The role of Lactobacillus probiotics in the treatment or prevention of urogenital infections: a systematic review
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CRD summary
The review found a significant benefit for treatment of recurrent bacterial vaginosis with certain Lactobacillus strains, but evidence in the prevention or treatment of urinary tract infection and or vulvovaginal or vaginal candidiasis was uncertain. Potential limitations in the review process and uncertainties about the quality of included studies make the reliability of the authors' conclusions unclear.

Authors' objectives
To evaluate the efficacy of Lactobacillus probiotics for prevention or treatment of bacterial vaginosis, vulvovaginal candidiasis and urinary tract infection.

Searching
PubMed, CINAHL, EMBASE, The Cochrane Library, DARE and American College of Physicians Databases and Google Scholar were searched for publications in English. Search dates spanned from inception to December 2007. Search terms were reported. The bibliography of each retrieved article was handsearched.

Study selection
All clinical controlled trials that evaluated use of Lactobacillus-containing probiotics compared with no treatment or a comparator in treatment or prevention of bacterial vaginosis, vulvovaginal candidiasis or urinary tract infection in adults were eligible for inclusion. Studies that focused on colonisation or restoration of normal vaginal flora were eligible. Studies were excluded if data were not provided to calculate relative risk. Most studies used intravaginal preparations of Lactobacilli, mostly pessaries or suppositories but also douches and tampons. One study used both oral and vaginal lactobacilli. The remaining studies used oral preparations (one used yogurt). Doses were no less than 1x10^6 CFU lactobacilli. Dosing frequency varied from once to twice daily to once weekly. Treatment duration ranged from four days to 19 months. Lactobacilli strains used included: L. acidophilus, L. rhamnosus (GG and GR-1), L. fermentum RC-14 (renamed L. reuteri), L. delbrueckii, L. crispatus and L. gasseri alone or in combination. (Further details of interventions were reported.) Definitions of criteria used for diagnosis of the three infections were provided. Bacterial vaginosis was evaluated using Amsel's criteria and/or Nugent's score. Normal vagina flora was evaluated using Nugent's score or modified Normal Flora Index (details were reported). Most studies were of women in an outpatient setting. Most participants were healthy premenopausal non-pregnant women. In a minority of the studies the women received concomitant antibiotics. Outcomes measured were prevention or cure from infection.

The authors did not state how many reviewers performed study selection.

Assessment of study quality
Methodological quality was assessed by two authors independently in terms of blinding, randomisation, follow-up time, loss to follow-up and use of a placebo.

Data extraction
The number of events for each outcome was extracted in order to calculate relative risk (RR) and 95% confidence intervals (CI). Two reviewers extracted data independently.

Methods of synthesis
A narrative synthesis was performed as the studies were heterogeneous. Results were summarised in a tabular form.

Results of the review
Twenty five relevant studies were identified (n=2,348): 17 randomised controlled trials (RCTs) (n=1,993), which comprised nine double-blind, one single-blind and nine placebo-controlled; and eight before-after studies with historical
controls (n=355), which comprised one double-blind and placebo-controlled studies.

Of two studies each of prevention and treatment of vulvovaginal candidiasis, only one prospective cross-over trial found a significant benefit for prevention (RR 0.39, 95% CI 0.17 to 0.70).

One RCT of the five studies of prevention of urinary tract infections found a significant benefit with both lactobacilli (RR 0.42, 95% CI 0.22 to 0.67) and lactobacilli growth factor (RR 0.63).

There were nine studies of treatment of bacterial vaginosis. Of these, five RCTs and one quasi-experimental trial showed a significant reduction in infection (RR range 0.03 to 0.43).

Data for adverse events were reported for seven studies: four reported no side effects; one reported headaches and increased appetite; and two reported itching or burning sensations.

Four RCTs (of seven studies) of Lactobacillus colonisation or restoration of normal vaginal flora found a significant positive benefit.

Authors’ conclusions
Use of certain Lactobacillus strains such as L. rhamnosus GR-1 and L. reuteri for prevention and treatment of recurrent urogenital infection had promise, especially for recurrent bacterial vaginosis. Scant data on use of probiotics for urinary tract infection and vulvovaginal candidiasis precluded definitive recommendations.

CRD commentary
The review addressed a well-defined question in terms of participants, interventions and study design, but minimal detail was given of relevant outcomes. Relevant sources were searched, but only for studies published in English and there was no apparent search for unpublished studies; therefore, studies may have been missed and associated biases introduced. Some relevant methodological quality data were provided, but not sufficient for the reader to judge study quality. Efforts were made to reduce error and bias during data extraction; it was unclear whether this applied to study selection and quality assessment. Relevant study details were reported, but no details of length of follow-up and minimal details of loss to follow-up were given. Minimal details were given of placebos used (for example whether they were different bacterial strains or did not contain live organisms). The chosen method of synthesis seemed appropriate since the authors considered the studies to be too heterogeneous to perform meta-analysis. In view of potential for missed studies, some potential error and bias during the review process and uncertainties about the quality of included studies, the extent to which the authors’ conclusions are reliable is unclear.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors identified a need for further research and larger studies on type of lactobacilli strains (using probiotics known to colonise vaginal epithelial cells or inhibit uropathogens), dosage, duration of treatment, optimal route and vehicle of administration, particularly for urinary tract infections and vulvovaginal candidiasis. Once this basic knowledge was established, adequately powered RCTs for vulvovaginal candidiasis and urinary tract infection would be recommended. Future studies should monitor adverse events carefully, including risk of bacteraemia from probiotics. Whether probiotics truly colonised the vagina or were just a transient presence also needed further investigation.

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contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on
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