Utility of antibiotic therapy in preterm premature rupture of membranes: a meta-analysis

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Authors' objectives
To examine the efficacy and effectiveness of antibiotic therapy on maternal outcomes in pre-term premature rupture of membranes (PROM) in pregnancy.

Searching
The following sources were searched: MEDLINE (search years unclear); the authors' reprint files; Current Contents over the past 5 years; indices of the American Journal of Obstetrics and Gynecology, Obstetrics and Gynecology, British Journal of Obstetrics and Gynecology, and Obstetrical and Gynecological Survey; and bibliographies of relevant trials. No search terms were provided.

Study selection
Study designs of evaluations included in the review
Placebo-controlled randomised controlled trials (RCTs) were included.

Specific interventions included in the review
Antibiotics administered included penicillin, ampicillin, erythromycin, synthetic penicillins, and triple antibiotic therapy. Duration of therapy ranged from 3 days to the end of pregnancy. Parenteral, oral and combination administration of antibiotics were included.

Participants included in the review
Women experiencing pre-term PROM were included. Infant gestational age across all the included trials ranged from 19 to 34 weeks. Babies were also included.

Outcomes assessed in the review
Endometritis, chorioamnionitis, maternal perinatal mortality, neonatal respiratory distress syndrome, neonatal necrotising enterocolitis, latency between membrane rupture and onset of labour greater than 48 hours, latency period greater than 168 hours, and neonatal sepsis.

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
Only placebo-controlled RCTs were included. The authors do not state how the papers were assessed for validity, or how many of the authors performed the validity assessment.

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?
Odds ratios (ORs) were combined by meta-analysis using fixed-effect and random-effects models.

How were differences between studies investigated?
A statistical test of homogeneity of ORs was performed.

**Results of the review**
Nine RCTs were included, with clinicians and patients blinded to group assignment (total n=957).

Endometritis: there was a non significant trend towards the reduction of endometritis (pooled random-effects OR 0.61, 95% confidence interval, CI: 0.34, 1.08; based on 6 studies).

Chorioamnionitis: antibiotic therapy was protective against chorioamnionitis (pooled random-effects OR 0.54, 95% CI: 0.31, 0.95; based on 6 studies). Antibiotic therapy was therefore protective against in utero infection.

Perinatal mortality: a reduction in perinatal mortality was found with fixed-effect meta-analysis (summary OR 0.50, 95% CI: 0.29, 0.85) and random-effects meta-analysis (summary OR 0.50, 95% CI: 0.26, 0.97). Antibiotic therapy therefore reduces the risk of perinatal death.

Respiratory distress syndrome (7 studies): no significant effect (fixed-effect summary OR 0.89, 95% CI: 0.65, 1.24; random-effects OR 0.89, 95% CI: 0.64, 1.25) was observed.

Necrotising enterocolitis: no significant effect (fixed-effect summary OR 1.06, 95% CI: 0.60, 1.88; random-effects OR 1.06, 95% CI: 0.640, 1.88) was observed.

Latency periods greater than 48 hours (4 studies): antibiotic therapy increased the likelihood of a latency period greater than 48 hours in the fixed-effect model (summary OR 2.18, 95% CI: 1.25, 3.80) but not the random-effects model (summary OR 1.50, 95% CI: 0.86, 2.64).

Latency periods greater than 168 hours (4 studies): antibiotic therapy increased the likelihood of a latency period greater than 168 hours in both the fixed-effect model (summary OR 3.53, 95% CI: 2.13, 5.85) and the random-effects model (summary OR 3.54, 95% CI: 2.12, 5.89).

Neonatal sepsis (6 studies): no significant reduction although a trend towards reduction in risk of sepsis was found (fixed-effect summary OR 0.69, 95% CI: 0.38, 1.26; random-effects OR 0.65, 95% CI: 0.33, 1.28).

Survival: 4 studies examined survival and found significant advantages for the antibiotic group in terms of survival. One study showed a significant difference in birth weight between the two groups. Two studies showed significant increases in the length of the latency period within the treatment groups.

**Authors' conclusions**
Antibiotic therapy in pre-term PROM improves the outcome for both mother and baby.

**CRD commentary**
It is unclear how rigorous this review is as there are few methodological details. The search strategy seems appropriate but search terms were not provided and there was little informations concerning the dates covered. Further relevant trials may have been identified through a wider search strategy, e.g. by including the Cochrane Collaboration Pregnancy and Childbirth Database, the Oxford Database of Perinatal Trials and the Cochrane Library. Authors did not report on how decisions on inclusion or exclusion of studies were taken, or how data extraction was performed. There was no information on the quality of the included studies, although only placebo-controlled RCTs were included. Heterogeneity tests were performed but not discussed.

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