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[Intervention Review]

Prophylactic use of ergot alkaloids in the third stage of labour

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ABSTRACT

Background

Previous research has shown that the prophylactic use of uterotonic agents in the third stage of labour reduces postpartum blood loss and moderate to severe postpartum haemorrhage (PPH). PPH is defined as a blood loss of 500 mL or more within 24 hours after birth. This is one of a series of systematic reviews assessing the effects of prophylactic use of uterotonic drugs; in this review prophylactic ergot alkaloids as a whole, and different regimens of administration of ergot alkaloids, are compared with no uterotonic agents. This is an update of a Cochrane Review which was first published in 2007 and last updated in 2011.

Objectives

To determine the effectiveness and safety of prophylactic use of ergot alkaloids in the third stage of labour by any route (intravenous (IV), intramuscular (IM), or oral) compared with no uterotonic agents, for the prevention of PPH.

Search methods

For this update, we searched the Cochrane Pregnancy and Childbirth Group's Trials Register, ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP) (19 September 2017); we also searched reference lists of retrieved studies.

Selection criteria

We included all randomised controlled trials or cluster-randomised trials comparing prophylactic ergot alkaloids by any route (IV, IM, or oral) with no uterotonic agents in the third stage of labour among women giving birth vaginally.

Data collection and analysis

Two review authors independently assessed trials for inclusion, extracted data and checked them for accuracy; they also assessed the risk of bias in included studies. Two review authors assessed the quality of the evidence using the GRADE approach.

Main results

There were eight included studies: three studies had a low risk of bias and five studies had high risk of bias. The studies compared ergot alkaloids with no uterotonic agents, with a total of 2031 women in the ergot alkaloids group and 1978 women in the placebo or no treatment group. Seven studies used the IV/IM route of administration and one study used the oral route.

Ergot alkaloids (any route of administration) versus no uterotonic agents

Use of ergot alkaloids in the third stage of labour decreased mean blood loss (mean difference (MD) -80.52 mL, 95% confidence interval (CI) -96.39 to -64.65 mL; women = 2718; studies = 3; moderate-quality evidence); decreased PPH of at least 500 mL (average risk ratio (RR) 0.52,

95% CI 0.28 to 0.94; women = 3708; studies = 5; $I^2 = 83\%$; low-quality evidence); increased maternal haemoglobin concentration (g/dL) at 24 to 48 hours postpartum (MD 0.50 g/dL, 95% CI 0.38 to 0.62; women = 1429; studies = 1; moderate-quality evidence); and decreased the use of therapeutic uterotonics (average RR 0.37, 95% CI 0.15 to 0.90; women = 2698; studies = 3; $I^2 = 89\%$; low-quality evidence). There were no clear differences between groups in severe PPH of at least 1000 mL (average RR 0.32, 95% CI 0.04 to 2.59; women = 1718; studies = 2; $I^2 = 74\%$; very low-quality evidence). The risk of retained placenta or manual removal of the placenta, or both, were inconsistent with high heterogeneity. Ergot alkaloids increased the risk of elevated blood pressure (average RR 2.60, 95% CI 1.03 to 6.57; women = 2559; studies = 3; low-quality evidence) and pain after birth requiring analgesia (RR 2.53, 95% CI 1.34 to 4.78; women = 1429; studies = 1; moderate-quality evidence) but there were no differences between groups in vomiting, nausea, headache or eclamptic fit.

Results for IV/IM ergot alkaloids versus no uterotonic agents were similar to those for the main comparison of ergot alkaloids administered by any route, since most of the studies (seven of eight) used the IV/IM route. Only one small study (289 women) compared oral ergometrine with placebo and it showed no benefit of ergometrine over placebo. No maternal adverse effects were reported.

None of the studies reported on any of our prespecified neonatal outcomes

Authors' conclusions

Prophylactic IM or IV injections of ergot alkaloids may be effective in reducing blood loss, reducing PPH (estimated blood loss of at least 500 mL), and increasing maternal haemoglobin. Ergot alkaloids may also decrease the use of therapeutic uterotonics, but adverse effects may include elevated blood pressure and pain after birth requiring analgesia. There were no differences between groups in terms of other adverse effects (vomiting, nausea, headache or eclamptic fit). There is a lack of evidence on the effects of ergot alkaloids on severe PPH, and retained or manual removal of placenta. There is also a lack of evidence on the oral route of administration of ergot alkaloids.

PLAIN LANGUAGE SUMMARY

Managing the end of childbirth (placenta delivery) with ergot alkaloid medications (e.g. ergometrine)

What is the issue?

The third stage of labour is the period from the birth of the baby to the expulsion of the placenta and membranes. As the placenta separates, there is inevitably some blood loss from the placental site until the muscles of the uterus clamp the blood vessels. Fit, healthy women cope with this normal blood loss without problems, but where poor nutrition, poor sanitation and limited or no access to clinical care are complications of pregnancy, severe morbidity and death can result from excessive blood loss at birth. This is very common in low- and middle-income countries. Active intervention, called 'active management of third stage', is recommended for the third stage of labour to reduce excess blood loss. Active intervention incorporates: 1) the administration of a uterotonic medication (medicine that stimulates contractions), given just before or just after the baby is born to help the muscles of the uterus contract; 2) cord clamping, performed approximately one to three minutes after birth; and 3) the use of controlled cord traction to deliver the placenta in settings where skilled birth attendants are available. This review of studies looked at the use of one group of uterotonic medications called ergot alkaloids (e.g. ergometrine) as part of this active management.

Why is this important?

A previous systematic review showed that the combination of ergometrine and oxytocin was associated with a significantly lower postpartum haemorrhage (PPH) rate (defined as blood loss of at least 500 mL) but a greater incidence of side-effects compared to the use of oxytocin alone. However, there was no review comparing ergometrine with no uterotonic medications and different routes or timings of administration for the prevention of PPH.

What evidence did we find?

We searched for evidence in September 2017 and included eight trials involving 4009 women receiving ergometrine by mouth (orally), into the muscle (intramuscularly (IM)) or into the vein (intravenously (IV)). Of eight trials, seven included studies were analysed in this updated review.

The evidence from the trials analysed suggests that ergot alkaloids may decrease mean blood loss, increase maternal haemoglobin levels in the blood, and may decrease both blood loss of at least 500 mL (PPH) and the use of therapeutic uterotonics. It is uncertain whether ergot alkaloids have any effect on numbers of women experiencing high blood loss of at least 1000 mL (severe PPH). The evidence also suggested that they may increase adverse effects such as increased blood pressure and pain after birth. They may make little or no difference between groups in terms of other adverse effects (vomiting, nausea, headache or eclamptic fit) and results were inconsistent on the risk of retained or manual removal of placenta. Most of the evidence came from trials that administered ergot alkaloids using the IM or IV route. There was only one small trial that looked at the use of oral ergot alkaloids and results were inconclusive. There were limited numbers of included studies and results between studies were not always consistent or precise. Overall quality of evidence across critical and important outcomes ranged from very low to moderate.

What does this mean?

The IV or IM route, although it may reduce blood loss and PPH, was associated with the adverse effects of raised blood pressure and pain due to contractions of the uterus. There was not enough evidence on the oral route of administering ergot alkaloids. There are other medications, namely oxytocin, syntometrine and prostaglandins (which are assessed in other Cochrane Reviews), that can be used and may be preferable.