

Review: Tegaserod or alosetron is effective for the irritable bowel syndrome

Brandt LJ, Bjorkman D, Fennerty MB, et al. Systematic review on the management of irritable bowel syndrome in North America. *Am J Gastroenterol.* 2002;97:S7-26.

QUESTION

In patients with the irritable bowel syndrome (IBS), what are the most effective therapies and diagnostic strategies?

DATA SOURCES

Studies were identified by searching 2 databases, reviewing the bibliographies of relevant studies, and contacting pharmaceutical companies for unpublished trials.

STUDY SELECTION

For IBS therapy, studies were selected if they were randomized controlled trials (RCTs) published in English, enrolled adults with IBS, compared an IBS treatment available in the United States with placebo or control therapy, and evaluated relief of IBS symptoms. Diagnostic studies were selected if they defined a cohort of patients with IBS using validated and published symptom-based criteria, used a diagnostic test with known properties, and quantified results as normal or abnormal.

DATA EXTRACTION

For therapy trials, data were extracted on study design and methodological features, patient characteristics, dosage and administration schedule, study duration, and results. The main outcome measure was patient-rated improvement in global IBS symptoms. For diagnostic studies, data were extracted on the test performed and its diagnostic standard, prevalence of confirmed organic gastrointestinal disease detected by the test, and test accuracy.

COMMENTARY

Many questions remain regarding the management of IBS. Design flaws, including use of varied definitions of IBS, different study endpoints, inadequate power, and short treatment duration make the early IBS literature difficult to interpret. Furthermore, high placebo responses increase the burden of proving superiority of therapies for IBS. Thus, the systematic review by Brandt and colleagues, which provides a critical review of the literature on the management of IBS, is important reading for health care providers treating this condition.

The review evaluated the quality of trials using criteria established by the Rome Committee, an international group of functional bowel disorder experts. Because these criteria were not available until 1999, it is not surprising that few available studies were of high quality. An important message from this review is that much of the current medical management of IBS is not evidence-based.

Based on low- to intermediate-quality data, several medications possibly improve individual IBS symptoms—loperamide for diarrhea, fiber for constipation, and tricyclic antidepressants for abdominal pain. Only recent studies evaluating alosetron for women with IBS and diarrhea and tegaserod for women with IBS and constipation were found to be

MAIN RESULTS

RCTs evaluated antispasmodics (dicyclomine and hyoscyamine), bulking agents (corn fiber, calcium polycarbophil, wheat bran, psyllium, and ispaghula husk), the anti-diarrheal agent loperamide, tricyclic antidepressants (desipramine, amitriptyline, trimipramine, and doxepin), the 5HT₄ (serotonin) receptor agonist tegaserod, the 5HT₃ (serotonin) receptor antagonist alosetron, and behavioral therapies. Of the trials that reported improvement in global IBS symptoms, the best results were seen with tegaserod (4 trials) for IBS with constipation and alosetron (1 trial) for IBS with diarrhea. Results for global IBS symptoms are in the Table.

6 studies of medium- to high-quality found a low prevalence of organic disease in

patients with IBS symptoms but no alarm features. Diagnostic tests (flexible sigmoidoscopy, colonoscopy, barium enema, complete blood count, serum chemistries, and fecal occult blood test) were unlikely to detect organic disease but may be useful in providing reassurance.

CONCLUSION

In patients with the irritable bowel syndrome (IBS), tegaserod improves IBS symptoms in patients with constipation and alosetron improves IBS symptoms in those with diarrhea.

Source of funding: Unrestricted educational grant from Novartis Pharmaceuticals.

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Interventions for the irritable bowel syndrome (IBS)*

Interventions	Number of trials	Quality	Number of patients	Number of trials showing improvement in global IBS symptoms
Antispasmodics	3	Low to int	196	1 (dicyclomine)
Bulking agents	13	Low to int	513	4 (ispaghula husk)
Antidiarrheal agents	3	Low to int	155	0
Tricyclic antidepressants	6	Low	638	2 (1 desipramine, 1 doxepin)
Tegaserod	4	High	3719	4
Alosetron	4	High	2441	1 (only 1 trial reported global IBS symptoms)
Behavioral therapy	16	Int	651	Not reported

*Int = intermediate.

of high quality. Alosetron and tegaserod, although indicated for different patient populations, offer similar therapeutic gains of 5% to 27% over placebo for the primary endpoints of their respective studies. In addition, each drug has shown efficacy for multiple IBS symptoms.

Safety issues have led to restricted use of alosetron in the United States. No serious safety issues have been reported with tegaserod (1). Although the therapeutic gain offered by these drugs is relatively small and confined to selected subgroups of patients, this is not surprising for such a heterogeneous condition as IBS, and the studies in this review show benefits for selected groups. Given our need to effectively identify subpopulations more likely to respond to specific agents, it is unlikely that any single drug will be a "magic bullet" for all patients with IBS.

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Reference

1. Tougas G, Snape WJ Jr, Otten MH, et al. *Aliment Pharmacol Ther.* 2002;16:1701-8.