Antibiotics for the Treatment of Functional Gastrointestinal Symptoms: A Case Series

by Anthony J. Lembo, Andrew W. DuPont, Brooks D. Cash, Charles I. Saperstein, and Christine L. Frissora

Treatment options for patients with irritable bowel syndrome (IBS) are limited. Recent randomized, double-blind, controlled studies and open-label trials have suggested a potential clinical benefit for antibiotics in the treatment of IBS and other functional gastrointestinal disorders. However, benefits observed in well-controlled studies may not be fully representative of results observed in clinical practice because of clinical trial inclusion and exclusion criteria, dose and duration of therapy, and the potential synergistic effects of other treatments. This case series describes the administration of antibiotics for the treatment of functional gastrointestinal symptoms in a “real-world” clinical setting. While no definitive conclusions can be drawn regarding the efficacy and safety of antibiotics in this setting, these cases illustrate the potential benefit of antibiotics for the management of functional gastrointestinal disorders and highlight areas for further study.

INTRODUCTION

Evidence continues to accumulate on the potential pathogenic role of bacteria in irritable bowel syndrome (IBS) (1). Therapeutic approaches that can positively impact bacterial growth and inflammatory host response may be beneficial in improving care for patients with functional gastrointestinal (GI) symptoms. Several open-label and randomized, double-blind, controlled trials indicate that antibiotics may be a useful treatment option for functional GI symptoms in patients with or without a clinical diagnosis of IBS (2–10). However, the efficacy and safety observed in clinical trials may not be fully representative of results observed in clinical practice because of clinical study inclusion and exclusion criteria, dose and duration of therapy, and the potential synergistic effects of other treatments. This case series describes the successful administration of antibiotics for the treatment of functional gastrointestinal symptoms in a “real-world” clinical setting. While no definitive conclusions can be drawn regarding the efficacy and safety of antibiotics in this setting, these cases illustrate the potential benefit of antibiotics for the management of functional gastrointestinal disorders and highlight areas for further study.
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functional GI symptoms in a “real-world” clinical setting. These relevant and useful observations help to supplement information gleaned from clinical trials. These observations do not, however, provide conclusive evidence to support the use of antibiotics in patients with functional bowel disorders.

CASES

Case 1: Patient With Alternating IBS
A 69-year-old female presented with a >40-year history of intermittent abdominal pain, gas and bloating, and diarrhea alternating with constipation. She indicated that significant worsening of gas and bloating and diarrhea occurred after a 2-day episode of gastroenteritis in the summer of 2003. It was presumed that the episode of gastroenteritis was caused by a viral infection, based on the predominant symptom of vomiting, the short duration of acute symptoms, and a similar report of symptoms by her spouse shortly after her illness presented. Results of a colonoscopy, in which random biopsies were analyzed for microscopic colitis, were normal. A lactulose breath test indicated an abnormal hydrogen level that supported a diagnosis of small intestinal bacterial overgrowth (SIBO).

The patient had tried several IBS medications, including hyoscyamine sulfate (Levsin®, Tablets, Schwarz Pharma, Inc., Milwaukee, WI), tegaserod maleate (Zelnorm®, Novartis Pharmaceuticals Corp, East Hanover, NJ), amoxicillin/clavulanate potassium (Augmentin®, GlaxoSmithKline, Research Triangle Park, NC), nortriptyline, and loperamide. The patient reported adverse effects with hyoscyamine sulfate (heart palpitations), nortriptyline (weight gain), tegaserod (light-headedness and diarrhea), and loperamide (increased bloating and constipation), and administration of amoxicillin/clavulanate did not improve symptoms. Thus, the patient was prescribed the antibiotic rifaximin (Xifaxan®, Salix Pharmaceuticals, Inc., Morrisville, NC) 400 mg three times daily for 10 days.

Overall, symptoms substantially improved during rifaximin treatment, with a marked decrease in stool frequency and resolution of abdominal pain. After completion of the initial course of rifaximin, the patient was prescribed rifaximin 200 mg twice daily for 6 months as maintenance therapy. Symptoms remained minimal during this time. During repeated attempts to discontinue rifaximin maintenance therapy, GI symptoms flared within 1 week of rifaximin cessation. However, symptoms improved again upon reinstatement of rifaximin therapy, with improvement noted within 3 days of retreatment. Therefore, maintenance therapy with rifaximin 200 mg twice daily was continued for an additional 6 months. All symptoms improved substantially, although the patient continued to experience some abdominal discomfort. In an attempt to further alleviate the abdominal discomfort, rifaximin 400 mg three times daily was prescribed for 7 consecutive days per month. However, IBS symptoms returned 3 days after completion of the first round of cyclic therapy, and the patient was prescribed rifaximin 200 mg twice daily, which lead to substantial improvement in symptoms. Patient has continued to receive rifaximin 200 mg twice daily as long-term maintenance therapy.

In this case, IBS refractory to previous treatments appeared to respond to rifaximin but flared after treatment discontinuation, raising the issue of identifying the optimal dose and duration of antibiotic therapy. Concerns about the risk for bacterial antibiotic resistance have generally discouraged the administration of antibiotics as maintenance treatment for functional bowel disorders. However, rifaximin differs from other antibiotics in that it is minimally absorbed (<0.4%) and has not been associated with clinically relevant resistance after >20 years of worldwide clinical use. Given this favorable profile, rifaximin may be an appropriate candidate for assessing the efficacy and safety of antibiotics as IBS maintenance therapy, and controlled studies are warranted.

Case 2: Patient With Diarrhea-Predominant IBS
A 56-year-old female presented in March 2004 with a 2.5-year history of abdominal pain and discomfort associated with diarrhea, bloating, and gas. The patient was diagnosed with diarrhea-predominant IBS, in accordance with Rome II criteria. The patient reported no history of gastroenteritis, and previous evaluations including computed tomography, endoscopy, serologic laboratory testing, stool sampling, and colonoscopy...
(2003) were normal. A fecal fat test performed in 2003 suggested a slightly elevated fecal fat level, and although repeat testing was negative, the patient received treatment with pancreatic enzymes. During her most recent evaluation, the patient reported an increase in the severity of abdominal bloating, gas, and pain, with no improvement following treatment (proton pump inhibitor and uncoated pancreatic enzymes; hyoscine as needed). A lactulose breath test was negative for the presence of SIBO. The patient was subsequently treated with concomitant desipramine hydrochloride (Norpramin®, sanofi-aventis, Bridgewater, NJ) at doses of 50 mg to 100 mg for 6 months with no improvement in GI symptoms. At that point, all IBS treatments were discontinued, and no appreciable change in symptoms was observed during 4 weeks of observation.

Because of continued complaints of bloating and loose, foul-smelling, floating stools and physician doubts regarding the diagnostic accuracy of the previous lactulose breath test, the patient received SIBO empiric therapy: metronidazole (Flagyl®, G.D. Searle LLC, Chicago, IL) 250 mg twice daily for 1 month. A slight improvement in symptoms was noted; however, symptoms recurred to previous levels of severity within 4 weeks after completion of metronidazole treatment, and the patient was subsequently treated with neomycin 500 mg twice daily and erythromycin 250 mg twice daily for 1 month. Multiple follow-up assessments conducted during and after this round of antibiotic therapy indicated a normalization of symptoms (i.e., substantial decrease in bloating, abdominal pain, and gas and improved stool consistency).

Approximately 3 months posttreatment, the patient relapsed with GI symptoms similar to those reported prior to empiric therapy (e.g., bloating and abnormal stool formation). Although repeated breath testing was not performed, SIBO was again suspected as the etiologic agent. An additional course of antibiotics was prescribed: erythromycin 250 mg twice daily for 1 month followed by erythromycin 250 mg once daily for 1 month. Symptoms were described as greatly improved during this therapy.

It would appear that IBS symptoms responded only to erythromycin-containing regimens, which raises the question of the mechanism by which erythromycin produced symptomatic improvement. Of note, results of a gastric-emptying study, performed during the 4-week period that the patient had discontinued all IBS medications, were within normal limits. It is possible that the effects of erythromycin on motility (11), rather than its antibacterial action, contributed to IBS symptom improvement. However, her original symptoms (i.e., foul-smelling diarrhea, bloating, and gas) and persistent improvement with antibiotic administration were consistent with the presence of SIBO, and potential inaccuracies during breath testing may have confounded a positive diagnosis.

Case 3: Patient With Diarrhea-Predominant IBS

A 47-year-old female presented in November 2004 with a 15-year history of IBS with predominant symptoms of diarrhea, abdominal pain, bloating, and gas. Symptom worsening prompted this consultation. Previous colonoscopy, laboratory tests, and stool samples were normal; the patient had no history of gastrointestinal, and her medical history indicated fibromyalgia and chronic fatigue syndrome. The patient had been previously treated with multiple IBS medications, including antispasmodics, antidepressants, and antidiarrheals, none of which relieved symptoms.

Based on symptom assessment, the presence of SIBO was suspected; a breath test was not performed. The patient was treated with rifaximin 200 mg twice daily for 14 days followed by maintenance treatment with tegaserod maleate 2 mg nightly for 3 months. Remarkable improvement in gas and bloating was observed after rifaximin treatment. The patient also reported decreased joint pain and an improvement in overall well-being. However, 3 months after completion of tegaserod maleate maintenance therapy, the patient experienced GI symptom relapse. The patient refused additional treatment and was lost to follow-up.

This patient was treated with antibiotic therapy on the basis of suspected SIBO and IBS. Whether empiric antibiotic therapy is the appropriate strategy for the treatment of SIBO and IBS is unclear. Tests, such as lactulose and glucose breath tests, may increase the certainty of a SIBO diagnosis and could help to guide treatment choices. The feasibility of routine breath testing in clinical practice warrants exploration.
Case 4: Patient With Constipation-Predominant IBS
A 58-year-old female presented in June 2005 with a 6-month history of severe abdominal pain and cramping, constipation, and excessive gas and bloating. Symptoms had emerged following a 5-day bout of gastroenteritis that was attributed to food poisoning. The patient also presented with dyspepsia characterized by epigastric discomfort and postprandial pain. Past medical history was unremarkable except for fallopian tubal ligation. Colonoscopy, endoscopy, celiac screening, and microbiologic testing did not identify a specific cause of symptoms. Previous treatments for GI symptoms had included antispasmodics, omeprazole, and fiber. Medications at the time of examination included omeprazole (Prilosec®, Merck & Co Inc., Whitehouse Station, NJ), dicyclomine hydrochloride (Bentyl®, Akorn Inc., Decatur, IL), and omeprazole plus ranitidine hydrochloride (Zantac®, GlaxoSmithKline, Research Triangle Park, NC).

Based on the information described above, the patient was diagnosed with postinfectious IBS and dyspepsia. In addition, SIBO was suspected based on GI symptoms, but a breath test was not performed. The patient discontinued previous therapies and was prescribed rifaximin 200 mg three times daily for 10 days. Ranitidine hydrochloride was also prescribed as needed. The patient was advised to avoid dairy products and to take a daily chewable multivitamin. Upon completion of rifaximin treatment, the patient was prescribed Saccharomyces boulardii lyo (Florastor®, Biocodex Inc, Creswell, OR) 250 mg daily. During a follow-up visit 8 weeks after initiation of rifaximin therapy, the patient reported a marked improvement in GI symptoms; abdominal pressure and bloating, in particular, had lessened. No adverse effects attributed to antibiotic treatment were reported. The patient was prescribed probiotic maintenance therapy 3 times weekly and rifaximin 200 mg as needed (e.g., 1–2 tablets/week) for recurrence of abdominal bloating and pressure.

This case illustrates the administration of concomitant probiotic and antibiotic maintenance therapy for functional bowel symptoms. The efficacy and role of probiotics in the management of SIBO and IBS have not been well established (12), but probiotics may positively impact colonic microflora, which can be disrupted in IBS. Although further research is needed, probiotics may be useful as adjunctive therapy with antibiotics or as maintenance therapy for IBS and SIBO after antibiotic treatment.

CONCLUSIONS
While no definitive conclusions about the efficacy of antibiotics for functional GI symptoms can be drawn on the basis of this case series alone, the cases, considered in context with published clinical studies (2–10), help illustrate potential future applications for antibiotics. Studies of antibiotic monotherapy and adjunctive therapy are warranted to further clarify the potential impact of antibiotics in IBS and SIBO.

References