Antimicrobial therapy in expectant management of preterm premature rupture of the membranes

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Authors' objectives
To assess the impact of antimicrobial treatment on maternal and foetal outcomes during expectant management of pre-term premature rupture of the membranes.

Searching
MEDLINE was searched from 1966 to 1994 and EMBASE from 1972 to 1994; the Cochrane Database of Systematic Reviews was also searched. The references of reviewed articles were examined. Unpublished data were also obtained.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) of systemic antimicrobial therapy after pre-term premature rupture of the membranes, were included.

Specific interventions included in the review
Antibiotic or antimicrobial therapy using penicillins, extended spectrum penicillins, cephalosporins, erythromycin, or multi-agent therapy with ampicillin, gentamicin and clindamycin.

Participants included in the review
Pregnant women, not in labour, less than 37 weeks' gestation, with pre-term premature rupture of the foetal membrane.

Outcomes assessed in the review
Obstetric outcomes: latency from membrane rupture, admission or randomisation to delivery; maternal infection (chorioamnionitis and febrile morbidity) after delivery; incidence of Caesarean delivery. Foetal/infant morbidity and mortality were also assessed.

How were decisions on the relevance of primary studies made?
Only studies in which the authors aimed to prolong gestation were included. Studies which included women at term and failed to sub-analyse pre-term women were excluded. Studies that included women in labour, and those in which intrapartum antimicrobial treatment was given solely for group B streptococcus prophylaxis were excluded. 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
Studies demonstrating potential bias, i.e. by use of retrospective controls, ill-defined outcomes, post-randomisation exclusion greater than 15%, or confounding treatments given only to one group, were excluded. The authors do not state how the papers were assessed for validity, or how many of the authors performed the validity assessment.

Data extraction
A single reviewer extracted the data using a computerised data-collection form from which data were exported to statistical software for analysis. Data were included on an intention-to-treat basis.

Methods of synthesis
How were the studies combined?
A series of meta-analyses was undertaken to compare the treatment and control groups; these used the Mantel-Haenszel
test with calculated odds ratios (ORs) and weighted 95% confidence intervals (CIs).

How were differences between studies investigated?
The Mantel-Haenszel test for heterogeneity of ORs was used to evaluate variability in outcomes between the trials.

**Results of the review**
Thirteen trials involving 1,594 women were included.

Obstetric outcomes.

Weighted mean latencies for treatment and control women were 8.9 and 5.7 days, respectively. Antimicrobial treatment significantly reduced the number of women who delivered within one week (OR 0.51, 95% CI: 0.41, 0.68). Treatment reduced chorioamnionitis and possibly postpartum infection, but did not reduce Caesarean delivery.

Foetal/infant outcomes.

Although foetal/infant mortality was not affected by antimicrobial treatment, the risk of infection was reduced. The OR for confirmed infant sepsis for placebo-controlled trials was 0.53 (95% CI: 0.30, 0.93); the figure for all trials was 0.57 (95% CI: 0.36, 0.88). ORs for specific aspects or types of infection (pneumonia, positive blood cultures, necrotising enterocolitis) were not significant, probably because the statistical power for these comparisons was insufficient.

Authors' conclusions
The significant prolonging of pregnancy, and reduction in maternal and infant infectious morbidity, is consistent with a direct protective effect of treatment with antimicrobial agents in the management of pre-term premature rupture of foetal membranes.

CRD commentary
The authors have taken steps to reduce the risk of bias and to investigate whether it has occurred by separate analyses, according to the methodology of trials. The findings of this review appear to be robust although some questions remain unanswered because of the low power of some comparisons.

**Bibliographic details**

**PubMedID**
7475723

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Anti-Bacterial Agents /therapeutic use; Bacterial Infections /diagnosis; Bias (Epidemiology); Ceftriaxone /therapeutic use; Cerebral Hemorrhage /diagnosis; Chemoprevention; Chorioamnionitis /diagnosis; Confounding Factors (Epidemiology); Delivery, Obstetric; Female; Fetal Death; Fetal Diseases /diagnosis; Fetal Membranes, Premature Rupture /therapy; Gestational Age; Humans; Infant, Newborn; Infant, Premature; Infant, Premature, Diseases /diagnosis; Placebos; Pneumonia /diagnosis; Pregnancy /drug effects; Pregnancy Outcome; Puerperal Infection /diagnosis; Randomized Controlled Trials as Topic

**AccessionNumber**
11995004023
Record Status
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