The efficacy of probiotics in the treatment of irritable bowel syndrome: a systematic review

CRD summary
This review concluded that probiotics appeared to be efficacious in the treatment of irritable bowel syndrome, but that the magnitude of benefit and the most effective probiotic species and strain remained uncertain. The review was generally well conducted and the authors' conclusions are likely to be reliable.

Authors' objectives
To assess the efficacy of probiotics in the treatment of irritable bowel syndrome.

Searching
The following databases were searched, with no language restrictions, from inception to June 2008: MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials. Search terms were reported. Conference proceedings of relevant abstract books (details not reported) were handsearched from 2001 to 2007. Reference lists of relevant publications were also screened.

Study selection
Randomised controlled trials (RCTs) that compared probiotics with a placebo or no treatment in adults (at least 16 years old) with irritable bowel syndrome (diagnosed using recognised criteria or doctors' opinions) were eligible for inclusion. To be eligible, trials had to have a minimum duration of treatment and a follow-up of seven days. Eligible trials were permitted to use other concomitant therapies if these were administered to both the intervention and control groups.

The primary review outcome was change in symptoms, reported as a dichotomous or continuous variable. Secondary outcomes were individual symptoms (abdominal pain, bloating, flatulence and urgency) and adverse events.

Most of the included trials recruited patients with Rome II irritable bowel syndrome. The included trials evaluated a number of probiotics, including Lactobacillus, Bifidobacterium, Streptococcus and a combination of probiotics; dose regimen varied between trials. Most of the included patients were female.

Two reviewers independently selected studies for inclusion, with any disagreement resolved by consensus or a third reviewer.

Assessment of study quality
The quality of included trials was assessed using the Jadad scale, a five-point scale evaluating randomisation, blinding and withdrawals.

Two reviewers independently performed the validity assessment.

Data extraction
For continuous outcomes, the mean and standard deviation were extracted to enable the calculation of mean differences (MDs) and 95% confidence intervals (CIs). For dichotomous outcome, event rates were extracted to enable the calculation of relative risks (RRs) with 95% confidence intervals. All data were extracted on the basis of intention-to-treat analyses. Trial authors were contacted for additional data where necessary.

Data were independently extracted by two reviewers and checked by a third reviewer.

Methods of synthesis
The trials were combined in a meta-analysis using a random-effects model. Pooled relative risks or standardised mean differences (SMDs), with 95% confidence intervals, were calculated. The numbers needed to treat (NNTs), with 95% confidence intervals, were also calculated. Statistical heterogeneity was assessed using $X^2$ and $I^2$ statistics.
Subgroup analyses were performed on different types of probiotics (Lactobacillus, Bifidobacterium, Streptococcus or a combination of probiotics). Sensitivity analyses were performed to assess the impact of removing one outlying trial and trial quality on the outcomes.

Publication bias was assessed using a funnel plot and the Egger test.

**Results of the review**

Eighteen RCTs (n=1,650 patients) were included in meta-analyses. The quality of trials was generally good, with eleven trials scoring at least 4 points.

Probiotics were associated with a significant reduction in the rate of irritable bowel syndrome persisting symptoms (RR 0.71, 95% CI 0.57 to 0.88; NNT 4, 95% CI 3 to 12.5; ten RCTs), a significant improvement of irritable bowel syndrome symptoms (SMD -0.34, 95% CI -0.60 to -0.07; 15 RCTs), and a significant improvement of pain scores (SMD -0.51, 95% CI -0.91 to -0.09; ten RCTs) compared with placebo. Significant heterogeneity was observed in all these outcomes. When one outlying trial was removed for both outcomes of improvement of symptoms as a continuous variable and pain scores, significant results for the treatment effect remained but heterogeneity was no longer statistically significant.

Sensitivity analyses did not materially alter the results for the continuous outcome of improvement of symptoms. However, for trials that reported a dichotomous outcome, trials with a Jadad score of at least 4 had a significantly less treatment effect than those with a Jadad score of less than 4 (p=0.02).

Evidence of publication bias was only observed for the outcome of rate of persisting symptoms. Results of other individual symptoms such as bloating, flatulence and urgency were also reported, as were results of subgroup analyses.

Six trials reported that there were no adverse events in the probiotic or the placebo groups. For three trials reporting overall adverse events, there was no significant difference in the rate of adverse events between the probiotic and placebo groups.

**Authors' conclusions**

Probiotics appeared to be efficacious in the treatment of irritable bowel syndrome, but the magnitude of benefit and the most effective probiotic species and strain remain uncertain.

**CRD commentary**

The inclusion criteria of the review were clear. Relevant databases were searched. Efforts were made to find both published and unpublished studies with no language restriction, minimising the possibility of publication and language biases. Sufficient attempts were taken to minimise the errors and biases in the review process.

Relevant criteria were used to assess the trial quality. Adequate details of the primary trials were provided. Statistical heterogeneity was assessed and appropriate methods were used to pool the results.

The review was generally well conducted and the authors' conclusions are likely to be reliable.

**Implications of the review for practice and research**

**Practice:** The authors stated that probiotic treatment is a promising treatment strategy for patients with irritable bowel syndrome.

**Research:** The authors stated that future studies are required to establish which species, strain and dose of probiotics are most effective for the treatment of irritable bowel syndrome. Factorial designed RCTs comparing individual bacterial species with combinations are required to evaluate whether probiotics have a synergistic effect.

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