Adjunctive antibiotic treatment in preterm labor and neonatal morbidity: a meta-analysis
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Authors' objectives
To determine the effects of prophylactic antibiotics on neonatal mortality and morbidity in patients with pre-term labour.

Searching
Eighteen medical databases were searched up to January 1995 including MEDLINE (from 1964) and EMBASE (from 1974); no search terms are provided in the review.

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

Specific interventions included in the review
Antibiotic treatment: intravenous (i.v.) ampicillin plus oral erythromycin; clindamycin followed by oral clindamycin; i.v. ampicillin plus i.v. sulbactam; i.v. ampicillin followed by oral ampicillin; i.v. ampicillin plus i.v. erythromycin followed by oral amoxicillin plus oral erythromycin; i.v. ampicillin followed by oral amoxicillin plus metronidazole suppository followed by oral metronidazole; ceftizoxime.

Participants included in the review
Women with pre-term labour defined as labour before 37 weeks' gestation. The gestational range on admission in the included trials was usually 24 to 34 weeks, although one study included women from 19 weeks. In all studies, women were excluded if there was clinical evidence of maternal infection, premature rupture of membranes, foetal distress or abnormal foetal testing, antepartum haemorrhage, and allergies or contraindications to antibiotic or adjunctive treatments. Patients with pregnancy-induced hypertension, severe maternal disease, uterine anomalies, foetal anomalies, placenta previa, foetal growth restriction, non vertex presentation, and recent use of antibiotics were also excluded.

Outcomes assessed in the review
Neonatal outcomes assessed: mortality, sepsis, pneumonia, respiratory distress syndrome or hyaline membrane disease, intraventricular haemorrhage, necrotising enterocolitis. Maternal outcomes assessed: treatment to delivery interval, chorioamnionitis, endometritis and maternal infection.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, although the inclusion criteria were provided, or how many of the authors performed the selection.

Assessment of study quality
Validity was assessed on the basis of baseline similarity between study groups, randomisation process, blindness, use of placebo and assessment of patient compliance. The authors do not state how the papers were assessed for validity, or how many of the authors performed the validity assessment.

Data extraction
Predefined data were abstracted. Patients with hyaline membrane disease and respiratory distress syndrome were combined as single outcomes. Patients where an intention-to-treat strategy was not followed were excluded from the analysis.
Methods of synthesis
How were the studies combined?
The RCTs were statistically pooled using a fixed-effect model when tests of heterogeneity confirmed this was appropriate. Odds ratios (ORs) and confidence intervals (CIs) were calculated for each outcome.

How were differences between studies investigated?
Chi-squared tests of heterogeneity were performed for each outcome. Studies were compared according to patient inclusion and exclusion criteria, baseline similarity of patients, characteristics of management including administration of antibiotics and management of patients with positive cervical cultures or chorioamnionitis, indications for induced delivery or Caesarean section, and management of infants.

Results of the review
Seven RCTs (795 patients) were included.

Two out of the 7 RCTs found that antibiotic treatment significantly prolonged the treatment to delivery interval. Antibiotic treatment had no significant effect on any maternal outcome in any of the studies reviewed. Combined ORs were not calculated because of inconsistent definitions.

ORs are presented for neonatal outcomes from combined RCT, where a beneficial treatment effect corresponds to an OR of less than 1; if the CI includes 1 the result is not statistically significant.

Mortality: OR 3.25 (95% CI: 0.93, 11.38).
Sepsis: OR 0.98 (95% CI: 0.34, 2.83).
Pneumonia: OR 0.45 (95% CI: 0.12, 1.72).
Respiratory distress syndrome: OR 0.93 (95% CI: 0.54, 1.87).
Intraventricular haemorrhage: OR 1.01 (95% CI: 0.2, 5.1).
Necrotising enterocolitis: OR 0.38 (95% CI: 0.14, 1.08).

None of the tests for heterogeneity were statistically significant.

Authors’ conclusions
The results of this meta-analysis do not support the routine use of adjunctive antibiotic treatment in patients with pre-term labour diagnosed on the basis of subjective uterine contractions and the resulting cervical changes.

CRD commentary
A very thorough systematic review. The methodological shortcomings of the included trials are discussed at length. The restriction to published trials may mean the results are subject to publication bias; this is acknowledged by the authors. In addition, inclusion of only English language papers potentially reduces the generalisability of the findings. The generalisability of the findings may also be limited by the very strict inclusion criteria applied. This notwithstanding, the authors’ conclusions are supported by the results of the review.

Implications of the review for practice and research
Routine use of prophylactic antibiotics in patients with pre-term labour is not indicated.

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