Premature rupture of membranes at term: a meta-analysis of three management schemes

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Authors' objectives
To compare rates of Caesarean birth, endometritis, chorioamnionitis, and serious neonatal infections among pregnancies complicated by premature rupture of membranes (PROM) at term and managed by immediate oxytocin induction, by conservative management (or delayed oxytocin induction), or by vaginal (or endocervical) prostaglandin E2 gel, suppositories, or tablets.

Searching
MEDLINE (1966 to April 1996, Health (1975 to April 1996, Aidsline (1980 to April 1996) and Cancerlit (1980 to April 1996) and the Cochrane Database for Systematic Reviews (CDSR)(1996 update) were searched. The reference lists of articles identified from MEDLINE and CDSR were cross-checked. The search terms used for electronic searches were: 'term', 'premature rupture' and 'fetal membranes'.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs). They were classified as either true randomised controlled trials (defined as those in which sealed envelopes or random number tables were used), or controlled clinical trials (in which the randomisation methods were less rigorous or were not detailed). In studies containing both randomised and non-randomised arms, only data from the randomised arms were included.

Specific interventions included in the review
Management of PROM at term by immediate oxytocin induction, by conservative management (or delayed oxytocin induction), or by vaginal (or endocervical) prostaglandin E2 gel, suppositories, or tablets.

Participants included in the review
Females at term gestation (term defined as 36 weeks or more completed menstrual weeks) with rupture of amniotic membranes before the onset of labour.

Outcomes assessed in the review
Rates of Caesarean birth, endometritis (clinical diagnosis), chorioamnionitis (clinical diagnosis), and serious neonatal infections (defined as culture-proven neonatal septicaemia, meningitis, or pneumonia).

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
The studies included in the review were assessed for the quality of their randomisation. 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 categories of data were extracted: treatment outcomes (Caesarean birth, endometritis, chorioamnionitis, and serious neonatal infections (specifically culture-proven neonatal septicaemia, meningitis, or pneumonia)); location of study; number of participants (by treatment and total); details of initial digital examination; Bishop score; parity; and method of treatment assignment. The authors do not state how the data were extracted for the review, or how many reviewers performed the data extraction.
Methods of synthesis
How were the studies combined?
The studies were combined using a quantitative synthesis. Meta-analyses were performed for the various interventions for each of outcome of interest using the DerSimonian and Laird (random-effects) technique to estimate the pooled (or combined) odds ratio (OR) plus 95% confidence interval (CI) for the individual trial results and for the pooled estimates (see Other Publications of Related Interest no.1). Results were confirmed using the Mantel-Haenszel (fixed-effect) pooled OR (see Other Publications of Related Interest no.2).

How were differences between studies investigated?
Homogeneity of ORs across the separate trials pooled in each analysis were tested for significant between-study variation. To examine the source of any heterogeneity subgroup analyses were carried out for studies in which the inclusion criteria included unfavourable cervices (Bishop's score less than 5), studies in which no digital examinations were performed before randomisation, and studies in which digital examinations were performed on all patients before randomisation, and separate analyses of RCTs and CCTs.

Results of the review
A total of 23 studies were included (n=7,493). A total of 3,030 participants had conservative management and delayed induction; 1,735 had vaginal prostaglandins, 2,722 had immediate oxytocin induction.

The ORs and 95% CIs derived from the random-effects (DerSimonian) analysis are given below by treatment comparison and by outcome:

Immediate oxytocin versus conservative management: chorioamnionitis OR 0.91 (95% CI: 0.51,1.62); endometritis OR 0.78 (95%:0.50,1.21; Caesarean birth OR 1.24 (95%CI: 0.89, 1.73), neonatal infection OR 0.73 (95% CI: 0.47, 1.13).

Prostaglandins versus conservative management: chorioamnionitis OR 0.68 (95% CI: 0.51,0.91); endometritis OR 0.81 (95%:0.53,1.23; Caesarean birth OR 0.95 (95%CI: 0.76,,1.20), neonatal infection OR 1.06 (95% CI: 0.67, 1.66).

Prostaglandins versus oxytocin: chorioamnionitis OR 1.55 (95% CI: 1.09,2.21); endometritis OR 0.78 (95%:0.23,2.62; Caesarean birth OR 0.67 (95%CI: 0.34,1.29), neonatal infection OR 1.50 (95% CI: 0.91, 2.45).

Therefore vaginal prostaglandins resulted in more chorioamnionitis than immediate oxytocin, but less than conservative management. These results were consistent with those obtained from the fixed-effect analysis, with the exception of the incidences of chorioamnionitis and endometritis in the immediate oxytocin/conservative management comparison (Mantel-Haenszel pooled ORs, respectively, 0.67, 95% CI: 0.52, 0.85 and 0.71, 95% CI: 0.51, 0.99).

There was significant heterogeneity among the trials pooled for the chorioamnionitis outcome (chi-squared (8) =23.99, tau=0.39. p<0.01). When only the 'true' RCTs were included in the analysis, the DerSimonian pooled ORs found a significantly lower incidence of chorioamnionitis with immediate oxytocin compared with conservative management and with vaginal prostaglandins compared with conservative management (ORs, respectively, 0.43, 95% CI: 0.31, 0.60 and 0.68, 95% CI:0.51, 0.91). Subgroup analyses found that in studies with no digital analyses found one significant treatment difference but this was based on a small number of patients. Other subgroup analyses did not reveal any further treatment differences.

Authors’ conclusions
Immediate induction with oxytocin currently appears to present the best prospect with respect to maternal and neonatal morbidity, although small increases in Caesarean births may be noted with this intervention. Conservative management may result in more maternal infections than immediate induction with oxytocin or prostaglandins.

CRD commentary
The review addressed an appropriate question and had well defined inclusion and exclusion criteria. The search of the literature was reasonably comprehensive although only a limited number of the electronic databases were used and the search terms may not have been sufficiently inclusive to capture all pertinent articles. No attempts to identify
unpublished studies were made. In addition, some studies may have been missed due to limiting the search to English language articles. The quality of the studies was not assessed formally except for classifying them according to the rigour of their randomisation. The details of the individual studies included in the review are well presented in a table, enabling identification of patient numbers by treatment, and study design. The meta-analysis was appropriate using both random-effects and fixed-effect analyses, with appropriate test for heterogeneity. The authors' conclusions reflect the trends in the data identified by the meta-analysis, although overall the data appear to indicate only small differences in treatment effects.

**Implications of the review for practice and research**

**Practice:** The authors state 'Immediate induction with oxytocin currently appears to present the best prospect with respect to maternal and neonatal morbidity, although small increases in Caesarean births may be noted with this intervention'.

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

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