Antibiotics for bacterial vaginosis or Trichomonas vaginalis in pregnancy: a systematic review

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CRD summary
This review assessed the effects of antibiotic treatment in pregnant women with bacterial vaginosis or Trichomonas vaginalis. The authors concluded that there was no evidence that antibiotics reduced pre-term delivery in women treated in the second or third trimester of pregnancy. The results were not consistent among studies and this casts doubt on the robustness of the authors' conclusions.

Authors' objectives
To assess the effects of antibiotic treatment for bacterial vaginosis or Trichomonas vaginalis on pre-term delivery and other adverse effects in pregnant women.

Searching
PREMEDLINE, MEDLINE (1966 to 2003), EMBASE (1980 to 2003) and the Cochrane Library were searched for studies published in the English language; the keywords were reported. Studies published as abstracts were excluded.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion. Studies were excluded if more than 20% of women in either treatment arm were lost to follow-up.

Specific interventions included in the review
Studies that compared antibiotics with no antibiotic or placebo were eligible for inclusion. The included studies used oral metronidazole with and without erythromycin, clindamycin vaginal cream and oral clindamycin.

Participants included in the review
Studies that included women in the second or third trimester of pregnancy at baseline with symptomatic or asymptomatic bacterial vaginosis or Trichomonas vaginalis, and reported results separately for this population, were eligible for inclusion. The studies had to be in women with intact membranes who were not in labour. The authors' diagnoses of bacterial infection were accepted by the reviewers. Where reported, the included studies were in women at high and low risk for premature delivery. The studies screened women at 8 to 26 weeks' gestation.

Outcomes assessed in the review
The studies had to report useable outcome data. The primary review outcome was pre-term delivery before 37 weeks. The review also assessed pre-term delivery before 35, 34, 32 and 28 weeks, very low birth weight (less than 1,500 g), pre-term prelabour rupture of membranes, chorioamnionitis, endometritis, peripartum infection, perinatal death, neonatal sepsis, admission to a neonatal intensive care unit, and eradication of the organism from the vagina.

How were decisions on the relevance of primary studies made?
One reviewer screened titles, while two reviewers independently screened identified abstracts and selected studies for inclusion. Any disagreements were resolved by consensus or with the help of a third reviewer.

Assessment of study quality
Studies were assessed for concealment of randomisation and use of placebo control. Two reviewers independently assessed drop-outs.
Data extraction
Two reviewers independently extracted the data. For each study, the relative risks (RRs) and 95% confidence intervals (CIs) were calculated.

Methods of synthesis
How were the studies combined?
The studies were grouped according to type of organism and combined using a random-effects model (DerSimonian and Laird). Pooled RRs and 95% CIs were calculated.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared statistic. A subgroup analysis was used to explore the influence of high-risk status, specific antibiotic, and confirmation or not of bacterial vaginosis at the time of randomisation. Other differences were apparent from the information tabulated.

Results of the review
Fourteen RCTs (n=6,728) were included.

Antibiotics for bacterial vaginosis.

Eradication of bacterial vaginosis (5 RCTs): Antibiotics significantly reduced the risk of persistent bacterial vaginosis (RR 0.32, 95% CI: 0.20, 0.52, P<0.001).

Pre-term birth before 37 weeks (11 RCTs): there was no statistically significant difference between the groups treated with antibiotics versus no antibiotics (RR 0.93, 95% CI: 0.70, 1.22, P=0.6). Statistically significant heterogeneity was detected (P<0.001). The results were similar for pre-term delivery before 35, 34, 32 and 28 weeks. There were no statistically significant differences between the groups treated with antibiotics versus no antibiotics for high-risk women (RR 0.75, 95% CI: 0.45, 1.24, P=0.30). Statistically significant heterogeneity was detected (P=0.001). There was also no statistically significant difference between metronidazole and no antibiotics for all women (RR 1.08, 95% CI: 0.73, 1.59, P=0.70). Statistically significant heterogeneity was detected (P=0.002).

Antibiotics for Trichomonas vaginalis.

Eradication of Trichomonas vaginalis (3 RCTs, 2 included in meta-analysis): antibiotics significantly reduced the risk of persistent Trichomonas vaginalis (RR 0.18, 95% CI: 0.07, 0.48, P<0.001).

Pre-term birth (1 RCT): the RCT found that, compared with no antibiotic, treatment with metronidazole was associated with an increased risk of pre-term delivery before 37 weeks for all women (RR 1.78, 95% CI: 1.19, 2.66, P=0.005) and for women at high risk (RR 1.84, 95% CI: 1.07, 3.18, P=0.03). The RCT found no statistically significant difference between treatments for pre-term delivery before 35 weeks for all women (the results were reported).

Authors' conclusions
There was no evidence that antibiotics for bacterial vaginosis or Trichomonas vaginalis in the second or third trimester of pregnancy reduce pre-term delivery or associated adverse effects in women at high or low risk of pre-term delivery.

CRD commentary
The review question was clear in terms of the study design, intervention, participants and outcomes. Three relevant databases were searched, but no attempts were made to minimise language or publication bias. Two reviewers independently selected studies and extracted the data, thus reducing the potential for bias and errors. Only RCTs with low drop-out rates were included; some other aspects of validity were discussed in the paper.

The studies were combined in a meta-analysis, regardless of the presence of statistically significant heterogeneity. A subgroup analysis was used to examine the influence on the results of some factors, but it was unclear to what extent
this reduced heterogeneity. The examination of the results would have been easier if meta-analyses graphs had been presented for all meta-analyses, and if statistical heterogeneity test results had been presented alongside the results of the relevant meta-analysis. Statistical heterogeneity was found for the main outcome; this showed that the results were not consistent among studies, and casts doubt on the robustness of the authors' conclusions.

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

**Practice:** The authors stated that there was no evidence to support treatment of asymptomatic Trichomonas vaginalis in pregnancy, and some evidence that treatment may be harmful.

**Research:** The authors stated that further adequately powered RCTs of antibiotic treatment started earlier in pregnancy are required to assess the effects on clinically important outcomes.

**Bibliographic details**


**PubMedID**

15802417

**DOI**

10.1097/01.AOG.0000157108.32059.8f

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Anti-Bacterial Agents /administration & dosage /adverse effects /therapeutic use; Female; Humans; Pregnancy; Pregnancy Complications, Infectious /drug therapy /pathology; Randomized Controlled Trials as Topic; Treatment Outcome; Trichomonas Vaginitis /drug therapy /pathology; Vaginosis, Bacterial /drug therapy /pathology

**AccessionNumber**

12005009900

**Date bibliographic record published**

30/04/2006

**Date abstract record published**

30/04/2006

**Record Status**

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