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[Intervention Review]

Prophylactic oxytocin for the third stage of labour to prevent postpartum haemorrhage

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ABSTRACT

Background

Active management of the third stage of labour has been shown to reduce the risk of postpartum haemorrhage (PPH) greater than 1000 mL. One aspect of the active management protocol is the administration of prophylactic uterotonics, however, the type of uterotonic, dose, and route of administration vary across the globe and may have an impact on maternal outcomes.

Objectives

To determine the effectiveness of prophylactic oxytocin at any dose to prevent PPH and other adverse maternal outcomes related to the third stage of labour.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (31 May 2013).

Selection criteria

Randomised or quasi-randomised controlled trials including pregnant women anticipating a vaginal delivery where prophylactic oxytocin was given during management of the third stage of labour. The primary outcomes were blood loss > 500 mL and the use of therapeutic uterotonics.

Data collection and analysis

Two review authors independently assessed trials for inclusion, assessed trial quality and extracted data. Data were checked for accuracy.

Main results

This updated review included 20 trials (involving 10,806 women).

Prophylactic oxytocin versus placebo

Prophylactic oxytocin compared with placebo reduced the risk of PPH greater than 500 mL, (risk ratio (RR) 0.53; 95% confidence interval (CI) 0.38 to 0.74; six trials, 4203 women; $T^2 = 0.11$, $I^2 = 78\%$) and the need for therapeutic uterotonics (RR 0.56; 95% CI 0.36 to 0.87, four trials, 3174 women; $T^2 = 0.10$, $I^2 = 58\%$). The benefit of prophylactic oxytocin to prevent PPH greater than 500 mL was seen in all subgroups. Decreased use of therapeutic uterotonics was only seen in the following subgroups: randomised trials with low risk of bias (RR 0.58; 95%

CI 0.36 to 0.92; three trials, 3122 women; $T^2 = 0.11$, $I^2 = 69\%$); trials that performed active management of the third stage (RR 0.39; 95% CI 0.26 to 0.58; one trial, 1901 women; heterogeneity not applicable); trials that delivered oxytocin as an IV bolus (RR 0.57; 95% CI 0.39 to 0.82; one trial, 1000 women; heterogeneity not applicable); and in trials that gave oxytocin at a dose of 10 IU (RR 0.48; 95% CI 0.33 to 0.68; two trials, 2901 women; $T^2 = 0.02$, $I^2 = 27\%$).

Prophylactic oxytocin versus ergot alkaloids

Prophylactic oxytocin was superior to ergot alkaloids in preventing PPH greater than 500 mL (RR 0.76; 95% CI 0.61 to 0.94; five trials, 2226 women; $T^2 = 0.00$, $I^2 = 0\%$). The benefit of oxytocin over ergot alkaloids to prevent PPH greater than 500 mL only persisted in the subgroups of quasi-randomised trials (RR 0.71, 95% CI 0.53 to 0.96; three trials, 1402 women; $T^2 = 0.00$, $I^2 = 0\%$) and in trials that performed active management of the third stage of labour (RR 0.58; 95% CI 0.38 to 0.89; two trials, 943 women; $T^2 = 0.00$, $I^2 = 0\%$). Use of prophylactic oxytocin was associated with fewer side effects compared with use of ergot alkaloids; including decreased nausea between delivery of the baby and discharge from the labour ward (RR 0.18; 95% CI 0.06 to 0.53; three trials, 1091 women; $T^2 = 0.41$, $I^2 = 41\%$) and vomiting between delivery of the baby and discharge from the labour ward (RR 0.07; 95% CI 0.02 to 0.25; three trials, 1091 women; $T^2 = 0.45$, $I^2 = 30\%$).

Prophylactic oxytocin + ergometrine versus ergot alkaloids

There was no benefit seen in the combination of oxytocin and ergometrine versus ergometrine alone in preventing PPH greater than 500 mL (RR 0.90; 95% CI 0.34 to 2.41; five trials, 2891 women; $T^2 = 0.89$, $I^2 = 80\%$). The use of oxytocin and ergometrine was associated with increased mean blood loss (MD 61.0 mL; 95% CI 6.00 to 116.00 mL; fixed-effect analysis; one trial, 34 women; heterogeneity not applicable).

In all three comparisons, there was no difference in mean length of the third stage or need for manual removal of the placenta between treatment arms.

Authors' conclusions

Prophylactic oxytocin at any dose decreases both PPH greater than 500 mL and the need for therapeutic uterotonics compared to placebo alone. Taking into account the subgroup analyses from both primary outcomes, to achieve maximal benefit providers may opt to implement a practice of giving prophylactic oxytocin as part of the active management of the third stage of labour at a dose of 10 IU given as an IV bolus. If IV delivery is not possible, IM delivery may be used as this route of delivery did show a benefit to prevent PPH greater than 500 mL and there was a trend to decrease the need for therapeutic uterotonics, albeit not statistically significant.

Prophylactic oxytocin was superior to ergot alkaloids in preventing PPH greater than 500 mL; however, in subgroup analysis this benefit did not persist when only randomised trials with low risk of methodologic bias were analysed. Based on this, there is limited high-quality evidence supporting a benefit of prophylactic oxytocin over ergot alkaloids. However, the use of prophylactic oxytocin was associated with fewer side effects, specifically nausea and vomiting, making oxytocin the more desirable option for routine use to prevent PPH.

There is no evidence of benefit when adding oxytocin to ergometrine compared to ergot alkaloids alone, and there may even be increased harm as one study showed evidence that using the combination was associated with increased mean blood loss compared to ergot alkaloids alone.

Importantly, there is no evidence to suggest that prophylactic oxytocin increases the risk of retained placenta when compared to placebo or ergot alkaloids.

More placebo-controlled, randomised, and double-blinded trials are needed to improve the quality of data used to evaluate the effective dose, timing, and route of administration of prophylactic oxytocin to prevent PPH. In addition, more trials are needed especially, but not only, in low- and middle-income countries to evaluate these interventions in the birth centres that shoulder the majority of the burden of PPH in order to improve maternal morbidity and mortality worldwide.

PLAIN LANGUAGE SUMMARY

Prophylactic oxytocin for the third stage of labour

Prophylactic oxytocin at any dose used routinely after birth can reduce blood loss with fewer side effects than ergot alkaloids.

The third stage of labour is that period from birth of the baby until delivery of the placenta, however, complications can continue to occur once the placenta is removed. The degree of blood loss during this stage depends, among other factors, on how quickly the uterine muscle contracts and the placenta separates from the uterine wall. Postpartum haemorrhage is a major problem, particularly where there is poor nutrition and lack of access to treatment. This review of 20 trials (involving 10,806 women) found that the routine use of prophylactic oxytocin, a drug that helps the uterus contract, may reduce the amount of blood loss during the third stage of labour. Prophylactic oxytocin is better at preventing blood loss compared with ergot alkaloids, however, no further improvement is seen when they were used together. More research is needed, especially in low- and middle-income countries, on the best method to implement this intervention in the third stage for women in all countries, on the dose to use, and the best route for administration (intramuscular or intravenous).