**Meta-analysis of smooth muscle relaxants in the treatment of irritable bowel syndrome**

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**Authors' objectives**

To assess the efficacy and tolerance of smooth muscle relaxants in the treatment of irritable bowel syndrome (IBS).

**Searching**

A search of MEDLINE and a manual search were combined. The keywords used were 'colonic disease', 'functional', irritable bowel syndrome' and 'randomised trial'. Additional studies were obtained by examining general reviews, references from published RCTs, and Current Contents, and by contacting pharmaceutical companies. In addition, recent meta-analyses in the Journal of Hepatogastroenterology were also used. Only published articles were considered for the review.

**Study selection**

**Study designs of evaluations included in the review**

Only double-blind, placebo-controlled RCTs were eligible for inclusion in the review.

**Specific interventions included in the review**

All smooth muscle relaxants were eligible, except those for which there was previous evidence of significant adverse effects, e.g. peppermint oil and dicyclomine bromide. Any smooth muscle relaxant for which there was only one randomised controlled trial (RCT) was also excluded from the review. The interventions used in the studies included in the review were: cimetropium (150 mg), hyoscine (30 or 40 mg), mebeverine (400 or 405 mg), otilonium (120 or 320 mg), pinaverium (150 mg) and trimebutine (300 or 600 mg). Only placebo-controlled studies were eligible for inclusion in the review.

**Participants included in the review**

Participants with IBS (diagnosis not specified) were eligible for inclusion in the review. Trials had to have included at least 51% of patients with IBS in the study population.

**Outcomes assessed in the review**

Studies included had to have assessed at least one of the following end points: global assessment of symptoms by the patient or physician; abdominal pain; constipation; or abdominal distension.

**How were decisions on the relevance of primary studies made?**

The authors do not state how the papers were selected for the review; however, this information may have been provided in the second publication (see Other Publications of Related Interest no.1).

**Assessment of study quality**

Each study was assigned a score for methodology using the methods detailed in a second publication from one of the authors (see Other Publications of Related Interest no.1). The authors do not state how the papers were assessed for validity; however, this information may have been provided in the second publication (see Other Publications of Related Interest no.1).

**Data extraction**

The authors do not state how the data were extracted for the review; however, this information may have been provided in the second publication (see Other Publications of Related Interest no.1).

**Methods of synthesis**
How were the studies combined?
The studies were pooled in a meta-analysis. For each end point, heterogeneity between control groups was assessed using the fixed-effect model of Peto (see Other Publications of Related Interest no.2) and the random-effects model of DerSimonian and Laird (see Other Publications of Related Interest no.3). The results of the two approaches were compared. The main end point was the percentage of patients with a global improvement in symptoms during the treatment period. Other end points were the percentage of patients with improvements in abdominal pain, constipation, transit, or abdominal distension, and the percentage of patients without adverse effects.

How were differences between studies investigated?
A sensitivity analysis was conducted when a significant difference was seen between the results of the fixed-effect and random-effects models. Sensitivity analyses were conducted according to the type of drug, treatment duration, prevalence of constipated patients and methodological quality (more or less than the median 9).

Results of the review
A total of 23 RCTs were included in the meta-analysis.

The mean percentage of patients with global improvement (21 trials) was 38% in the placebo group and 56% in the smooth muscle relaxant group. The pooled Peto odds ratio (OR) was 2.13 (95% confidence interval, CI: 1.77, 2.58, P=0.001) and the mean risk difference was 22% (95% CI: 13, 32, P<0.001).

The percentage of patients with pain improvement (11 trials) was 41% in the placebo group and 53% in the smooth muscle relaxant group. The Peto OR was 1.65 (95% CI: 1.30, 2.10, P<0.001) and the risk difference was 18% (95% CI: 7, 28, P<0.001).

The mean percentage of patients with improvement for abdominal distension was 35% in the placebo group, compared with 44% in the smooth muscle relaxant group. The Peto OR was 1.46 (95% CI: 1.10, 1.94, P=0.008).

There were no significant differences for improvements in constipation or transit, or for adverse events.

Authors' conclusions
Smooth muscle relaxants were superior to placebo in the treatment of IBS.

CRD commentary
This review addressed an appropriate question using clearly defined inclusion and exclusion criteria. The exclusion of smooth muscle relaxants for which there was previous evidence of significant adverse effects was not clearly defined; this may have introduced some subjective bias into the review. Similarly, the exclusion of those interventions that were studied in only a single RCT did not seem warranted, given that the meta-analysis pooled the results from all smooth muscle relaxants. Also, the diagnosis of IBS, which is multi-faceted, was not defined in this review.

The search strategies were not comprehensive, but this was counteracted to some extent by the authors use of previous meta-analyses and their inclusion of non-English language studies. The methodology of the review was not described in detail but may be available in another publication (see Other Publications of Related Interest no.1). As this review included only double-blind placebo-controlled RCTs, the basic quality of the included studies can be assumed to be adequate. The review presented adequate details of the primary studies, and the methods used for the meta-analysis appear to have been appropriate.

The authors’ conclusions were supported by the data presented. The possibility of the introduction of bias should be borne in mind. The review was supported in part by SOLVAY pharmaceutical company (manufacturers of mebeverine and pinaverium).

Implications of the review for practice and research
Practice: The authors state the need for muscle relaxants in the management of IBS.
Research: The authors state the need to include non-English language trials in any meta-analysis.

**Bibliographic details**

**PubMedID**
11207510

**Other publications of related interest**

This additional published commentary may also be of interest. Chey WD. Review: smooth muscle relaxants improve symptoms and reduce pain in irritable bowel syndrome. Evid Based Med 2001;6:153.

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Abdominal Pain /drug therapy /etiology; Adult; Colonic Diseases, Functional /drug therapy /pathology; Female; Humans; Male; Middle Aged; Odds Ratio; Parasympatholytics /pharmacology /therapeutic use; Placebos; Treatment Outcome

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**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.