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Maintenance treatments for opiate-dependent pregnant women

Oxytocin injected into a vein or muscle for reducing blood loss after vaginal birth

Maintenance treatments for opiate-dependent pregnant women

Authors: Minozzi S, Amato L, Jahanfar S, Bellisario C, Ferri M, Davoli M

Review question

This review summarised research studies comparing different types of pharmacologic maintenance treatments for pregnant women with opioid dependence

Key messages:

Methadone and buprenorphine may be substantially similar in efficacy and safety for the treatment of opioid-dependent pregnant women and their babies. There is not enough evidence to make conclusions for the comparison between methadone and slow-release morphine. Overall, the body of evidence is too small to make firm conclusions.

Background

Some women continue to use opiates when they are pregnant, yet heroin readily crosses the placenta. Opiate-dependent women experience a sixfold increase in maternal obstetric complications and may give birth to low-weight babies. The newborn may experience narcotic withdrawal (neonatal abstinence syndrome) and have development problems. There is also increased neonatal mortality and a 74-fold increase in the risk of sudden infant death syndrome. Maintenance treatment with methadone provides a steady concentration of opiate in the pregnant woman's blood, and so prevents the adverse effects on the fetus of repeated withdrawals. Buprenorphine is also used.

Search date

The evidence is current to 18 February 2020.

Study characteristics

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Only four randomised controlled trials with 271 participants satisfied the inclusion criteria for the review: two from Austria (outpatients), one from the USA (inpatients) and the fourth a multicentre, international study conducted in Austria, Canada and the USA. The trials continued for 15 to 18 weeks. Three compared methadone with buprenorphine (223 participants) and one compared methadone with oral slow-release morphine (48 participants).

Study funding sources

The National Institute on Drug Abuse funded two studies, one received a grant from the Mayor of Vienna, and in the fourth study Schering Plough provided an educational grant to the first author to employ personnel required to conduct this study.

Key results

This review found few differences in newborn or maternal outcomes for pregnant, opiate-addicted women who were maintained on methadone, buprenorphine or oral slow-release morphine from a mean gestational age of 23 weeks to delivery.

Comparing methadone with buprenorphine, there is probably little or no difference in the number of women who dropped out of treatment. There may be little or no difference in the use of a primary substance and the number of newborns treated for neonatal abstinence syndrome between the methadone and buprenorphine groups. We are very uncertain whether newborns with mothers receiving buprenorphine could have a heavier birth weight.

Comparing methadone with oral slow-release morphine, there were no dropouts in the only study included. The use of heroin in the third trimester may be lower with slow-release morphine. However, there may be little or no difference in infant birth weight or duration of neonatal abstinence syndrome.

The number of participants in the trials was small and may not be sufficient to draw firm conclusions. All the included studies ended immediately after the baby was born. No severe complications were noted.

Quality of evidence

In the comparison of methadone with buprenorphine, the quality of the evidence ranged from moderate to very low because of inconsistency in the results of the studies for some outcomes, high rates of participants who dropped out from the studies, and small sample sizes of the included studies. In the comparison of methadone with slow-release morphine, the quality of the evidence was low because of the small sample size of the study.

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Oxytocin injected into a vein or muscle for reducing blood loss after vaginal birth

Authors: Oladapo OT, Okusanya BO, Abalos E, Gallos ID, Papadopoulou A

We set out to look for evidence from randomised controlled trials on the effectiveness and safety of oxytocin injected into a vein, compared with injection into muscle, to prevent excessive bleeding immediately after vaginal birth.

What is the issue?

Most maternal deaths occur within the first 24 hours after delivery. Up to one-fourth of them are caused by excessive bleeding (called postpartum haemorrhage). In low-income countries, drugs to prevent or treat postpartum haemorrhage (uterotonics) are not always available. Oxytocin is one such drug. Oxytocin prevents excessive postpartum bleeding by helping the uterus to contract. It is given to the mother by injection into a vein or into muscle during or immediately after the birth of her baby.

Why is this important?

Blood loss after the birth of the baby depends on how quickly the placenta separates from the uterus and how well the uterus contracts to close the blood vessels that carried blood to the placenta.

Oxytocin given directly into a vein has an almost immediate effect which lasts for a relatively short time. When injected into muscle, oxytocin takes a few minutes to act, but the effect is longer-lasting. Giving injections into a vein requires special skills and sterile equipment that may not always be available. In contrast, injection into muscle is quick and requires relatively less skill.

Oxytocin injected into a vein may sometimes cause serious side effects, such as a sudden drop in blood pressure, especially when given rapidly in a small amount of solution (undiluted).

What evidence did we find?

We searched for evidence from randomised controlled trials on 19 December 2019 and identified seven studies (involving 7817 women). The studies compared oxytocin injected into a vein with injection into muscle during or immediately after the vaginal birth of the baby. All studies were conducted in hospitals and mostly recruited women giving birth vaginally to one baby at term. In all but two studies, both women and hospital staff were aware of how the oxytocin was given. This may have had an impact on results. Overall, the included studies were at moderate or low risk of bias, and the certainty of the generated evidence was generally moderate to high.

We found that women receiving oxytocin through a vein were at lower risk for blood loss of 500 mL or more (six trials; 7731 women) and blood transfusion (four trials; 6684 women) compared with women receiving oxytocin into muscle. There was high-certainty evidence for both of these outcomes. The administration of oxytocin through a vein probably reduced the risk for severe blood loss of 1000 mL or more, compared with oxytocin

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into muscle (four trials; 6681 women; moderate-certainty evidence). The two highest-quality studies (1512 women) found that oxytocin injection into a vein reduced the risk for blood loss of 1000 mL or more, compared with oxytocin injection into muscle. Although the two ways of giving oxytocin may have been similar in terms of women requiring additional medications to contract the uterus, we have little confidence in these results (six trials; 7327 women; low-certainty evidence). Both routes of oxytocin were safe with probably same number of women experiencing side effects, including low blood pressure (four trials; 6468 women; moderate-certainty evidence). Probably fewer women receiving oxytocin through a vein experienced serious complications related to excessive bleeding, such as admission to intensive care, loss of consciousness, or organ failure (four trials; 7028 women; moderate-certainty evidence). No mother died in any of the included studies.

The studies did not report on women's and health personnel's satisfaction with either route of oxytocin administration.

What does this mean?

Oxytocin is more effective when given through a vein than oxytocin injected into muscle for preventing excessive bleeding soon after vaginal birth. Giving oxytocin into a vein did not cause additional safety concerns and had similar side effects compared with oxytocin injected into muscle. Future studies need to consider the acceptability of the two different ways of giving oxytocin to women and healthcare providers as important study outcomes. It is also important to investigate whether the benefits of giving oxytocin into a vein outweigh the higher cost.

If you have any questions or comments with regard to the above document please feel free to contact me.

Kind regards

Dr Vanessa Jordan PhD

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