PCSS Guidance

Topic: Pregnancy and buprenorphine treatment.

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Guideline coverage:
This topic is also addressed in:
1) TIP 43: Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs, chapter 13, SAMHSA/CSAT, 2005.
2) TIP 40: Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction, pp.68-70.

http://www.kap.samhsa.gov/products/manuals/tips/numerical.htm

Clinical questions:
1) If a female patient of child-bearing age is requesting buprenorphine treatment, what should I do? (i.e. informed consent, birth control, etc)
2) If a patient is already on buprenorphine, should I keep her on it during a pregnancy?
3) Does it matter whether she is given the mono (buprenorphine) or combo (buprenorphine/naloxone) product?
4) If a new opioid dependent patient is pregnant and requests buprenorphine treatment, what should I do?
5) Is buprenorphine treatment during pregnancy safe?
6) How can detoxification (medically supervised withdrawal) be carried out if a pregnant patient wants to stop all opioids, including buprenorphine?
7) How does buprenorphine treatment compare with methadone treatment for pregnant women?
8) Does treatment of pregnant women change depending on whether the patient abuses heroin or prescription opioids?
9) Is breastfeeding safe while taking buprenorphine?
10) What neonatal withdrawal is expected when mothers take buprenorphine?

Background:
Heroin abuse during pregnancy is often closely associated with a multitude of environmental factors that can contribute to adverse consequences including fetal growth restriction, premature labor, miscarriage and low birth weight, an important risk factor for later developmental delay. Methadone maintenance has been the treatment of choice for opioid dependent women since the 1970s, and

given in the context of comprehensive care improves outcomes compared to heroin. Prenatal methadone exposure may result in a neonatal withdrawal syndrome (sometimes called neonatal abstinence syndrome). This withdrawal syndrome is a generalized disorder characterized by signs and symptoms indicating dysfunction of the autonomic nervous system, gastrointestinal tract and respiratory system.[1] With appropriate intervention, withdrawal signs can be alleviated without damaging consequences. If a withdrawal syndrome occurs, it typically, peaks at three days after birth, and even in carefully managed patients on split dosing requires treatment in over 40 percent of cases.[2] There are case studies showing that buprenorphine is safe and effective.[3,4] A large non-randomized observational prospective study comparing methadone and buprenorphine showed similar neonatal outcomes with both medications.[5]

There are two small randomized, double-blind study comparing methadone to buprenorphine, showing comparable, or slightly better neonatal outcomes with buprenorphine.[6,7] There is a multi-site study in progress based on these results. The case reports and prospective studies of women maintained on buprenorphine indicate that neonatal withdrawal occurs in over half of the infants, peaking at roughly 72 hours after birth. Percentages requiring treatment are similar to methadone maintenance studies, between 40-55 percent. There are no specific studies examining maternal and neonatal outcomes following buprenorphine treatment during pregnancy using women who were dependent on prescription opioids.

Buprenorphine is pregnancy category C, because of limited data in humans. Physicians should use buprenorphine in pregnancy using a risk/benefit analysis, informing the patient about the still unproven status of buprenorphine treatment. Methadone is also a pregnancy category C medication, although with longer clinical use, and methadone maintenance is the current standard of care in the US. Repeated episodes of fetal withdrawal are considered harmful, hence tapering or detoxification is relatively contraindicated. Breastfeeding while in treatment with buprenorphine is likely safe, due to its known poor oral bioavailability, in spite of the package insert statement that it is not recommended.

Recommendations: Level of evidence: Low -based on case studies and two limited controlled trials

Pregnant patients should be offered methadone maintenance when available. If they refuse, or if methadone maintenance is not available, they should be informed that buprenorphine is not a proven treatment during pregnancy, and the clinician should get the patient's signature documenting her refusal of methadone maintenance and her understanding of the unproven status of buprenorphine treatment during pregnancy. Pregnant opioid-dependent women should be co-managed with an obstetrician familiar with high-risk pregnancy and neonatal withdrawal treatment.

If a patient is taking buprenorphine during pregnancy, every effort should be made to prevent fetal withdrawal. The way to do this is to prevent maternal withdrawal by encouraging regular and adequate dosing, and by discouraging tapers. Surrogate markers for fetal withdrawal are maternal withdrawal, including craving, and increase in fetal motion.

If a patient absolutely refuses maintenance and desires medically supervised withdrawal, this should be carried out in collaboration with obstetric care, if possible with fetal monitoring. It is thought that the second trimester is the safest time to carry out MSW in order to avoid miscarriage or premature labor.

If the patient is being maintained on buprenorphine during pregnancy, most experts recommend that she be given the mono product. In the case of unstable patients, smaller prescriptions, observed dosing, or more frequent visits are recommended, to avoid injection abuse of the mono product.

Most experts recommend breastfeeding for mothers who are on buprenorphine.

References:

1. Finnegan, L.P., Kaltenbach, K., 1992. Neonatal abstinence syndrome. In: Hoekelman, R.A., Nelson, N.M. (eds), Primary Pediatric Care. 2nd ed. Mosby Yearbook, Inc., St Louis, pp 1367-1378.

2. McCarthy, J., M. Leamon, et al. (2005). "High-dose methadone maintenance in pregnancy: maternal and neonatal outcomes." American Journal of Obstetrics and Gynecology 193(3 Pt 1): 606-610.

3. Johnson, R., H. Jones, et al. (2003). "Use of buprenorphine in pregnancy: patient management and effects on the neonate." Drug and Alcohol Dependence 70 (2 Suppl): S87-S101.

4. Lacroix, L., C. Berrebi, et al. (2004). "Buprenorphine in pregnant opioid-dependent women: first results of a prospective study." Addiction 99: 209-214.

5. Lejeune C, Simmat-Durand L, Gourarier L, Aubisson S; the Groupe d'Etudes Grossesse et Addictions (GEGA). Prospective multicenter observational study of 260 infants born to 259 opiate-dependent mothers on methadone or high-dose buprenophine substitution. Drug Alcohol Depend. 2005 Oct 26;

6. Jones, H., R. Johnson, et al. (2005). "Buprenorphine versus methadone in the treatment of pregnant opioid-dependent patients: effects on the neonatal abstinence syndrome." Drug and Alcohol Dependence 79(1): 1-10.

7. Fischer G, Ortner R, Rohrmeister K, Jagsch R, Baewert A, Langer M, Aschauer H. Methadone versus buprenorphine in pregnant addicts: a double-blind, double-dummy comparison study. Addiction. 2006 Feb;101(2):275-81.

Additional references:

Connaughton, J. J., D. Reeser, et al. (1977). "Perinatal addiction: outcome and management." American Journal of Obstetrics and Gynecology 129(6): 679-686.

Finnegan, L., D. Reeser, et al. (1977). "The effects of maternal drug dependence on neonatal mortality." Drug and Alcohol Dependence 2(2): 131-140.

Kaltenbach, K. and L. Finnegan (1987). "Perinatal and developmental outcome of infants exposed to methadone in-utero." Neurotoxicol Teratol 9(4): 311-313.

Kandall, S., S. Albin, et al. (1977). "The narcotic-dependent mother: fetal and neonatal consequences." Early Human Development 1(2): 159-169.

PCSS Guidances use the following levels of evidence*:
High = Further research is very unlikely to change our confidence in the estimate of effect.
Moderate = Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low = Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low = Any estimate of effect is very uncertain.

Type of evidence:
Randomized trial = **high**
Observational study = **low**
Any other evidence = **very low**

* Grading quality of evidence and strength of recommendations
British Medical Journal, 2004;328;1490-