Literature Review

Buprenorphine-Naloxone versus Buprenorphine in Pregnancy

Jeanmarie Roberts

Cummings Graduate Institute for Behavioral Health Studies

Dr. Cara English

September 11, 2022

Literature Review: Buprenorphine-Naloxone versus Buprenorphine in Pregnancy

For the past 20 years, prescribers of buprenorphine-naloxone and buprenorphine were taught that only plain buprenorphine should be used during pregnancy because of risk of spontaneous pregnancy termination and other negative consequences from the naloxone. However, recently we have been told that the naloxone in the combination drug does not cause fetal harm or spontaneous pregnancy termination.

Many pregnant women who are on the combination drug request to be switched to monotherapy, citing the old information. Wanting to offer the latest in evidence-based literature, the question has been posed: should pregnant females with opioid use disorder who are currently taking buprenorphine-naloxone be switched to plain buprenorphine in order to have better pregnancy outcomes? This literature review hopes to answer that question.

Review of the Literature

Perry et al. (2020) studied this exact situation, directly comparing neonatal outcomes in two groups: one taking buprenorphine-naloxone and one taking only buprenorphine. This study was completed in the United States. According to Perry, this is the first study of its kind. What they found was buprenorphine-naloxone was found to not be significantly different from buprenorphine only; this supports a positive reason to use the combination drug in terms of neonatal outcomes, that the combination drug cannot get a person “high” if injected like the monotherapy drug can. It does indicate that there are no more negative results in using the combination therapy rather than the monotherapy. A negative to this study is that it was a small study, using only one study site. One wonders if such a small study can be used for the entire population.

Mullens, et al. (2020) repeated the research done by Perry. It was also completed in the United States. Their primary outcome was the rate of neonatal abstinence syndrome, also studied by the Perry group. The Mullens group found it more favorable to use the combination drug, citing less neonatal abstinence syndrome than in the monotherapy drug, although a hypothesis of what caused this outcome was not given. Like Perry, all other measures were about equal, thus giving credence to using the combination therapy during pregnancy. And of course, diversion is more difficult with the combination product. This was also a small study, but it did come up with the same findings as in the Perry study. So far, this seems to be answering the hypothesis question positively.

In trying to find more information regarding buprenorphine-naloxone versus buprenorphine alone in pregnancy, many studies looked at one or the other against another medication; generally methadone. In the study completed by Nechanska et al. (2018), it combined the two drugs and then looked at them against methadone. This was done in the Czech Republic and Norway with approximately 550 participants. They did not differentiate between the combination drug and monotherapy in any of the outcomes. Methadone is the gold standard for use in pregnancy and in neonates that have neonatal abstinence syndrome. What these researchers found was that there was no statistical difference between the two groups. But there were also no differences found between the combination buprenorphine-naloxone and the monotherapy buprenorphine. This adds weight to the answer of plain buprenorphine not being any better than the combination drug in treating OUD during pregnancy and with similar neonatal outcomes.

Link et. al. (2020) looked pecifically at the use of the combination drug in pregnancy through a systematic review and meta-analysis. This study was done in the United States. They

compared the combination drug to any other form of medication assisted treatment for opioid use disorder being used in pregnancy in 1,875 mothers and their babies. They concluded what the others are saying: that there is no significant difference in terms of NAS in infants in using the combination drug versus monotherapy. It did show, as others did as well, that neonatal abstinence syndrome was less apparent with the combination drug that with anything else in the study. Another positive vote for using the combination drug during pregnancy.

Finally, Nguyen et al. (2018) looked retrospectively at 26 mothers and their babies in a chart review regarding combination therapy exposure. This study was conducted in the United States. They found what the other researchers found: that there was no statistically significant difference between the two medications in treating prenatal OUD. They also concurred that the rate of neonatal abstinence syndrome was less with the combination product than with any of the other medications they investigated, including the monotherapy product. These researchers also talked about the higher diversion rate of plain buprenorphine. Apparently that is how the reasoning for using monotherapy began. The concern was that if the combination drug was injected, it would cause withdrawal symptoms in both the mother and the baby; however, this is not true.

Analysis

It appears that using buprenorphine-naloxone during pregnancy for opioid use disorder has no more negative effects than buprenorphine, with a decreased risk of diversion. The findings in each of the studies supported the others, and the findings were opposite than expected, having been taught that buprenorphine-naloxone is bad for pregnancy. Not only did that not turn out to be true, but there are other benefits to buprenorphine-naloxone in the way of decreased neonatal abstinence syndrome versus using buprenorphine.

Therefore, using the combination drug to treat OUD in pregnancy should be seen in a new light. There is no evidence that this medication is harmful to the fetus at all, so the research question raised has been definitively answered with a resounding "no." Based on the literature, there is an evidence-based recommendation to use buprenorphine-naloxone to treat OUD in pregnancy, due to its studied benefits to the mother, low risk to the fetus, and low risk of NAS in the newborn.

References

Link, H.M., Jones, H., Miller, L., Kaltenback, K., and Seligman, N. (2020). Buprenorphine-naloxone use in pregnancy: a systematic review and metaanalysis. *American Journal of Obstetrics & Gynecology MFM*. 2 (3). Retrieved from: https://doi.org/10.1016/j.ajogmf.2020.100179.

Mullins, N., Galvin, S.L., Ramage, M., Gannon, M., Lorenz, K., Sager, B., and Coulson, C. (2020). Buprenorphine and naloxone versus buprenorphine for opioid use disorder in pregnancy: a cohort study. *Journal of Addiction Medicine*. 14 (3). P. 185-192.

Nechanska, B., Mravcik, V., Skurtveit, S., Lund, I.O., Gabrhelik, R., Engeland, A., and Handal, M. (2018). Neonatal outcomes after fetal exposure to methadone and buprenorphine: National registry studies from the Czech Republic and Norway. *Society for the Study of Addiction*. 113. P. 1286-1294.

Nguyen, L., Lander, L.R., O'Grady, K.E., Marshalek, P.J., Schmidt, A., Kelly, A.K., and Jones, H.E. (2018). Brief report: treating women with opioid use disorder during pregnancy in Appalachia: initial neonatal outcomes following buprenorphine + naloxone exposure. *American Academy of Addiction Psychiatry*. 27. P. 92-96.

Perry, B.N., Vais, S., Miller, M., and Saia, K.A. (2020). Buprenorphine-naloxone versus Buprenorphine for treatment of opioid use disorder in pregnancy. *Obstetrics &*

Gynecology. 135. P.51S.