Opioid Use Disorder During Pregnancy: The Role of Naltrexone in Decreasing Rates of Neonatal Abstinence Syndrome

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Background

Opioid use disorder (OUD) during pregnancy has been linked with serious negative health outcomes for pregnant women and neonates, including preterm birth, stillbirth, maternal mortality, and neonatal abstinence syndrome (NAS). What is NAS? 1

- Neonatal withdrawal from opioids or other substances that the neonate was exposed to in utero.
- Symptoms commonly include neonatal irritability, temperature dysregulation, poor feeding, failure to thrive, and in some cases seizures.
- Affected neonates may show signs and symptoms of withdrawal for up to 10 weeks and are often admitted to the NICU for prolonged periods of time.

NAS/NOWS and Maternal Opioid Use Disorder on the Rise Rates per 1000 Hospital Births

- Naltrexone is the third treatment option for nonpregnant patients with OUD, yet it is associated with the poor neonatal outcomes observed in neonates exposed to illicit opioids.
- MAT is the current standard of care for pregnant women, however its safety for both the mother and the neonate is promising.

Opioid Use Disorder Treatment Options

Medication Assisted Treatment (MAT)

- Prevents cravings, but patient maintains opioid dependence.
- Methadone

Agnostic at the mu-opioid receptor.

Buprenorphine

Mixed opioid receptor agonist-antagonist.

Medication Assisted Withdrawal (MAW)

- Prevents cravings and does not produce dependence.
- Naltrexone

Opioid antagonist. *8-7-day opioid free period before start.

Rationale

- MAT is the current standard of care for pregnant women, yet it is associated with the poor neonatal outcomes observed in neonates exposed to illicit opioids.
- Naltrexone is the third treatment option for nonpregnant patients with OUD, yet it is minimally offered as an option for pregnant patients due to insufficient research, risk of relapse and fear of maternal withdrawal.
- This research will help to identify whether NAS is entirely linked to action of opioid agonist treatment or naltrexone.

Limitations

- Sample size and study type. The clinical use of naltrexone during pregnancy is in its infancy and therefore the research is limited to case studies and prospective and retrospective studies. Due to this, cohorts were relatively small and came from single centers. This may have skewed, or biased results based on demographics in the area.

- Randomization. Focusing an individual to alter her medication use based on a randomization arm would be unethical.

Provider Reluctance. Providers practice evidence-based medicine. MAT has been the standard of care for pregnant women with OUD for over 50 years with overall good outcomes for mother and child. There is minimal evidence for use of naltrexone for pregnant women with OUD.

- Of note: Kelty et al. did not control for the concurrent use of other drugs of addiction. Therefore, NAS in the naltrexone exposed neonates may have been a result of other drugs that the mother was taking during gestation as it is a diagnosis of general withdrawal, not just opioid withdrawal.

PICO

In opioid dependent pregnant women, does medically assisted withdrawal with naltrexone result in reduced incidence of neonatal abstinence syndrome and better birth outcomes in comparison to the standard medication assisted treatment with methadone or buprenorphine?

Conclusions

- Overall, these results suggest that if a mother is willing to endure the symptoms of withdrawal for a five-to-seven-day period, naltrexone can lead to lower rates of NAS and better birth outcomes in comparison to opioid agonist treatment.
- Due to the size of the studies and the lack of diversity the research is not yet viable enough to suggest naltrexone as a first line treatment for pregnant women, however it is safer for both the mother and the neonate is promising.

Future Directions

- More information is needed on the long-term effects of withdrawal as gestation as a result of the naltrexone treatment.
- Future research would benefit from a randomized, multicenter study in order to verify patient populations as well as long-term following of the neonate in order to evaluate for later effects of the gestational naltrexone.
- Future studies should also exclude multi drug users in order to make an accurate conclusion on the rates of NAS in naltrexone exposed neonates.

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References


Figure 1: The CDC reported that OUD has risen more than 4 times among pregnant women and neonates, including preterm birth, stillbirth, maternal mortality, and neonatal abstinence syndrome (NAS).

Figure 2: The CDC reported that OUD has risen more than 4 times among pregnant women and neonates, including preterm birth, stillbirth, maternal mortality, and neonatal abstinence syndrome (NAS).

Figure 3: *** p<0.001

Kelty et al. The NAS rate was significantly lower in the naltrexone group than MAT group (0/6 [0%] vs 12/13 [92%];P<0.001)

Kelty et al. The length of hospital stay was significantly lower in the naltrexone group than MAT group (3.2 days vs 10.9 days;P<0.001)

Kelty et al. The length of hospital stay was significantly lower in the naltrexone group than MAT group (5.5 days vs 9.65 days;P<0.01)

Kelty et al. The length of hospital stay was significantly lower in the naltrexone group than MAT group (5.5 days vs 20.8 days;P<0.01)

Kelty et al. The NAS rate was significantly lower in the naltrexone group than MAT group (5/38 [13%] vs 13/32 [41%];P<0.001)

Kelty et al. The NAS rate was significantly lower in the naltrexone group than MAT group (0/5 [0%] vs 12/13 [92%];P<0.001)

Figure 4: *** p<0.001, ** p<0.01

Kelty et al. The length of hospital stay was significantly lower in the naltrexone group than MAT group (5.5 days vs 9.65 days;P<0.01)

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Figure 5: CDC: Strategies for addressing OUD in the Pregnant Woman.