Treatment of vaginal infections to prevent preterm birth: a meta-analysis

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CRD summary
The review evaluated the role of antibiotic treatment for vaginal infections in pregnancy to determine benefits and harms of treatment. The authors concluded that there is little evidence to suggest treatment can reduce the risk of adverse pregnancy outcomes, and further research is needed. The conclusions are broadly based on the evidence presented and can be considered reliable.

Authors' objectives
To determine the role of antibiotic treatment of vaginal infections in pregnancy to prevent pre-term birth.

Searching
MEDLINE (1966 to May 2004) and EMBASE (1974 to May 2004) were searched using the terms reported. The bibliographies of all relevant articles were also checked.

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

Specific interventions included in the review
Studies of antibiotic treatment compared with placebo were eligible for inclusion. The infections included in the review were group B Streptococcus, Chlamydia trachomatis, Ureaplasma urealyticum, Trichomonas vaginalis and bacterial vaginosis. The treatments evaluated in the included studies were metronidazole, erythromycin, vaginal or oral clindamycin, azithromycin and cefixime.

Participants included in the review
Studies of women at less that 37 weeks' gestation who were not in labour and had intact amniotic membranes were eligible for inclusion. The gestational age at treatment ranged from 12 to 30 weeks.

Outcomes assessed in the review
Studies that reported gestational age at delivery and any of the following outcomes were eligible for inclusion: low birth weight (less than 2,500 g), number with premature rupture of the membrane (PROM), and the number of pre-term births when the mother had a prior pre-term delivery.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed the eligibility of studies for inclusion. Any disagreements were resolved by discussion and consensus.

Assessment of study quality
Each study was assigned a quality score (1 being the lowest and six the highest) to assess the description of randomisation, double-blinding, withdrawals and drop-outs, and analysis according to intention-to-treat principles. Additional points were added or deducted for the use of appropriate or inappropriate randomisation or blinding. Studies scoring less than 3 points were considered to be of a poor quality. The authors did not state how the papers were assessed for quality, or how many reviewers performed the quality assessment.

Data extraction
[A: Two reviewers independently extracted data and disagreements were resolved by consensus]. Data on the occurrence
of each outcome were extracted from the individual studies and used to calculate an odds ratio (OR) with 95% confidence intervals (CIs).

**Methods of synthesis**

How were the studies combined?
The results were combined in a meta-analysis. A fixed-effect model was used in the absence of statistical heterogeneity, and a random-effects model in the presence of statistical heterogeneity. Pooled ORs with 95% CIs were calculated separately for each type of bacterial infection and for each outcome where there was more than one study. For infections where there was only one study, the OR with 95% CI was presented.

How were differences between studies investigated?
Statistical tests of homogeneity were performed as part of the meta-analysis (significance threshold P<0.10). Subgroup analyses were performed to determine the impact of antibiotic use, route of administration and obstetrical history on outcome for those bacterial infections for which there were a sufficient number of included studies.

**Results of the review**

Sixteen RCTs (n=11,412) were included in the review.

Group B Streptococci (1 RCT, n=938): no statistically significant difference was found in the likelihood of a low birth weight (OR 1.43, 95% CI: 0.86, 2.37), pre-term delivery (OR 0.91, 95% CI: 0.61, 1.36) or pre-term PROM (OR 1.0, 95% CI: 0.46, 2.11).

Chlamydia trachomatis (1 RCT, n=414): no statistically significant difference was found in the likelihood of a low birth weight (OR 0.74, 95% CI: 0.38, 1.45), pre-term delivery (OR 0.89, 95% CI: 0.49, 1.62) or pre-term PROM (OR 0.70, 95% CI: 0.19, 2.49).

Ureaplasma urealyticum (1 RCT, n=1,181): no statistically significant difference was found in the likelihood of a low birth weight (OR 1.36, 95% CI: 0.85, 2.17) or pre-term delivery (OR 1.02, 95% CI: 0.67, 1.54).

Trichomonas vaginalis (2 RCTs, n=2,469): there was an increased likelihood of a low birth weight (OR 1.68, 95% CI: 1.11, 2.53) and pre-term birth (OR 1.71, 95% CI: 1.19, 2.46). There was no evidence of statistical heterogeneity for either outcome.

One RCT found no statistically significant difference in the likelihood of pre-term PROM (OR 1.1, 95% CI: 0.5, 2.3).

Bacterial vaginosis (11 RCTs, n=6,410): no statistically significant difference was found in the likelihood of a low birth weight (OR 0.92, 95% CI: 0.60, 1.40), pre-term birth (OR 0.89, 95% CI: 0.66, 1.20) or pre-term PROM (OR 0.77, 95% CI: 0.33, 1.81); these results were based on 6, 11 and 5 studies, respectively. There was evidence of statistical heterogeneity in all of the analyses.

The subgroup analyses on antibiotic use, route of administration, and obstetrical history did not impact on the outcomes for bacterial vaginosis.

**Authors' conclusions**

There was little evidence to suggest that the treatment of bacterial infections lowered the risk of outcomes associated with pre-term birth. Certain groups of women may benefit from treatment and other subgroups may be harmed by treatment.

**CRD commentary**

The review addressed a clear research question and the inclusion criteria appeared appropriate. Relevant sources were used to identify studies. However, no attempts were made to identify unpublished studies. Methods were used to minimise bias when selecting studies for inclusion and for data extraction. Quality was assessed using established
criteria, although details of the quality assessment were not fully reported or considered in the presentation of results.

Limited details were provided on the populations evaluated in the included studies, e.g. it was unclear whether women were screened and treated for infection. This makes it difficult to comment on the generalisability of the review findings. The authors performed tests of heterogeneity and explored possible reasons for differences in appropriate subgroup analyses. Given the paucity of studies for most bacterial infections and the heterogeneity in the results of studies of bacterial vaginosis, the authors' tentative conclusion and recommendations for further research are appropriate based on the evidence presented.

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

**Practice:** The authors state that caution is advised in treating BV to prevent pre-term birth.

**Research:** The authors stated that future research is needed to determine which women may benefit or be harmed from treatment, and to investigate the possible role of anti-inflammatory agents in addition to antibiotics in the presence of infection.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.