Meta-analysis: long-term therapy with rifaximin in the management of uncomplicated diverticular disease

CRD summary
This review concluded that treatment with rifaximin plus fibre supplementation was effective in obtaining symptom relief and could prevent more complications at one year in patients with symptomatic uncomplicated diverticular disease. This conclusion reflects the results presented, but the small number of included trials and the potential for missed data mean that it should be interpreted with some caution.

Authors' objectives
To determine the long-term efficacy of rifaximin plus fibre supplementation versus fibre supplementation alone in patients with symptomatic uncomplicated diverticular disease on symptom relief and complication rate.

Searching
PubMed and Cochrane Central Register of Controlled Trials (CENTRAL) were searched for articles published in full up to September 2010 with no language restrictions. Search terms were reported. Reference lists of relevant publications were searched. The authors stated that they searched conference abstracts and contacted authors for additional data, although only articles published in full were included.

Study selection
Randomised controlled trials (RCTs) of treatment with a poorly absorbed antibiotic compared with no treatment in patients with symptomatic uncomplicated diverticular disease were eligible for inclusion. The primary outcome was symptom relief/pain at end of follow-up. Complication rate (local and/or systemic) within one year from first examination was considered as a secondary outcome. Trials were required to report both primary and secondary outcomes to be eligible for inclusion. Diverticulitis was defined as abdominal pain attributed to diverticular disease plus one of the following criteria: treated with antibiotics, hospitalisation, or surgery; or described as severe or acute or presenting with fever, requiring medication, or evaluated with computed tomography. Cross-over trials appear to have been excluded post-hoc.

The antibiotic treatment used in all included trials was rifaximin (400mg twice daily for seven days every month). All patients in the treatment and control groups received a standard supplement of dietary fibres (glucomannan 2 to 4g) or unspecified dietary fibre (20g/daily). One control group received placebo. The diagnosis of symptomatic uncomplicated diverticular disease was made by double contrast barium enema and/or colonoscopy in all included trials. In most trials, clinical evaluation was performed on admission and at two to four months intervals for up to 12 months (24 months in one trial). Different symptom scores based on a number of clinical variables were used across the included trials; the review focused only on the presence or absence of any symptom. Side effects were reported.

Four reviewers selected trials for inclusion in the review; any disagreements were resolved through consensus.

Assessment of study quality
Two reviewers assessed the quality of the included trials using the Cochrane risk of bias tool (randomisation, allocation concealment, blinding, reporting of data and other sources of bias) and the 5-point Jadad scale. Disagreements were resolved through consensus and were referred to a third reviewer if necessary.

Data extraction
Four reviewers independently abstracted data to calculate risk differences (RDs) onto a standardised form. Where additional data was required trial investigators were contacted. Disagreements were resolved by consensus.

Methods of synthesis
Summary risk differences and associated 95% confidence intervals (CIs) were estimated using the DerSimonian and Laird random-effects model. Number needed to treat (NNT) was calculated. Heterogeneity was assessed using the Q
statistic and $I^2$, as well as a visual display representing results on the L'Abbe plot. A therapeutic effect was considered significant only where no evidence of heterogeneity was found (p<0.10).

Publication bias was assessed according to the fail-safe file-drawer method.

**Results of the review**
Four RCTs were included in the review (n=1,660 patients, 970 in the rifaximin group and 690 in the control group). One trial was blinded. Three trials had adequate sequence generation. All trials had adequate allocation concealment. Incomplete outcome data was addressed and all included trials were considered to be free of selective reporting and other bias. The Jadad scores ranged from 2 to 4 points.

A significant increase in symptom relief was found in favour of rifaximin plus fibre supplementation compared with control groups (RD 29.0%, 95% CI 24.5 to 33.6; four RCTs; NNT=3).

A statistically, but not clinically, significant reduction in complication rate was found in the rifaximin group compared with the control group (RD -1.7%, 95% CI -3.2 to -1.5; four RCTs; NNT=59). No evidence of statistical heterogeneity was found ($I^2$=0%). When only acute diverticulitis was considered, the pooled risk difference in the control group for complication rate was -1.9% (95% CI -3.4 to -0.57; four RCTs; NNT=50).

Three out of four trials reported side effect data; the authors reported that no significant differences were found between treatment and control groups.

No evidence of publication bias was found.

**Authors’ conclusions**
Treatment with rifaximin plus fibre supplementation was effective in obtaining symptom relief and preventing complications at one year than fibre supplementation alone in patients with symptomatic uncomplicated diverticular disease.

**CRD commentary**
The review question was supported with clearly defined criteria. However, the authors appear to have excluded cross-over trials post-hoc without explanation. The literature search was somewhat limited; two electronic databases were searched. While it appeared that the authors may have searched for unpublished studies, study selection was restricted to published data, so potentially relevant trials may have been missed. Publication bias was addressed, but with so few included trials it was difficult to assess meaningfully. Each stage of the review process was conducted in duplicate, which reduced the potential for reviewer error or bias. The quality of the trials was assessed using appropriate criteria and the results were reported.

The authors’ conclusion follows from the results presented, but the small number of included trials and the potential for missed data mean that it should be interpreted with some caution.

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

**Research:** The authors stated that further trials on the role of rifaximin in modifying the clinical course of the disease (in reducing complication rate in a population with a higher probability of the event) were warranted.

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Not reported.

**Bibliographic details**

**PubMedID**
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.