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[Intervention Review]

Maintenance agonist treatments for opiate-dependent pregnant women

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ABSTRACT

Background

The prevalence of opiate use among pregnant women can range from 1% to 2% to as high as 21%. Heroin crosses the placenta and pregnant, opiate-dependent women experience a six-fold increase in maternal obstetric complications such as low birth weight, toxaemia, third trimester bleeding, malpresentation, puerperal morbidity, fetal distress and meconium aspiration. Neonatal complications include narcotic withdrawal, postnatal growth deficiency, microcephaly, neuro-behavioural problems, increased neonatal mortality and a 74-fold increase in sudden infant death syndrome.

Objectives

To assess the effectiveness of any maintenance treatment alone or in combination with psychosocial intervention compared to no intervention, other pharmacological intervention or psychosocial interventions for child health status, neonatal mortality, retaining pregnant women in treatment and reducing the use of substances.

Search methods

We searched the Cochrane Drugs and Alcohol Group Trials Register (September 2013), PubMed (1966 to September 2013), CINAHL (1982 to September 2013), reference lists of relevant papers, sources of ongoing trials, conference proceedings and national focal points for drug research. We contacted authors of included studies and experts in the field.

Selection criteria

Randomised controlled trials assessing the efficacy of any maintenance pharmacological treatment for opiate-dependent pregnant women.

Data collection and analysis

We used the standard methodological procedures expected by The Cochrane Collaboration.

Main results

We found four trials with 271 pregnant women. Three compared methadone with buprenorphine and one methadone with oral slow-release morphine. Three out of four studies had adequate allocation concealment and were double-blind. The major flaw in the included studies was attrition bias: three out of four had a high drop-out rate (30% to 40%) and this was unbalanced between groups.

Methadone versus buprenorphine: the drop-out rate from treatment was lower in the methadone group (risk ratio (RR) 0.64, 95% confidence interval (CI) 0.41 to 1.01, three studies, 223 participants). There was no statistically significant difference in the use of primary substance between methadone and buprenorphine (RR 1.81, 95% CI 0.70 to 4.69, two studies, 151 participants). For both, we judged the quality of evidence as low. Birth weight was higher in the buprenorphine group in the two trials that could be pooled (mean difference (MD) -365.45 g (95% CI -673.84 to -57.07), two studies, 150 participants). The third study reported that there was no statistically significant difference. For APGAR score neither of the studies which compared methadone with buprenorphine found a significant difference. For both, we judged the quality of evidence as low. Many measures were used in the studies to assess neonatal abstinence syndrome. The number of newborns treated for neonatal abstinence syndrome, which is the most critical outcome, did not differ significantly between groups. We judged the quality of evidence as very low.

Methadone versus slow-release morphine: there was no drop-out in either treatment group. Oral slow-release morphine seemed superior to methadone for abstinence from heroin use during pregnancy (RR 2.40, 95% CI 1.00 to 5.77, one study, 48 participants). We judged the quality of evidence as moderate.

Only one study which compared methadone with buprenorphine reported side effects. For the mother there was no statistically significant difference; for the newborns in the buprenorphine group there were significantly fewer serious side effects.

In the comparison between methadone and slow-release morphine no side effects were reported for the mother, whereas one child in the methadone group had central apnoea and one child in the morphine group had obstructive apnoea.

Authors' conclusions

We did not find sufficient significant differences between methadone and buprenorphine or slow-release morphineto allow us to conclude that one treatment is superior to another for all relevant outcomes. While methadone seems superior in terms of retaining patients in treatment, buprenorphine seems to lead to less severe neonatal abstinence syndrome. Additionally, even though a multi-centre, international trial with 175 pregnant women has recently been completed and its results published and included in this review, the body of evidence is still too small to draw firm conclusions about the equivalence of the treatments compared. There is still a need for randomised controlled trials of adequate sample size comparing different maintenance treatments.

PLAIN LANGUAGE SUMMARY

Maintenance treatments for opiate-dependent pregnant women

Some women continue to use opiates when they are pregnant, yet heroin readily crosses the placenta. Opiate-dependent women experience a six-fold increase in maternal obstetric complications and 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. These treatments reduce illicit drug use, improve compliance with obstetric care and improve neonatal birth weight but they are still associated with neonatal abstinence syndrome.

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. Only four randomised controlled trials with 271 participants trials satisfied the inclusion criteria for the review: two from Austria (outpatients), one from the USA (inpatients) and the fourth a multi-centre, 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). The number of women who dropped out from treatment was lower in the methadone group. However, there was no difference in the use of primary substance between the methadone and buprenorphine groups. The number of newborns treated for neonatal abstinence syndrome did not differ significantly between groups. Birth weight was higher in the buprenorphine group in two trials and no different in the third. Oral slow-release morphine seemed superior to methadone in terms

of the number of women who used heroin in their third trimester. However, there was no clear improvement 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.