Prostaglandin analogues for postpartum haemorrhage

Objectives:
The objective of this evidence summary is to clarify the evidence base for or against the use of prostaglandin analogues in the treatment of PPH due to uterine atony.

Background:
Postpartum haemorrhage is the single most important cause of maternal death worldwide and one of the major causes of maternal death in developed and developing countries. It is estimated that it causes 125,000 deaths per year, affects 5-15% of women after giving birth and increases morbidity in about 20 Million women undergoing delivery. Prostaglandin analogues are being increasingly used in the treatment of postpartum haemorrhage particularly when atonic uterus is suspected.

Prostaglandin analogues are used to treat postpartum haemorrhage because they induce powerful uterine contractions. RCTs and observational studies have found promising results using prostaglandin analogues in women who continue to bleed after having received first line treatment including traditional uterotonics (oxytocin with or without ergometrine), as well as an add-on treatment to conventional uterotonics. Prostaglandin analogues are generally expensive and they usually require refrigeration and additional sterile equipment for their administration. However, misoprostol is a prostaglandin analogue that is inexpensive, can be stored at room temperature and, can be easily administered (i.e. mouth, vaginal or rectal administration).

Evidence summary:
In immediate postpartum haemorrhage (first 24 hours after delivery):
A Cochrane review (Search date April 2002) assessed the effects of treatments for primary postpartum haemorrhage. It found no RCTs or quasi-randomised trials comparing uterotonics versus no treatment or placebo. The review found one small trial (64 women) comparing syntometrin plus oxytocin infusion versus misoprostol. The trial found that misoprostol reduced the proportion of women with persistent bleeding or needing other medical interventions to control bleeding. However, the study was small and underpowered to determine the effects of treatments in other clinically important outcomes providing insufficient evidence to guide a particular recommendation.

A subsequent RCT (237 women) was also underpowered and failed to establish the benefits and harms associated to the use of misoprostol in women with postpartum haemorrhage.

Two placebo-controlled randomised trials showed reduced measured blood loss of 500 ml or more with misoprostol (Relative Risk (RR) 0.57, 95% confidence interval (CI) 0.34 to 0.96), increased pyrexia (RR 6.40, 95% CI 1.71 to 23.96) and shivering (RR 2.31, 95% CI 1.68 to 3.18), and no significant differences in other substantive outcomes.

In delayed postpartum haemorrhage:
A Cochrane review (Search date January 2004) assessed the effects of treatments in women with secondary (between 24 hours and 12 weeks after delivery) postpartum haemorrhage. It found no RCTs or quasi randomised studies assessing the effects of treatments (including uterotonics) for secondary postpartum haemorrhage.

Observational studies and expert opinion suggest that prostaglandin analogues (i.e. carboprost, dinoprostone, sulprostone and misoprostol) may be useful in treating postpartum haemorrhage. They may have a role as an add-on treatment to conventional uterotonics or
as a last resort when other measures has been unsuccessful or there is no access to traditional oxytocics. Misoprostol, in particular, may have a role in the prevention and treatment of postpartum haemorrhage in situations where parenteral medications are not available, such as home deliveries in isolated areas.\(^{(3)}\)

**Recommendation:**
None of the prostaglandin analogues have been evaluated rigorously to identify benefits and harms in the treatment of PPH. Of these, misoprostol has been evaluated in two RCTs and there seems to be an effect on reducing further blood loss although the evidence regarding substantive outcomes is lacking. The safety of these prostaglandin analogues have not been established conclusively. Misoprostol has been used and evaluated more widely than others and it may be used to treat PPH while we await the results of ongoing research. Adverse events should be carefully monitored and recorded for any prostaglandin analogue used for this purpose.

**References:**


WHO Department of Reproductive Health and Research, 07 February 2005