The efficacy and safety of rifaximin for the irritable bowel syndrome: a systematic review and meta-analysis

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CRD summary
The authors concluded that treatment with rifaximin was more effective than placebo for global symptoms and bloating in patients with irritable bowel syndrome. The modest therapeutic gain was similar to that of other therapies. The authors' conclusion for short-term treatment compared with placebo reflects the evidence presented and seems reliable; the comparison with other treatments is not substantiated.

Authors' objectives
To evaluate the efficacy and tolerability of rifaximin in patients with irritable bowel syndrome (IBS).

Searching
PubMed, EMBASE, The Cochrane Library and Web of Science were searched up to May 2011. There were no language restrictions. Search terms were reported. Reference lists of identified articles and bibliographies of relevant gastrointestinal meetings (reported in the paper) were handsearched.

Study selection
Double-blind randomised controlled trials (RCTs) that compared the efficacy of rifaximin versus placebo in patients with IBS were eligible for inclusion. IBS had to be defined by accepted symptom-based criteria such as Manning, Kruis, Rome I, Rome II or Rome III. The primary outcome of interest was improvement in global IBS symptoms.

The dosages of rifaximin were 400mg or 550mg twice or three times daily. Treatment duration ranged from 10 days up to 14 days. Most included studies used Rome II criteria to assess IBS symptoms. Patient with all subtypes of IBS were included. Bloating was analysed as a secondary outcome. Adverse events were reported.

Two researchers independently screened studies for eligibility.

Assessment of study quality
Study quality was assessed based on the Cochrane risk of bias tool for sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and other sources of bias. It was unclear how many reviewers were involved in the quality assessment.

Data extraction
Two reviewers independently extracted data to enable calculation of odds ratios and 95% confidence intervals for outcomes at 10 to 14 days after completion of therapy. Disagreements were resolved by a third reviewer.

Methods of synthesis
Pooled odds ratios and 95% confidence intervals were calculated using the DerSimonian and Laird random-effects model to reflect both within-study and between-study variability. The number needed to treat (NNT) was calculated. Heterogeneity was assessed using the $X^2$ test and $I^2$ statistic ($I^2 \geq 25\%$ was considered evidence of heterogeneity). Publication bias was assessed using funnel plot. Meta-regression was performed to estimate the summary odds ratio adjusting for covariate differences across studies and treatment group.

Results of the review
Five studies were included in the review (1,803 participants). Two studies appeared to be subsets of the same population. All studies reported low risks of bias for sequence generation, allocation concealment, blinding and incomplete outcome data. One study reported high risk of bias for selective outcome reporting and one study for other source of bias. Follow-up periods ranged from 10 days to 12 weeks.

Compared to placebo, rifaximin was associated with a significant improvement in global IBS symptoms (OR 1.57, 95%
CI 1.22 to 2.01; I²=26%; five RCTs; therapeutic gain 9.8%; NNT=10.2) and bloating (OR 1.55, 95% CI 1.23 to 1.96; I²=22.9%; four studies; therapeutic gain 9.9%; NNT=10.1). The authors reported that there was no evidence of publication bias.

A summary of odds ratios adjusted for different covariance across studies was reported.

Four studies reported adverse effects data. The authors reported that no significant differences were found between treatment and placebo group. The most frequently reported adverse effects were headache, upper respiratory infection, nausea, nasopharyngitis, diarrhoea and abdominal pain.

Authors' conclusions
Rifaximin proved more effective than placebo for global symptoms and bloating in IBS patients. The modest therapeutic gain was similar to that yielded by other currently available therapies for IBS.

CRD commentary
The review question was clearly stated and inclusion criteria were appropriately defined. Several relevant sources were searched and attempts were made to minimise publication and language bias. Methods were used to minimise reviewer errors and bias in study selection and data extraction; methods were unclear for the assessment of validity. Included studies were quality assessed and appropriate methods were used for pooling the data. Some studies were small.

The authors' conclusion reflects the evidence presented and seems reliable in relation to treatment compared with placebo for the short term (≤12 weeks). The authors' conclusion in relation to comparison with other treatments is not substantiated in this review.

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

Funding
Division of Gastroenterology, University of Michigan Health System, USA.

Bibliographic details

PubMedID
22045120

DOI
10.1038/ajg.2011.355

Original Paper URL
http://www.nature.com/ajg/journal/v107/n1/abs/ajg2011355a.html

Indexing Status
Subject indexing assigned by NLM

MeSH
Anti-Infective Agents /therapeutic use; Humans; Irritable Bowel Syndrome /drug therapy; Randomized Controlled Trials as Topic; Rifamycins /therapeutic use

AccessionNumber
12012003066

Date bibliographic record published
22/02/2012
Date abstract record published
10/01/2014

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.