Meta-analysis of probiotics for the treatment of irritable bowel syndrome
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CRD summary
This review concluded that probiotic use may be associated with improvement in irritable bowel syndrome symptoms compared to placebo, but these results should be interpreted with caution. This cautious conclusion accurately reflects the nature of the evidence and the results of the review, and appears likely to be reliable.

Authors' objectives
To determine the overall efficacy of probiotics in the treatment of irritable bowel syndrome (IBS).

Searching
MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), Current Controlled Trials and ClinicalTrials.gov databases and Google Scholar were searched. Reference lists of identified studies, reviews, commentaries, books and meeting abstracts were searched. Search terms were reported. Studies published in full or as abstracts in peer-reviewed journals were eligible for inclusion.

Study selection
Randomised controlled trials (RCTs) of probiotic treatment of patients with IBS were eligible for inclusion. Trials were required to be blinded. The primary outcome was the proportion of patients with improvement in global IBS symptoms. Secondary outcomes were the proportion of subjects with improvements in one of the three common IBS symptoms of abdominal pain, bloating and flatulence. Adverse effects were reported. Outcomes were defined by self-report or clinician assessment.

All included studies were placebo controlled. Daily doses of probiotic treatment ranged from 450 to 1x10^{12} colony-forming units/day (median=9x10^9). Most studies had a short duration; 90% lasted eight weeks or less (median of four weeks). Probiotics used in the included studies included four types of Lactobacillus, Bifidobacterium infantis, Saccharomyces boulardii and Streptococcus faecium and mixes of different strains.

Two reviewers independently selected the studies for the review.

Assessment of study quality
Two independent reviewers assessed the studies for validity using the Linde Internal Validity Scale of six points based on the criteria: method of allocation, allocation concealment, baseline comparability of groups, blinding of patients and outcome assessors, and use of intention-to-treat (ITT) analysis. Disagreements were resolved through discussion. Studies that scored fewer than three points were excluded from the meta-analysis.

Data extraction
Data were extracted to permit the calculation of relative risks (RR) with 95% confidence intervals, on an ITT basis where possible. Authors were contacted for missing data where necessary.

Two reviewers independently extracted the data. Differences were resolved through discussion.

Methods of synthesis
Studies were pooled using a random-effects model if statistically significant heterogeneity were detected and a fixed-effect model in the absence of such heterogeneity. Heterogeneity was assessed using the X^2 test and the I^2 statistic. Numbers needed to treat (NNT) were calculated. Sensitivity analysis of studies weighted by quality score rather than sample size was conducted. Another sensitivity analysis excluded a large study. Characteristics of studies that showed strong effects of probiotics were compared with studies that did not show such effects. Funnel plot analysis and Begg's test were used to assess possible publication bias.
Results of the review

Twenty RCTs (n=1,404) that comprised 23 probiotic interventions were included in the review. Median sample size was 54 (range 25 to 363). There were some minor discrepancies in reported sample sizes between text and tables. Study quality was variable. Quality scores ranged from 3 to 6 points (median 4 points). None of the studies performed ITT analysis or adequately accounted for withdrawals and dropouts.

Global IBS symptoms were statistically significantly reduced in the probiotic groups compared with the placebo groups (RR 0.77, 95% CI 0.62 to 0.94, NNT=7.3; 14 RCTs; $I^2=68\%$). Probiotics were also associated with lower incidence of abdominal pain (RR 0.78, 95% CI 0.69 to 0.88, NNT=8.9; 11 RCTs; $I^2=73\%$). There was no evidence of statistically significant publication bias in either analysis.

Fourteen RCTs stated that there were no serious adverse reactions reported; three reported no safety data and three provided limited data on reactions including increased intestinal symptoms, epistaxis, aftertaste, anxiety and angina.

Authors’ conclusions

Probiotic use may be associated with improvement in IBS symptoms compared to placebo, but these results should be interpreted with caution.

CRD commentary

The review question and inclusion criteria were clear. Several relevant sources were searched. The restriction to studies published in peer-reviewed journals may have increased risks that relevant studies were omitted and publication bias was introduced into the review. The authors reported that they used methods designed to reduce reviewer bias and error at all stages of the review process. The use of meta-analysis and the exploration of heterogeneity appeared reasonable.

The authors’ cautious conclusions appeared likely to be reliable.

Implications of the review for practice and research

Practice: The authors stated that it was too soon to recommend use of probiotics for treatment of IBS in clinical practice. However, clinicians should consider discussing the evidence of benefits and risks of probiotics with patients with IBS.

Research: The authors stated that further larger studies over a longer period of time of probiotics in the treatment of IBS were required. Such studies should attempt to adhere to ITT principles and minimise loss to follow-up while using standardised outcome assessments.

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