Misoprostol in preventing postpartum hemorrhage: a meta-analysis

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CRD summary

This review assessed the effectiveness of misoprostol for the prevention of postpartum haemorrhage. The author concluded that conventional uterotonic drugs should not be used to set the lowest accepted level of effectiveness in settings where they are unsuitable. Whilst this was a reasonably well-conducted systematic review, the author's conclusions are not directly based on the findings and, therefore, cannot be verified.

Authors' objectives

The author stated that the objective was to assess the effectiveness of misoprostol for the prevention of postpartum haemorrhage (PPH) in developing countries, where no alternatives exist. However, the review included studies conducted in both developing and developed countries.

Searching

The author searched PubMed, the Cochrane CENTRAL Register and the Population Council's bibliographic website for studies published before May 2005; the search terms were reported. In addition, the reference lists of identified articles were handsearched. The author contacted primary authors in an attempt to identify unpublished studies. No language restrictions were applied.

Study selection

Study designs of evaluations included in the review

Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review

Studies of misoprostol were eligible for inclusion, irrespective of the dose and route of administration (with the exception of vaginal administration). The studies were not restricted by type of control substance. In the included studies, misoprostol was administered orally, rectally or sublingually at doses ranging from 400 to 600 micrograms. The control groups were given methylergometrine, oxytocin, oxytocin and ergometrine or placebo.

Participants included in the review

Studies of women giving birth vaginally during the third trimester of pregnancy were eligible for inclusion. The studies were conducted in England, USA, Canada, Belgium, Switzerland, France, Turkey, India, Hong Kong, South Africa, Mozambique, Zimbabwe, Nigeria and Ghana.

Outcomes assessed in the review

The outcomes of interest were blood loss of 500 mL or more, blood loss of 1,000 mL or more, and the need for additional uterotonic agents.

How were decisions on the relevance of primary studies made?

The author did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality

The studies were assessed for methodological quality based on the following criteria: appropriate research objective; explicit inclusion and exclusion criteria; exclusion of patients with labour augmentation or induction; randomisation method; similarity of the groups at baseline; masking of the attending physician; measurement of blood loss; reporting of all raw data; losses to follow-up; and criteria for the administration of additional uterotonic drugs. Each study was given a score from 0 to 10. The author did not state how the papers were assessed for quality, or how many reviewers performed the quality assessment.

Data extraction

One reviewer extracted the data from each study; the reviewer was not blinded to study details. Data from each study were compiled in 2x2 tables. One study only reported percentages, therefore cell counts were calculated.

Methods of synthesis

How were the studies combined?

For each outcome, a pooled risk ratio (RR) comparing misoprostol with oxytocics or placebo was calculated using the Mantel-Haenszel fixed-effect model. When significant heterogeneity was detected, the DerSimonian and Laird random-effects model was used to pool the outcomes. All doses and routes of administration were pooled together.

Publication bias was assessed using Egger's weighted regression and Begg's rank correlation.

How were differences between studies investigated?

Heterogeneity was assessed using the chi-squared and I-squared tests. Sensitivity analyses were conducted to investigate the influence of individual studies on the summary statistic by omitting each study in turn.

Results of the review

Twenty-two RCTs (n=30,017) were included in the review.

The quality assessment scores ranged from 5 to 9, with most studies scoring 7 or 8.

Misoprostol versus placebo.

Four trials that compared misoprostol with placebo and reported results for blood loss of 1,000 mL or more and one trial that reported results for blood loss of 500 mL or more were pooled. There was no statistically significant difference between the misoprostol and placebo groups (RR 0.85, 95% confidence interval, CI: 0.63, 1.14). There was no significant heterogeneity.

Patients given placebo were statistically significantly more likely to require additional uterotonic agents than those given misoprostol (4 trials; RR 0.69, 95% CI: 0.53, 0.90).

Misoprostol versus oxytocics.

Blood loss of 500 mL or more was statistically significantly greater in the misoprostol group than in the oxytocics group (15 trials; RR 1.40, 95% CI: 1.21, 1.62), representing an excess risk of 5% greater incidence of blood loss. There was slight heterogeneity across the studies; however, the fixed-effect and random-effects estimates were similar.

Blood loss of 1,000 mL or more was also statistically significantly greater in the misoprostol group than in the oxytocics group (11 trials; RR 1.36, 95% CI: 1.19, 1.56), representing an excess risk of 1% greater incidence of severe PPH.

There was no statistically significant difference in the requirement for additional uterotonic agents between patients in the misoprostol group and those in the oxytocics group (17 trials; RR 1.23, 95% CI: 0.93, 1.63). A subgroup analysis of oral and sublingual misoprostol also revealed no statistically significant difference between misoprostol and oxytocics (RR 1.13, 95% CI: 0.81, 1.56).

There was no evidence of significant publication bias for any outcome.

Authors' conclusions

Conventional uterotonic drugs should not be used to set the lowest accepted level of effectiveness in settings where they are entirely unsuitable. Continuing to weigh the benefits of one effective drug against another only delays the distribution of misoprostol in countries where it is the only feasible choice and must be measured against no treatment at all.

CRD commentary

The review question was clear in terms of the study design, participants, interventions and outcomes of interest. The search strategy was fairly limited, although attempts were made to identify unpublished studies, thus reducing the potential for publication bias. Publication bias was assessed and was not found to be significant. No language restrictions were applied, thereby reducing the potential for language bias. The author did not report the processes used for the study selection or quality assessment. Only one reviewer performed the data extraction, thus increasing the potential for reviewer bias and errors. Adequate details of the included studies were presented. The quality of the included studies was assessed using adequate criteria and quality assessment scores were reported. Appropriate measures of effect were calculated and heterogeneity was assessed. Whilst this was a reasonably well-conducted systematic review, the author's conclusions are not directly based on the findings and, therefore, cannot be verified.

Implications of the review for practice and research

The author did not state any implications for practice or further research.

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