

# Studies suggest possible overlap of IBS symptoms and inflammatory bowel disease

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Research unveiled today at the American College of Gastroenterology's (ACG) 77th Annual Scientific meeting in Las Vegas suggests a possible overlap of symptoms of two prevalent GI disorders: irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD) and further suggests a possible link between subtle GI tract inflammation and IBS symptoms—a link that is also the focus of the first systemic review of the literature on this topic and an editorial both published in this month's *American Journal of Gastroenterology*.

One study presented today found that mesalamine granules, an anti-inflammatory drug used to treat [ulcerative colitis](#), improved [abdominal pain](#) and stool consistency in diarrhea-predominant IBS. In the second study, researchers found that tricyclic antidepressants (TCAs)—which are commonly used to treat IBS [patients](#)—may be effective in managing moderately-severe functional symptoms such as abdominal pain and diarrhea in patients with [inflammatory bowel disease](#).

Crohn's disease (CD) and ulcerative colitis (UC) are two of the most common forms of inflammatory bowel disease which affects about 1.4 million Americans, with approximately 30,000 new cases diagnosed each year, according to the Crohn's and Colitis Foundation of America. UC is marked by inflammation of the lining of the colon and rectum, together known as the [large intestine](#) while CD can cause inflammation anywhere from the mouth to the anus anywhere along the lining of the digestive tract. It most commonly affects the [small intestine](#) and the colon.

"This inflammation can lead to symptoms of abdominal pain and diarrhea, symptoms which are typical of many IBS patients, for instance those IBS patients with diarrhea predominant symptoms or mixed diarrhea and constipation," said Brian E. Lacy, M.D., Ph.D., Professor of Medicine at the Dartmouth Medical School and the Director of the GI Motility Laboratory at the Dartmouth-Hitchcock Medical Center in Lebanon, New Hampshire.

"One theory is that IBS develops subsequent to an inflammatory process or infectious process in the GI tract. Microscopic inflammation can then persist in the lining of the GI tract, or the adjacent lymph nodes. This inflammation may produce symptoms of pain and diarrhea similar to those experienced by patients with Crohn's disease. Thus, it is quite likely that an overlap exists between IBS and IBD, both with respect to etiology and symptoms," added Dr. Lacy.

### **Some IBS Patients Find May Find Relief from Anti-Inflammatory Drug Used in IBD**

IBS is a chronic functional gastrointestinal disorder which for many sufferers is marked by abdominal discomfort, bloating, constipation and/or diarrhea and can be categorized based on these symptoms: IBS-D is accompanied by diarrhea, IBS-C is accompanied by constipation and IBS-M includes both diarrhea and constipation. Research suggests that IBS is caused by changes in the nerves and muscles that control sensation and motility of the bowel. IBS affects 10 to 15 percent of the U.S. population and is 1.5 times more common in women than in men, according to the National Digestive Diseases Information Clearinghouse.

Patients with IBS-D showed a statistically significant improvement in abdominal pain and diarrhea after a 12-week course of mesalamine granules (1500 mg), a form of mesalamine or 5-aminosalicylic acid (5-ASA) which is an anti-inflammatory drug used to treat inflammatory

disorders of the digestive tract such as ulcerative colitis and mild-to-moderate Crohn's disease.

Researchers from California Pacific Medical Center in San Francisco conducted the prospective randomized, double-blind, placebo-controlled multicenter study to investigate the efficacy of mesalamine granules in the treatment of IBS-D after a review of uncontrolled, publicly available data suggested aminosalicylate therapy may be of benefit to patients with IBS-D.

In the study, "Mesalamine Granules 1500 mg Once daily for 12 Weeks Provides Adequate Relief of [IBS Symptoms](#) in [Irritable Bowel Syndrome](#) with Diarrhea: Results from a Phase 2 Trial," 148 patients with IBS-D (by Rome III criteria) were randomized to receive MG 750 mg (47 patients) and MG 1500 mg (51 patients) or placebo (50 patients) once daily for 12 weeks. An intent-to-treat analysis of patients who were monthly responders in both abdominal pain and stool consistency for two months or more during the three-month treatment period was compared between groups by a Logistics regression model. A weekly responder in abdominal pain was defined as a 30 percent or more improvement from baseline in the weekly average abdominal pain score on a 10-point scale. A weekly responder in stool consistency was defined as a 50 percent reduction in number of days in a week with stool consistency of Type 6 or 7 compared with baseline using the Bristol Stool Scale. Monthly responders were patients who were weekly responders in abdominal pain and stool consistency for at least 2 out of 4 weeks.

In the primary endpoint analysis, a significantly greater proportion of patients (47 percent) were monthly responders for at least 2 months in the MG 1500mg group compared with placebo (28 percent). However, statistically significant differences were not observed in the mesalamine granules 750mg group (31.9 percent) compared with the placebo (28 percent).

"In a post-hoc analysis of the data, those subjects who had greater inflammation as measured by a median C-reactive protein level greater than 2.2mg/L had a 65.4 percent improvement in pain and stool consistency at 12 weeks when compared to a 25 percent response to placebo," said co-investigator Jeffrey Aron, M.D. "IBS is a more mild expression of intolerance of the person's immune system to the environment of the gut in that it disturbs function rather than destroying structure in certain anatomical and pathologic patterns as seen in ulcerative colitis and Crohn's disease. Control of inflammation, to me, is the key to treating these disorders."

"Mesalamine granules at a dosage of 1500mg once a day for 12 weeks provided statistically significant improvement in abdominal pain and stool consistency in patients with IBS-D and emphasized the role of treating inflammation in this disorder," added Dr. Aron. "These results confirm earlier observations that aminosalicylates may have a therapeutic role in symptomatic treatment of IBS-D but further large-scale studies may be warranted in this population."

### **Common IBS Antidepressant Therapy May Help Reduce Abdominal Pain, Diarrhea in IBD Patients**

In the study, "Tricyclic Antidepressants in the Management of IBD Patients with Functional GI Symptoms," researchers from Washington University in St. Louis conducted a retrospective study of open-label antidepressant therapy to learn whether tricyclic antidepressants would reduce IBS-type symptoms in patients with IBD. "We often see patients with IBD in remission or with mild disease activity on anti-inflammatory therapies who are presenting with functional GI symptoms, such as abdominal pain and diarrhea," said co-investigator Heba Iskandar, M.D.

Abdominal pain and diarrhea were equally common with baseline symptom scores moderate-severe in the study's two cohorts: 81 IBD

patients in clinical remission or with mild inflammation who also had persistent GI symptoms (average age 41.3 years; 56 female/25 male; 58 CD/23 UC); and a comparator group of 65 Symptomatic IBS patients without IBD (average age 43.9 years; 51 female/14 male).

Approximately half of the patients in both groups experienced at least moderate improvements with tricyclic antidepressant therapy, according to the study. "Within the IBD group, ulcerative colitis patients had a significantly better response than Crohn's disease patients, perhaps reflecting differences in their underlying pathophysiology," said Dr. Iskandar.

"IBD presents itself differently in each patient so the disease is often difficult to manage and there is no one-size, fits-all treatment approach. Our main focus with this study was whether IBD patients could improve with a well-tolerated and effective symptom-based therapy since many of them are already on maximal anti-inflammatory regimens to control their disease," explained Dr. Iskandar. She noted that IBD patients often have to take several types of medications in various combinations and dosages such 5-aminosalicylate acid (5-ASA), immunosuppressants, corticosteroids and biologics to keep the disease under control.

"This study suggests that IBD patients with persistent symptoms despite treated inflammation may benefit from a tricyclic antidepressant," said Dr. Iskandar. "But these drugs should be considered as an adjunctive therapy for IBD patients with minimal disease activity —not a replacement for their current treatment regimens." She added that the results of this study need prospective validation where patients could be randomized and followed over time to establish their response duration.

## **IBS-Type Symptoms May Pose Challenge for Physicians Caring for IBD Patients**

"IBS-type symptoms may pose a challenge for the physician caring for the patient with IBD, especially, when they occur in the context of apparent remission of IBD. In this situation, IBS-type symptoms may represent ongoing but clinically unapparent inflammation. New diagnostic methods such as measuring fecal calprotectin levels may prove helpful in addressing these clinical dilemmas," says Eamonn M.M. Quigley, M.D., FACG, Professor of Medicine and Human Physiology and a Principal Investigator at the Alimentary Pharmabiotic Centre at the National University of Ireland, Cork, Ireland.

Dr. Quigley co-authored an editorial in the October issue of *The American Journal of Gastroenterology*, "[Irritable Bowel Symptoms" in IBD: Diagnostic Uncertainty Meets Pathological Reality.](#)" He and Alexander C. Ford, M.D. discussed the prevalence of IBS symptoms in IBD with Journal co-editor Paul Moayyedi, MD, FACG in this month's [AJG Author Podcast](#). Dr. Ford is the co-investigator of the [recent systematic review and meta-analysis](#) that demonstrated that prevalence of symptoms compatible with IBS in patients with IBD is as high as 40 percent.

Provided by American College of Gastroenterology

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