCare) filled opioid prescriptions during 2009. From 1995–2009, pregnancy-related use of opioid analgesics nearly doubled among TennCare participants (5). From 2009–2011, the rate of NAS among infants in TennCare increased from 6.0–10.7 per 1000 births (6) and to 11.6 in 2013 (4) – representing a 16-fold increase since 2000. This commentary focuses on opioid agonist treatment as a significant component of the management of prescription opioid use disorder during pregnancy in Tennessee, of particular interest, as this state ranked second nationally in the rate of prescriptions written for opioid pain relievers, at 1.4 per person in 2012 (7). In rural and southeastern regions of the United States, such as Tennessee, where opioid addiction is predominantly characterized by non-injection use of prescription opioids, available therapeutic choices for opioid use disorder have become limited to buprenorphine instead of methadone, seemingly a policy decision, not one guided by the available scientific evidence which supports the efficacy of both medications.

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The Tennessee approach: criminalization to “encourage” treatment but no Medicaid access to methadone

Even these very high rates of NAS in Tennessee likely underestimate the use of opioids during pregnancy because of significant underreporting due to stigma associated with drug use disorders. This stigma is greatly exacerbated by recent Tennessee legislation which “allows prosecution of a woman for assault for the illegal use of a narcotic drug while pregnant, if her child is born addicted to or harmed by the narcotic drug and the addiction or harm is a result of her illegal use of a narcotic drug taken while pregnant” (<http://state.tn.us/sos/acts/108/pub/pc0820.pdf>). This legislation clearly may deter pregnant women from seeking prenatal care for fear of being reported. However, the law should also be viewed as offering incentive for addiction treatment and recovery as it next states that, “It is an affirmative defense to a prosecution . . . that the woman actively enrolled in an addiction recovery program before the child is born, remained in the program after delivery, and successfully completed the program, regardless of whether the child was born addicted to or harmed by the narcotic drug.” Interpretation of this legislation is challenging based on recent findings that opioid type, including methadone and buprenorphine maintenance, and tobacco and SSRI antidepressant use all significantly increase risk of NAS (6).

In order to attempt to contain the prescription opioid epidemic in the state, the Tennessee Department of Health has implemented a Controlled Substance Monitoring Database (CSMD) program and mandatory education for prescribers (<http://health.state.tn.us/boards/ControlledSubstance/index.shtml>). This program mandates that pharmacies record all controlled drug prescriptions in a centralized database that physicians must search in real-time prior to providing a prescription for a controlled drug to any patient. However, the high incidence of NAS has not diminished, so much so that the first statewide surveillance system for NAS was recently implemented by the Tennessee Department of Health to allow study of prevention of this serious complication of prescription opioid dependence (4).

Options for management of opioid use disorder during pregnancy include maintenance on an opioid agonist approved for addiction treatment or detoxification (1). With careful monitoring, the prescribed opioid analgesic may also be continued or discontinued slowly by tapering. Detoxification from opioids during pregnancy has not been the recommended course for more than 40 years, particularly not for women with the most severe form of opioid use disorder, namely those who use intravenous opioids; such pregnant women are very unlikely to be able to avoid relapse without pharmacological support (8). Methadone maintenance treatment, as currently widely employed throughout the United States, remains the standard of care for agonist treatment of opioid use disorder in pregnancy (1). Although consensus holds methadone maintenance as the standard against which other treatments of pregnant women with opioid use disorder must be compared, TennCare does not cover the cost of methadone maintenance. Tennessee is not alone: approximately a third of states do not provide for methadone maintenance treatment of pregnant women (9).

Policy rather than evidence-guided clinical practice?

Disparities among states in Medicaid support for treatment of these pregnant women is not easily understood by examining the published evidence alone. Does excluding methadone from the therapeutic armamentarium for pregnant opioid-addicted women reflect simply an ill-advised political decision or are these appropriate regional policies because relevant evidence supporting methadone maintenance in their populations is not readily available? State laws and regulations pose significant implications for practitioners in that policy might influence clinical practice in a manner that is not entirely consistent with recommendations in the scientific literature (10).

Without opioid agonist treatment, which reduces drug craving and use, those who are addicted to intravenous opioids are recognized to be at a particularly high risk of relapse and consequently opioid overdose, premature labor triggered by repeated episodes of withdrawal, exposure to intravenously transmitted infections, and consequences of involvement with the criminal justice system. Evidence-based treatment includes administration of a therapeutic daily dose of methadone provided within the context of a comprehensive treatment program comprising psychiatric and obstetrical prenatal care, counseling and group therapy, and social work services (11). Methadone maintenance in comparison with active intravenous opioid addiction has been shown to result in improved adherence to prenatal care, increased fetal growth, and decreased risk of HIV infection, preeclampsia, and foster care placement of the neonate. Nevertheless, NAS of significant severity to require treatment with morphine is still observed in well over 50% of pregnancies on methadone maintenance (12). Hence, if absence of NAS is one criterion for treatment efficacy, as inferred from the above-mentioned Tennessee law, methadone maintenance, while it is evidence-based practice, may not be the best we can do. Also, focusing solely on NAS, as the Tennessee law does, misses the possibility that women who relapse during pregnancy may never even reach delivery because of complications of accelerated opioid use disorder (13,14).

Changing face of opioid addiction

By not covering methadone costs, TennCare, like Medicaid in the other non-methadone states, limits access to methadone, but it does ensure that opioid-dependent Tennesseans can receive buprenorphine during pregnancy at a limited daily dose, with prior authorization (<http://www.tn.gov/tenncare/forms/ben11001.pdf>). This policy may be a reflection of the changing face of opioid addiction among pregnant women due to an ever-expanding prescription opioid epidemic (1). From a problem affecting predominantly disenfranchised inner city women using intravenous heroin, a much larger, demographically diverse population addicted to prescription opioid analgesics has become widely distributed throughout smaller urban and rural regions of the United States. This increase in prescription opioid use disorder is characteristic of southeastern states, including Tennessee. Not only is the pattern of opioid use different in the Southeast and in rural regions, but this pattern of opioid addiction represents a considerably larger challenge in absolute numbers than do

injection opioid users. For example, in 1997, annual quantities of opioid pain relievers prescribed were equivalent to 96 mg of morphine per individual; by 2007, rates had reached the equivalent of 700 mg of morphine per person. In 2010, 2,004,000 persons aged 12 or older initiated non-medical opioid pain reliever use (almost as high as the 2,426,000 for marijuana) compared to only 140,000 for heroin (15). These trends suggest that management of non-injection prescription opioid use during pregnancy will continue as a major clinical challenge and that states like Tennessee may be legislating care based upon epidemiologic data. However, methadone treatment in pregnancy standards were established in large urban areas from which most of the NIH-funded research guiding practitioners, to date, has been conducted.

Management of non-injection vs. injection opioid addiction

Although non-injection opioid addiction has fewer severe medical complications than injection drug use (16), overdose deaths due to opioid analgesics recently surpassed heroin and cocaine, rivaling death rates from motor vehicle accidents in absolute terms as reported by the CDC (17). So, while ingested prescription opioids have been considered a “safer” dosage form compared to intravenously administered opioids, consequences of these drugs are far from benign and cannot be ignored. In fact, an increasingly common clinical trajectory is to switch to intravenous or smoked heroin from prescription opioids (13,14) based upon changing supply and demand, unintended consequences of tighter regulation of prescribing.

Despite the fact that we do not really know which patients (injection or non-injection) do better on methadone or on buprenorphine, TennCare and the Medicaid formularies of many demographically similar states provide buprenorphine rather than methadone for opioid use disorder treatment. While it would be ideal to determine for each individual whether a partial (buprenorphine) or full (methadone) mu opioid agonist combined with structured psychosocial care of the mother during gestation can result in a healthier neonate at the point when opioid exposure stops at delivery (1), the other extreme, a public health approach, attempts to reach the greatest number of patients with an evidence-based approach (18).

The risk-benefit analysis supporting methadone maintenance for intravenous opioid addicted pregnant women is very compelling (8,19,20), but comparable studies in non-injection opioid use disorder patients, who obtain these drugs from the street or by prescription from their doctors for pain control, are only now emerging from other rural states like Vermont. The findings suggest that buprenorphine is equal to, or may be even better, for prescription opioid addicted pregnant women (21). The situation is somewhat more complicated by the fact that the route of heroin administration has change dramatically in the past 10 years due to the purity of the drug that allows for smoking or snorting (22). It may be argued that some of these women addicted to prescription opioids may well be detoxified or tapered off the opioid, thus avoiding NAS for their child. However, the likelihood of continued abstinence without maintenance treatment is not very high in oral prescription opioid use disorder either (23); hence, the

risks of repeated cycles of intoxication and withdrawal, albeit less severe, do exist with prescription opioids as well. A case can thus be made for maintenance with an opioid agonist to reduce craving and risky use, but these women may not require the intensive (expensive and time-consuming) daily monitoring mandated by law for methadone maintenance.

Buprenorphine maintenance: the practical choice for pregnant prescription opioid addicts

Buprenorphine appears to be a particularly appropriate choice for management of the pregnant prescription opioid addict because it has been approved for office-based maintenance of opioid addiction, thus eliminating barriers associated with daily visits to a methadone clinic. Buprenorphine can be used during pregnancy with little risk to the fetus, and pregnancy outcomes are not significantly different from those obtained with methadone (24). Buprenorphine, a partial mu opioid agonist and kappa opioid antagonist, causes less activation of, and has greater affinity for the mu-opioid receptor than methadone. Additionally, there is less placental transfer of buprenorphine than methadone. These considerations, in theory, should lead to decreased physical dependence of the fetus with buprenorphine and less severe associated NAS upon delivery. The MOTHER study, a randomized controlled trial comparing buprenorphine and methadone exposure during pregnancy, provided some support for these predictions (12). Infants exposed to buprenorphine during gestation were found to spend fewer days in the hospital and required lower morphine doses over a shorter treatment period for NAS than those exposed to methadone, while both opioid agonists were equally well tolerated and effective in decreasing illicit drug use.

Further research is needed to determine the appropriate clinical threshold for opioid prescribing in pregnancy, including opioid agonist maintenance in women who are addicted to prescription opioids and use them only via non-injection routes. This is possibly a different population than that from which most of the existing research guiding treatment is currently available.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

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