Indications for therapy and treatment recommendations for bacterial vaginosis in nonpregnant and pregnant women: a synthesis of data
Koumans E H, Markowitz L E, Hogan V

Authors' objectives
To investigate the efficacy of treatments for bacterial vaginosis (BV) in pregnant and nonpregnant women, and the resulting reduction in adverse pregnancy outcomes.

Searching
MEDLINE (from 1976 onwards) and the references of retrieved articles were searched. Search terms relating to the interventions and outcomes were reported.

Study selection
Study designs of evaluations included in the review
Studies using a randomised or controlled design, which stated the inclusion and exclusion criteria, were eligible for inclusion in the assessment of efficacy in nonpregnant women. For the review of therapy in pregnant women, cohort studies of at least 200 women and case-control studies were eligible for inclusion.

Specific interventions included in the review
Studies evaluating the treatment of BV, namely 7 to 10 days' oral metronidazole, metronidazole gel, 2% clindamycin cream, clindamycin ovules and chlorhexidine, were eligible for inclusion. The dose of oral metronidazole was 400 to 500 mg two or three times daily for 5 to 7 days, or a single dose of 2 g. The included studies were either comparisons of two or more active treatments, or active treatment and a placebo.

Participants included in the review
Both pregnant and nonpregnant women diagnosed as having BV (met at least two of the Amsel criteria, see Other Publications of Related Interest no.1) were eligible for inclusion. Trials that evaluated the therapy of partners were also eligible for inclusion.

Outcomes assessed in the review
Studies reporting efficacy outcomes at least 21 days after treatment, and a definition of 'cure' that included at least 2 of the Amsel criteria, were eligible for inclusion. The outcomes reported in the review included cure rates, premature or pre-term delivery, premature rupture of membranes, and post- or peripartum infections.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the extraction. The extracted data included the study design, inclusion or exclusion criteria, definition of cure or improvement, period of follow-up, loss to follow-up, treatment regimen and cure rate. The BV diagnosis method, intervention and reported findings were given for studies reporting adverse pregnancy outcomes.

Methods of synthesis
How were the studies combined?
The review was a narrative synthesis in which the studies were tabulated according to the intervention.

How were differences between studies investigated?
The effects of the loss to follow-up were investigated using a best-case worst-case sensitivity analysis. Sensitivity analyses were also performed for studies that only followed up responders.

Results of the review
The review included 59 published articles (n=30,197), including 40 randomised controlled trials (n=9,024), 9 cohort studies (n=18,419), 3 case-control studies (n=1,044), one controlled trial (n=100), one prospective comparative trial (n=1,138), one part-randomised trial (n=43) and one non-randomised trial (n=429).

Efficacy of treatment for BV.
Treatment with an oral regimen of metronidazole (400 to 500 mg, 2 to 3 times daily) gave a cure rate of between 76 and 100%, compared to 5 and 11% in those receiving a placebo. This regimen was as effective (cure rate: 80 to 100%) as a single 2-g dose of metronidazole (cure rate: 47 to 92%).

The cure rate of an oral regimen of metronidazole (500 mg, 2 to 3 times daily), was very similar to that observed in those using metronidazole gel (cure rate: 71 to 93%) or 2% clindamycin cream (cure rate: 61 to 95%). The cure rate was also similar between the oral regimen of metronidazole (400 to 500 mg, 2 to 3 times daily) and other regimens; the exception was pivampicillin which had a cure rate of 57%, compared to 74% for those on metronidazole.

The cure rate of BV when using metronidazole vaginal gel was 58 to 77% for once-daily application and 61 to 87% for twice-daily applications. The cure rate in women using 2% clindamycin cream was 58 to 94%, compared to 25 to 35% in those using a placebo and 66% in those using clindamycin ovules.

Effect of BV treatment on adverse pregnancy outcomes.
Oral therapy for BV in pregnant women showed no significant effect on the incidence of pre-term birth. However, for those in high-risk groups, BV treatment significantly reduced the incidence of pre-term birth (P<0.05).

Intravaginal therapy with 2% clindamycin increased the incidence of pre-term delivery. It also significantly increased the incidence of sepsis and pneumonia in newborns (P=0.013).

Authors’ conclusions
Oral therapy (7 days' metronidazole) for BV effectively reduces upper tract infections and adverse outcomes of pregnancy. There was no evidence to support the treatment of low-risk women for BV. The use of intravaginal clindamycin increases the risk of adverse outcomes of pregnancy, particularly for the newborn.

CRD commentary
The authors restricted their search to MEDLINE and the references of retrieved articles, and made no attempt to find unpublished data. This may have led to the introduction of publication bias. It was difficult to assess the methodological quality of this review, as the authors did not state how the studies were selected, how the data were extracted, or how quality was assessed. The authors did, however, state that the quality and follow-up rates of studies varied widely and undertook sensitivity analyses to investigate the effect of loss to follow-up. The authors undertook a narrative synthesis of the data, which was appropriate considering the clinical heterogeneity of the included studies. The review evaluated several treatments and regimens of these treatments, with a limited number of studies evaluating the same regimen. The conclusions for individual treatment regimens were, therefore, drawn from limited evidence.

Implications of the review for practice and research
Practice: The authors stated that pregnant women being treated for BV should be prescribed 250 mg of metronidazole,
3 times daily for 7 days. Alternatively, 300 mg of clindamycin twice daily is recommended. The authors did not recommend a single 2-g oral dose of metronidazole or any intravaginal regimen during pregnancy.

Research: The authors made the following recommendations.

Studies in low-risk asymptomatic women are needed, including: the systemic therapy of pregnant women for a minimum of 4 days; screening for BV early in pregnancy; addition of macrolide therapy; and the assessment of infectious morbidity.

Future research should report an intention-to-treat analysis, to remove the potential for bias arising from a lack of compliance or losses to follow-up.

More confidence can be placed in comparative studies that adopt the guidelines for the evaluation of therapy efficacy for new drugs (see Other Publications of Related Interest no.2).

Studies should have an adequate sample size and follow-up period.

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Other publications of related interest

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Record Status
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.