Prostaglandine E2 par voie vaginale dans les ruptures prematurees des membranes a terme avec col defavorable: meta-analyse [Vaginal administration prostaglandin E2 in premature ruptured membranes at term with an unfavorable cervix]

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Authors' objectives
To compare the immediate induction of labour using vaginal prostaglandins (PG) with either the immediate induction of labour using oxytocin, or expectant management, in women with premature rupture of the membranes at term.

Searching
MEDLINE and the Cochrane Library were searched and the bibliographies of the retrieved papers were examined. Studies published as conference proceedings were also sought.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs), published as full papers or conference abstracts, were included if they reported the following comparisons: the induction of labour using PG versus expectant waiting (8 to 24 hours); and the induction of labour using PG versus induction with oxytocin.

Specific interventions included in the review
Trials of PG given vaginally, as either gel or pessaries, were included. In every case, the preparation used was natural PGE2. Evaluations of PG administered by general or cervical routes, or preparations of PG other than natural PGE2, were excluded. The PG regimens varied across the trials and included the following:

1 mg given as an initial dose and repeated 6 hours later;
1 mg given as an initial dose and repeated 6, 12 and 18 hours later;
1 mg given as an initial dose, followed by 3 mg given 1 hour and 4 hours later;
2 mg as an initial dose followed by 1 mg 6 hours later;
3 mg given as single dose;
two 3 mg doses given 4 hours apart;
two 3 mg doses given 6 hours apart; and
4 mg given as a single dose.

In all the included trials, it was stated that those patients that initially received PG were later given oxytocin if induction by PG failed. The interval between PG failure and oxytocin administration varied between the trials (range: 8 to 24 hours). In patients receiving expectant management, the interval between rupture of membranes and the induction of labour was within the range 8 to 24 hours, where the spontaneous onset of labour had not occurred. In patients receiving oxytocin, the starting dose by infusion varied between 1 and 3 mUI/minute, and increased by 1 to 2.5 mUI/minute every 10 to 30 minutes. The maximum doses, where reported, were either 24 or 56 mUI/minute, depending on the trial. Two trials described the use of antibiotics in cases where the time between the rupture of the membranes and the onset of labour exceeded 12 or 24 hours.

Participants included in the review
Trials recruiting women with premature rupture of membranes after 34 weeks' gestation were included. Cervical status
was assessed using either the Bishop's score or by measuring cervical dilatation. The Bishop's score was determined by vaginal examination, whilst cervical dilatation was determined by either vaginal dilatation or the use of a speculum. All of the included trials recruited women with a singleton pregnancy, cephalic presentation, no previous Caesarean section, and a due date calculated according to the last menstrual period or early ultrasound scan. All of the trials excluded women with the following:

uterine contractions indicating the beginning of labour;

contraindications of induction, due to disproportion between the foetus and pelvis, diabetes, foetal distress, non-cephalic presentation, multiple birth, delayed growth, or haemorrhage;

the possibility of infection; and

maternal illness requiring immediate delivery.

Outcomes assessed in the review

There were no specific selection criteria relating to the outcomes of the primary studies. The following outcomes were assessed in the included trials:

the risk of maternal or foetal infection;

maternal fever peripartum and/or postpartum, defined as a temperature above 37.5 degrees C or 38 degrees C, depending on the trial;

delivery within 18 to 24 hours following induction;

recourse to administration of oxytocin;

delivery by Caesarean section;

instrumental delivery;

transfer to neonatal intensive care unit (ICU);

neonatal infection;

incidence of hypertonic uterus and ruptured uterus.

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 reviewers performed the selection.

Assessment of study quality

Each trial was coded using a checklist based on the method of Chalmers et al. (see Other Publications of Related Interest nos. 1-2), and scored out of a maximum of 26 points. The methodological quality of each trial was presented as the percentage of the maximum score. The checklist assessed the trials on the basis of the following criteria: explanation of the primary outcome; clear explanation of the patient selection criteria; the numbers of patients seen and excluded; reasons for exclusion or loss to follow-up; the methods used for blinding patients; the methods used for blinding investigators; the method of randomisation; whether statistical power calculations were performed; the analysis and discussion of co-variables; the appropriateness of statistical methods; the handling of study withdrawals; and whether an intention-to-treat analysis was performed. The authors do not state how the papers were assessed for quality, or how many of the reviewers performed the quality assessment.

Data extraction
The following data were extracted and tabulated for each included trial: authorship and year; the numbers of patients per treatment group; cervical status and method of examination; the method of diagnosing premature rupture of membranes; the minimum number of weeks' gestation to be achieved prior to inclusion in the trial; the type of PG (gel or pessary); the PG regimen (initial and subsequent doses); the interval allowed between failed induction with PG and oxytocin administration; the oxytocin infusion regimen used; the criteria used to judge the effectiveness of oxytocin; and the methodological quality score, expressed as a percentage of the total score.

Odds ratios (ORs) with associated 95% confidence intervals (95% CIs) were generated for each outcome for each trial, on an intention-to-treat basis, using the method of Yusuf et al. (see Other Publications of Related Interest no.3). The authors do not state how many of the reviewers performed data extraction.

Methods of synthesis
How were the studies combined?
Pooled ORs with the associated 95% CIs were generated for each outcome using the method of Yusuf et al. (see Other Publications of Related Interest no.3).

How were differences between studies investigated?
Between-trial heterogeneity was assessed using the chi-squared test.

Results of the review
Ten RCTs (n=1,004) were included. Two trials had three arms, comparing PG, oxytocin and placebo. The remaining 8 trials all had two arms; of these, 2 trials compared PG with expectant management, 2 compared PG with placebo, and 4 compared PG with oxytocin. Overall, 470 patients received PG, 150 received placebo, 180 received expectant management, and 204 received oxytocin.

Trials comparing PG with oxytocin achieved quality scores ranging from 31 to 54% of the maximum score, whilst those comparing PG with expectant management achieved scores ranging from 42 to 77%. The scores were lower for trials comparing PG with oxytocin because of the absence of blinding.

PG versus expectant management.
The OR for delivery within 18 to 24 hours of induction (3 RCTs) was 2.20 (95% CI: 1.54, 3.13).
The OR for recourse to oxytocin use (5 RCTs) was 0.36 (95% CI: 0.25, 0.51).
The OR for peripartum fever (4 RCTs) was 0.82 (95% CI: 0.39, 1.74).
The OR for postpartum fever (5 RCTs) was 0.35 (95% CI: 0.13, 0.90).
The OR for maternal infection (6 RCTs) was 0.61 (95% CI: 0.34, 1.08).
The OR for the overall rate of delivery by Caesarean section (6 RCTs) was 0.72 (95% CI: 0.38, 1.37).
The OR for instrumental delivery (1 RCT) was 6.91 (95% CI: 0.97, 49.1).
The OR for transfer to the neonatal ICU (4 RCTs) was 0.98 (95% CI: 0.45, 2.14).
The OR for neonatal infection (6 RCTs) was 0.21 (95% CI: 0.05, 0.98).

PG versus oxytocin.
The OR for delivery within 18 to 24 hours of induction (2 RCTs) was 1.16 (95% CI: 0.64, 2.09).
The OR for peripartum fever (5 RCTs) was 0.53 (95% CI: 0.11, 2.60).
The OR for postpartum fever (5 RCTs) was 0.34 (95% CI: 0.09, 1.20).

The OR for maternal infection (5 RCTs) was 0.45 (95% CI: 0.17, 1.17).

The OR for the overall rate of delivery by Caesarean section (6 RCTs) was 0.35 (95% CI: 0.17, 0.73).

The OR for instrumental delivery (4 RCTs) was 0.45 (95% CI: 0.22, 0.93).

The OR for transfer to the neonatal ICU (4 RCTs) was 1.97 (95% CI: 0.33, 11.80).

The OR for neonatal infection (6 RCTs) was 6.60 (95% CI: 0.40, 109.2).

Incidence of hypertonic uterus and uterine rupture.

A single case of hypertonic uterus was reported with PG use, versus four cases with placebo (2 RCTs); this difference was non-significant. In another RCT, a single case of ruptured uterus was reported following the administration of PG gel, necessitating hysterectomy.

**Authors' conclusions**
A policy of inducing labour, in cases of premature rupture of membranes at term with unfavourable local conditions, is justified by a desire to reduce the infection rates. In comparison with expectant management, the use of vaginal PG resulted in the following benefits: fewer cases of maternal and neonatal infection with no increase in Caesarean section delivery rates, and a shorter interval between premature rupture of membranes and delivery. When compared with induction using oxytocin, PG use resulted in fewer Caesarean and instrumental deliveries.

**CRD commentary**
The search strategy was very limited. Only two databases were accessed, and details of the dates and search terms used were not provided. The authors did not mention whether they conducted handsearches, accessed specialist sources, or attempted to identify unpublished literature. It would not be possible to replicate the search strategy from the information given. In addition, it is possible that relevant trials could have been missed from the review.

The methodological quality of each trial was assessed using a published checklist, and each was assigned a score. The quality score, and other details of the individual studies were tabulated clearly. The selection criteria for the primary studies were described, apart from those for the outcomes. The methods used to synthesis the data were appropriate. The authors mentioned using a statistical test to assess the between-trial heterogeneity, but the results of this were not presented. No details relating to the review process were provided; for example, it was not stated how many of the reviewers were involved in selecting the studies, assessing the methodological quality and extracting the data, and the methods used to resolve any disagreements were not described.

Due to the limited search strategy used, the lack of information about heterogeneity, and the poor methodological quality of some of the primary studies, more caution should be applied to the findings of this review than have been expressed by the authors in their conclusions.

**Implications of the review for practice and research**
The authors did not state any implications for further research and practice.

**Bibliographic details**
Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Administration, Intravaginal; Cesarean Section; Dinoprostone /therapeutic use; Female; Fetal Membranes, Premature Rupture /drug therapy; Humans; Labor, Induced /methods; Odds Ratio; Oxytocics /therapeutic use; Oxytocin /therapeutic use; Pregnancy; Pregnancy Outcome; Pregnancy Trimester, Third

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.