Misoprostol for cervical ripening and labor induction: a meta-analysis
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Authors' objectives
To examine the efficacy and perinatal and maternal safety of misoprostol as a cervical ripening and labour induction agent.

Searching
Searches for the years 1986 to 1995 of the Bibliographic Retrieval Service, MEDLINE, Current Contents and Silver Platter were made (search terms given). The reference lists of studies and review articles were screened for further references.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs; comparative and placebo-controlled) were included.

Specific interventions included in the review
The use of misoprostol for cervical ripening and labour induction compared to the use of other prostaglandins, oxytocin or placebo.

Participants included in the review
Pregnant women undergoing cervical ripening and labour induction were included.

Outcomes assessed in the review
Maternal and perinatal outcomes included: the need for oxytocin augmentation, start of induction-to-vaginal delivery interval, incidence of tachysystole and hyperstimulation syndrome, Caesarean rate, proportion of subjects delivered within 24 hours, vaginal delivery within 24 hours of drug application, occurrence of active labour during the ripening period, abnormal Apgar scores and neonatal intensive care unit admission.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The validity of primary studies was evaluated according to the Moher checklist for RCTs (Control Clin Trials 1995; 16:62-73). Each study's methodological attributes were assessed for quality by two investigators, who were blinded to study authorship and institutional affiliation.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were combined statistically to estimate the odds ratio (OR) and risk difference for dichotomous outcomes, using both a random-effects and a fixed-effect model. No substantial difference in results was noted in the results obtained by either method, and only the fixed-effect results are presented. Continuous outcomes were pooled using a variance weighted average of the within-study difference in means between the misoprostol and control groups. The
weight assigned to each study was the inverse of the variance of the difference in means for that study. A fixed-effect model was used for pooling means.

How were differences between studies investigated?
The trials were reviewed to determine their clinical comparability based on their inclusion/exclusion criteria, as well as similarity in misoprostol regimens. Differences between studies were examined using logistic regression analysis, with misoprostol dose and study location as covariates. A chi-square test showed that some heterogeneity was present (P = .069). Following logistic regression analysis, only study location appeared to be a potential source of heterogeneity (OR 1.97, 95% CI 1.30, 2.99).

Results of the review
Eight studies were included, with a total of 966 patients (488 treated with misoprostol and 478 controls).

The results of the analysis demonstrated that women receiving misoprostol had a lower Caesarean rate than controls (15% vs. 21.5%; OR 0.67, 95% CI 0.48, 0.93; P = .02) and were significantly more likely to experience vaginal delivery within 24 hours (OR 2.64, 95% CI 1.87, 3.71). Misoprostol use was associated with a 4.6 hour reduction in the interval from first dose to delivery (all deliveries) (95% CI, -3.5, -5.7; P<.001) and a 5.6 hour reduction in the interval from first dose to vaginal delivery (95% CI, -3.8, -7.5; P=0.028). The incidence of spontaneous labour was significantly higher in the misoprostol group (OR 8.20, 95% CI 5.70, 11.78) and the percentage of women requiring oxytocin administration was significantly lower (OR 0.29, 95% CI 0.21, 0.41).

No differences in the incidence of low 5-minute Apgar scores and admissions to the neonatal intensive care unit were noted between groups. Women receiving misoprostol were significantly more likely than controls to experience tachysystole (OR 2.70, 95% CI 1.80, 4.04), although the incidence of hyperstimulation syndrome (foetal heart rate abnormalities associated with tachysystole) were not significantly different between groups, OR 1.91 (95% CI, 0.98, 3.13).

Authors' conclusions
Published data demonstrate the safety and efficacy of intravaginal misoprostol for cervical ripening and labour induction.

CRD commentary
Overall this is a high quality systematic review. The literature search was well described and fairly comprehensive, although no attempt was made to search for grey literature or unpublished material. However little information on the inclusion and exclusion criteria for the review was presented. Validity assessment of the studies was conducted in a blinded manner by two authors using a recognised quality assessment scale. Details regarding methodological quality and outcomes were presented in table format, although insufficient information was provided regarding the actual interventions used. The data synthesis was conducted in an appropriate manner, using both random-effects and fixed-effect models, and the potential reasons for any differences between studies were investigated statistically.

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Other publications of related interest

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