Pre-induction of labour: comparing dinoprostone vaginal insert to repeated prostaglandin administration - a systematic review and meta-analysis

Facchinetti F, Fontanesi F, Del Giovane C

CRD summary
The review concluded that in nulliparous women with an unprepared cervix, dinoprostone vaginal inserts performed better than repeated vaginal doses but were associated with more uterine hyperstimulation. The review noted serious bias concerns in some included trials; the authors’ conclusions should not be considered reliable as they appear over-optimistic.

Authors’ objectives
To assess the efficacy and safety of the dinoprostone vaginal insert compared to repeated prostaglandin administration (including dinoprostone and misoprostol) in women at term.

Searching
PubMed, EMBASE and The Cochrane library were searched to August 2011 without language restrictions; keywords were reported. Reference lists and conference proceedings were also examined to identify further studies. Known trialists were contacted to identify unpublished studies.

Study selection
Randomised controlled trials (RCT) of dinoprostone vaginal insert compared to repeated prostaglandin administration (including dinoprostone and misoprostol) in women at term were eligible. The primary efficacy outcome was caesarean section rate and the primary safety outcome was uterine hyperstimulation requiring immediate delivery. Secondary efficacy outcomes were also defined in the paper. Data had to be reported separately according to parity (nulliparous and/or multiparous). Women had to have an unfavourable cervix (Bishop Score of less than 5) and intact membranes.

Most studies were of nulliparous women; the remainder were a mix of nulliparous and multiparous women. Gestational ages in most studies ranged between 37 and 42 weeks. Dinoprostone was given for 12 or 24 hours and was followed by oxytocin (though at different time points); oxytocin was frequently administered following amniotomy. Most of the comparator treatments consisted of two or three doses of vaginal gel, sometimes with prior intracervical gel, followed by oxytocin (often with amniotomy).

Two reviewers independently selected studies for inclusion, with disagreements resolved by a third reviewer.

Assessment of study quality
Study quality was assessed using the Cochrane risk of bias tool, evaluating the risk of bias arising from methods of randomisation, allocation concealment, blinding, completeness of outcome data and whether a trial was multi-centre. The authors did not state how many reviewers performed the assessment.

Data extraction
Two reviewers extracted data to calculate risk ratios or mean differences with 95% confidence intervals. Authors were contacted for missing data when necessary.

Methods of synthesis
Meta-analyses were performed to calculate pooled risk ratios with 95% confidence intervals, using a random-effects model. Heterogeneity was assessed using $I^2$. Analyses were performed separately for nulliparous and multiparous women.

Results of the review
Seven RCTs were included (911 participants). Sequence generation was adequate in four trials but allocation concealment was only adequate in two trials. Blinding was adequate in one trial and inadequate in the remainder. Completeness of follow up was adequate in all trials.
Dinoprostone vaginal inserts significantly reduced caesarean section rate in nulliparous women by 24% compared to control administrations (RR 0.76, 95% CI 0.59 to 0.98; six RCTs). There was no statistically significant difference for the analysis of the two studies including multiparous women.

The risk of oxytocin use was reduced with the vaginal insert (RR 0.64, 95% CI 0.42 to 0.99; five RCTs). The risk of uterine hyperstimulation was significantly higher in nulliparous women using the vaginal insert than the control administrations (RR 2.17, 95% CI 1.08 to 4.33; three RCTs).

For nulliparous women, there were no significant differences between groups for vaginal delivery within 12 hours (four RCTs), vaginal delivery within 24 hours (four RCTs), instrumental vaginal delivery (three RCTs), induction to delivery interval (two RCTs) and hospitalisation length (one RCT). The overall result for vaginal delivery had borderline statistical significance (RR 1.09, 95% CI 1.00 to 1.20; six RCTs). Results for multiparous women were also reported.

There was no evidence of heterogeneity or publication bias.

Authors' conclusions
In nulliparous women with unprepared cervix and intact membranes vaginal insert performed better than repeated vaginal doses, since it was associated with more vaginal deliveries and less oxytocin use. Vaginal insert was associated with more uterine hyperstimulation, but showed a protective effect toward caesarean section.

CRD commentary
The review addressed a clear question and was supported by reproducible eligibility criteria. Attempts to identify all relevant studies in any language were undertaken by searching electronic databases and checking references. Searches were also made to identify unpublished studies. Duplicate processes were employed to reduce the risks of reviewer error and bias during data extraction and study selection, but authors did not report on whether such methods were used to assess risk of bias.

Risk of bias was assessed, but results were used little to inform the review conclusions, even though they highlighted some serious bias concerns. Appropriate methods were used to pool data and to assess heterogeneity. However, it was unclear why one study (the largest) was excluded from the meta-analyses. In light of limited use of risk of bias assessment results, the authors' conclusions should not be considered reliable as they appear over-optimistic.

Implications of the review for practice and research
Practice: The authors stated that, in view of the risk of hyperstimulation, active surveillance should be used during the application periods of vaginal inserts. They suggested that vaginal insert releasing dinoprostone should be used for women where labour induction was expected to be less responsive in terms of time to labour onset, as well as requiring repeated stimulation procedures.

Research: The authors did not state any implications for research.

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