

Opioid agonist treatment during pregnancy: review of methadone and buprenorphine

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Session description:

Opioid misuse and addiction have been a public health concern since the 1990s. This workshop will focus on the management of opioid use disorders during pregnancy. The prevalence and effects of perinatal opioid use will be reviewed. This will be followed by pregnancy-specific recommendations for the use of opioid agonists. Finally, best practice recommendations for the management of the opioid-exposed infant will also be reviewed.

Learning Objectives:

1. To review the prevalence of perinatal opioid use disorders.
2. To discuss the effects of perinatal opioid use.
3. To describe an approach to the comprehensive management of opioid use disorders in pregnancy.
4. To review benefits and risks of opioid agonist treatment during pregnancy.
5. To describe pregnancy-specific recommendations for the use of methadone and buprenorphine.
6. To review best practice recommendations for the management of the opioid-exposed infant.

Synopsis of workshop

Opioid misuse and addiction have been a growing public health concern since the 1990s. Opioids include all substances derived from the poppy such as morphine and codeine as well as, synthetic opioids such as heroin, oxycodone, hydromorphone, and methadone.

PREVALENCE

In Canada, the use of opioids has also reached concerning levels. National population surveys found that up to 2% of Canadian adults report abusing opioids in 2015. Specifically, Ontario has the highest rate of opioid use in Canada, and has one of the highest prescription opioid uses in the world. Provincial surveys have reported that past year nonmedical use of prescription opioids was up to 4% in Ontario.

Data on opioid use during pregnancy is more limited. Canadian estimates stem from the Canadian Maternity Experiences Survey which found that 7% of women reported street drug use in the 3 months prior to pregnancy which was then reduced to 1% once aware of pregnancy. More data is available from the USA based on the National Survey on Drug Use and Health survey which reported that up to 2% of pregnant women used prescription opioids and heroin in the past 30 days.

EFFECTS

The risks of opioid use disorder during pregnancy include both obstetrical and neonatal complications. Negative pregnancy outcomes are related to the recurrent cycles of opioid highs and lows and consist of miscarriage, growth restriction, premature labour and even neonatal death. Newborns exposed to opioids in utero are at risk of having withdrawal in the immediate post delivery period. These effects may be compounded by concomitant polysubstance use, mental health disorders and social stressors.

MANAGEMENT OF OPIOID USE DISORDERS DURING PREGNANCY

Pregnant women with opioid use disorders face numerous barriers to treatment including personal, system and societal barriers. Pregnancy represents a window of opportunity - a moment when women are more likely to access long-term substance abuse treatment programs such as methadone maintenance program.

Comprehensive care consisting of integrated obstetrical and addictions care along with social services represents an optimal method of managing pregnant substance-using women. The standard of care for opioid use disorder during pregnancy is opioid agonist treatment (OAT) with either methadone or buprenorphine since the benefits of OAT outweighs any associated risks. Several studies have shown that OAT leads to improved maternal and neonatal outcomes including reducing the risk of newborn withdrawal also known as neonatal abstinence syndrome (NAS). Based on these recent findings, methadone and buprenorphine are both effective for managing opioid addiction and there is promising evidence that buprenorphine may reduce the overall severity of NAS. Therefore, methadone and buprenorphine may be offered for opioid use disorders during pregnancy after a discussion about its benefits and risks. Geographic variations in availability of opioid agonist treatments will determine which agent will be used for pregnant women.

The safety of buprenorphine-naloxone combination product during pregnancy is uncertain. To date, there are only a few published reports. Preliminary findings indicate that infants were born at term with normal birth parameters and no birth defects. The rate of NAS was comparable to the rate seen with buprenorphine monoproduct.

NEONATAL ABSTINENCE SYNDROME (NAS)

NAS occurs when infants are no longer exposed to any opioids. NAS is a constellation of symptoms and signs such as neurological, gastrointestinal and autonomic system dysfunction. Signs include increased muscle tone, tremor, high-pitched cry, poor feeding, poor weight gain, diarrhea, temperature instability, nasal stuffiness and irritability. Seizures have also been described in newborns.

The onset of clinical symptoms depends on the duration of action of each particular opioid. For example, with methadone or buprenorphine, withdrawal symptoms and signs commence around 48 – 72 hours of age with late presentations up to 5-7 days after birth. There is evidence that the severity of NAS is not related to mother's dose of medication; therefore, women can be reassured to continue on the required dose of either medication during pregnancy.

SUMMARY RECOMMENDATIONS

1. Management of substance use during pregnancy consists of comprehensive care including obstetrical, addiction and psychosocial supports. Interventions should address the cluster of risks and include inter-professional collaboration.
2. The standard of care for opioid use disorders during pregnancy is opioid agonist treatment with methadone or buprenorphine.
3. Women who become pregnant while on methadone should continue on MMT and should not switch to buprenorphine due to the risk of opioid withdrawal.
4. Women who become pregnant while on buprenorphine/naloxone should be switched to buprenorphine monoprodut. The buprenorphine/naloxone combination product should be continued until the monoprodut becomes available.
5. Infants who are exposed to opioids in utero require observation and possible treatment for neonatal abstinence syndrome.
6. Substance-exposed children should be monitored for growth and development.

REFERENCES

1. World Health Organization. Guidelines for the identification and management of substance use and substance disorders in pregnancy. Geneva: WHO; 2014.
2. College of Physicians and Surgeons of Ontario. Methadone maintenance treatment: Program Standards and Clinical Guidelines. 4th Edn. Toronto: CPSO; 2011.
3. Jones HE, Kaltenbach K, Heil SH, Stine SM, Coyle MG, Arria AM, et al. Neonatal abstinence syndrome after methadone or buprenorphine exposure. *NEJM* 2010; 363(24): 2320-2331.
4. Minozzi S, Amato L, Bellisario C, Ferri M, Davoli M. Maintenance agonist treatments for opiate-dependent pregnant women. *Cochrane Database of Systematic Review* 2013, Issue 12. Art. No.: CD006318. DOI: 10.1002/14651858.CD006318.pub3.
5. Brogly SB, Saia KA, Walley AY, Du HM and Sebastiani P. Prenatal buprenorphine versus methadone exposure and neonatal outcomes: systematic review and meta-analysis. *Am J Epidemiol* 2014; 180(7): 673-686.
6. Debelak K, Morrone WR, O'Grady KE, Jones HE. Buprenorphine + naloxone in the treatment of opioid dependence during pregnancy – Initial patient care and outcome data. *American Journal on Addictions* 2013; 22: 252-254.
7. Wiegand SL, Stringer EM, Stuebe AM, Jones H, Seashore C, Thorp J. Buprenorphine and naloxone compared with methadone treatment in pregnancy. *Obstetrics & Gynecology* 2015; 125(2): 363-368.
8. Dooley J, Gerber-Finn L, Antone I, Guilfoyle J, Blakelock B, Balfour-Boehm J, et al. Buprenorphine-naloxone use in pregnancy for treatment of opioid dependence Restrospective cohort study of 30 patients. *Canadian Family Physician* 2016; 62: e194-e200.
9. Pritham UA. Breastfeeding promotion for management of neonatal abstinence syndrome. *JOGNN* 2013; 42: 517-526.
10. Welle-Strand GK, Skurtveit S, Jansson LM, Bakstad B, Bjarkø L, Ravndal E. Breastfeeding reduces the need for withdrawal treatment in opioid-exposed infants. *Acta Paediatr.* 2013;102(11):1060-1066.
11. O'Connor AB, Collett A, Alto WA, O'Brien LM. Breastfeeding rates and the relationship between breastfeeding and neonatal abstinence syndrome in women maintained on buprenorphine during pregnancy. *Journal of Midwifery & Women's Health* 2013; 58: 383-388.
12. Provincial Council for Maternal and Child Health. Neonatal abstinence syndrome clinical practice guidelines. Revised 2016. www.pcmch.on.ca