Small intestinal bacterial overgrowth: Management

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INTRODUCTION

Small intestinal bacterial overgrowth (SIBO) is a condition in which the small bowel is colonized by excessive aerobic and anaerobic microbes that are normally present in the colon. The majority of patients with SIBO present with bloating, flatulence, abdominal discomfort, or diarrhea. This topic will review the management of SIBO. The etiology, pathogenesis, clinical manifestations, and diagnosis of SIBO are presented separately. (See "Small intestinal bacterial overgrowth: Clinical manifestations and diagnosis".)

INITIAL APPROACH

The mainstay of therapy for SIBO are antibiotics to reduce (rather than eradicate) small intestinal bacteria. In addition, some patients require treatment of underlying nutritional deficiencies and associated ileitis/colitis.

Antibiotic therapy — Antibiotic therapy is typically begun on an empiric basis. The selection of antimicrobial regimens is based on the pattern of bacterial overgrowth, the prevalence of risk factors for drug-resistance (recent or repeated prior exposure), relevant antibiotic allergies, and cost [1]. It is unnecessary to repeat breath testing if symptoms resolve with treatment. (See "Small intestinal bacterial overgrowth: Clinical manifestations and diagnosis", section on 'Carbohydrate breath test'.)

- **Hydrogen-predominant bacterial overgrowth** – In patients with hydrogen predominant bacterial overgrowth without excess methane production, we use rifaximin (1650 mg/day for 14 days). Rifaximin is non-absorbable rifamycin derivative. It is well tolerated and has been

demonstrated to be effective in the treatment of SIBO [2-8]. However, the high cost of rifaximin has limited its use.

- **Methane-predominant bacterial overgrowth** – In patients with methane-predominant bacterial overgrowth, a combination of neomycin 500 mg twice daily and rifaximin 550 mg three times daily for 14 days [9].

Alternative antibiotic regimens for the treatment of SIBO are listed in the table (table 1). There are few randomized trials of antibiotics to treat bacterial overgrowth and the evidence for use of specific antibiotics is largely from observational studies [2-8]. Studies suggest that clinical response rates may be higher with rifaximin than other antibiotics. In a randomized controlled trial in which 142 patients with SIBO were randomized to seven days of rifaximin (1200 mg/day) or metronidazole (750 mg/day), glucose breath test normalization rates at one month were significantly higher in patients treated with rifaximin compared with metronidazole (63 versus 44 percent).

Correction of micronutrient deficiency — Deficiencies of vitamin B12, fat-soluble vitamins, iron, thiamine, and niacin can be associated with severe SIBO and should be corrected when present. (See "Small intestinal bacterial overgrowth: Clinical manifestations and diagnosis", section on 'Laboratory findings' and "Treatment of vitamin B12 and folate deficiencies", section on 'Vitamin B12' and "Vitamin D deficiency in adults: Definition, clinical manifestations, and treatment", section on 'Vitamin D repletion' and "Overview of water-soluble vitamins".)

Treatment of associated ileocolitis — SIBO-associated ileitis or colitis is usually mild and resolves with treatment of SIBO. However, severe cases require treatment that is the same as for patients with inflammatory bowel disease [10]. The management of Crohn disease is discussed in detail separately. (See "Overview of the medical management of mild (low risk) Crohn disease in adults".)

TREATMENT RESPONSE AND RECURRENCE

Approximately 40 percent of patients with small intestinal bacterial overgrowth (SIBO) have persistent symptoms after initial antibiotic treatment [11]. Recurrent SIBO is also frequent after antibiotic treatment. In a study involving 80 patients with SIBO, recurrence rates three, six, and nine months after successful treatment with rifaximin were 13, 28, and 44 percent, respectively [11]. Recurrence was more likely in older adults, those with a history of an appendectomy, and with chronic proton pump inhibitor (PPI) use.

INADEQUATE RESPONSE TO INITIAL THERAPY OR RECURRENCE

Evaluation — We empirically treat patients with a second course of antibiotics if they have a partial improvement in symptoms or early recurrence (<3 months). For patients with recurrent symptoms ≥3 months after initial antibiotic treatment, a repeat breath test can confirm recurrence of SIBO. Patients with no improvement in symptoms after two courses of antibiotic therapy or progressive symptoms should be evaluated for alternative diagnoses. (See "Evaluation of the adult with abdominal pain" and "Approach to the adult with chronic diarrhea in resource-rich settings".)

Subsequent antibiotic regimen — In patients with partial response to recurrent SIBO, the choice of antibiotic therapy should be guided by the patient's initial treatment regimen. Antibiotics included in the initial regimen should generally be avoided. However, patients with an inadequate initial response or recurrent SIBO after treatment with rifaximin can be retreated with a two-week course of rifaximin [12]. Alternative antibiotic regimens are also summarized in the following table (table 1). Compliance with antibiotic therapy should be reinforced.

Elemental diet — We reserve the use of an elemental diet to patients who cannot tolerate antibiotics or have failed to respond to antibiotic therapy for SIBO. Limited observational data suggest that an elemental diet can induce remission of symptoms in patients with SIBO. However, elemental diets are expensive and compliance is limited by palatability. In a retrospective study, 124 patients with methane- or hydrogen-predominant SIBO were treated exclusively with elemental diet for at least two weeks [13]. Patients continued the diet for a total of three weeks if the breath test did not normalize by week two. At two weeks, 74 of 93 patients (80 percent) had a normal breath test. Five of 19 subjects who were treated with an elemental diet for an additional week had a normal breath test by day 22 for a cumulative response of 85 percent. Patients who normalized their breath test had a significant improvement in symptoms as compared with those with persistently abnormal breath tests (66 versus 12 percent). Fourteen patients discontinued the elemental diet and were excluded from the analysis.

PREVENTION OF RECURRENCE

Treat the underlying etiology in all patients — All patients should receive therapy directed against the underlying etiology of SIBO (table 2). As examples, medications that can decrease intestinal motility (eg, narcotics, benzodiazepines) or cause achlorhydria should be avoided when possible. Prokinetics are a useful adjunct in patients with SIBO due to an underlying dysmotility. In the case of iatrogenic surgical causes of SIBO and for fistulas between the proximal and distal intestine, surgery may be necessary in patients who fail to respond to antibiotics and have significant weight loss and diarrhea. Patients with dilated segments of bowel with poor motility may benefit from intestinal tapering procedures. (See "Small intestinal bacterial overgrowth: Clinical manifestations and diagnosis", section on 'Evaluation to determine the etiology'.)

Antibiotic prophylaxis in selected patients — Antibiotic prophylaxis for SIBO should be reserved for patients with ≥4 distinct and well-documented episodes within one year and risk factors for recurrent SIBO (eg, short bowel syndrome, jejunal diverticulosis). In such patients we administer antibiotics on a periodic basis (5 to 10 days out of every month or every other week). Antibiotics are changed to prevent the development of resistance to a specific drug. The frequency with which antibiotics are rotated varies from monthly to every six months.

Interventions with unclear role

- **Low FODMAP diet** – Fermentable oligo-, di-, and monosaccharides and polyols (FODMAPs) are short-chain carbohydrates that are poorly absorbed and are osmotically active in the intestinal lumen where they are rapidly fermented by small intestinal bacteria. A diet low in FODMAPs improves bloating and gas in patients with irritable bowel syndrome, however, evidence to support a low FODMAP diet in the prevention or management of patients with SIBO are lacking. (See "Obesity in adults: Dietary therapy".)

- **Probiotics** – There are limited data to support probiotics in the treatment of SIBO [10,14-17]. In a 2017 meta-analysis that included 18 studies there was no significant difference in the incidence of SIBO in patients on probiotics as compared with the control group [17]. Patients with SIBO who were treated with probiotics had higher rates of gut decontamination and decrease in breath hydrogen concentration and abdominal pain but there was no significant improvement in diarrhea.

- **Statins** – Statins have been shown to inhibit growth and production of methane in several Methanobrevibacter isolates [18]. However, studies in patients with SIBO are lacking.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Small intestinal bacterial overgrowth".)

SUMMARY AND RECOMMENDATIONS

- Small intestinal bacterial overgrowth (SIBO) is a condition in which the small bowel is colonized by excessive aerobic and anaerobic microbes that are normally present in the colon. The majority of patients with SIBO present with bloating, flatulence, abdominal discomfort, or watery diarrhea. (See 'Introduction' above.)

- We suggest antibiotic treatment for SIBO with rifaximin (**Grade 2C**). In patients with methane-predominant bacterial overgrowth, we use a combination of neomycin and rifaximin. Adequate antimicrobial coverage can also be achieved with other antibiotic combinations (table 1). Deficiencies of vitamin B12, fat-soluble vitamins, iron, thiamine, and niacin are usually associated with severe SIBO and require supplementation when present. (See 'Antibiotic therapy' above.)

- Approximately 40 percent of patients with SIBO have persistent symptoms after initial antibiotic treatment and 40 percent have recurrent SIBO within nine months of antibiotic treatment. (See 'Treatment response and recurrence' above.)

- We empirically treat patients with a second course of antibiotics if they have a partial improvement in symptoms or early recurrence (<3 months). For patients with recurrent symptoms ≥3 months after initial antibiotic treatment, we perform a repeat carbohydrate breath test to diagnose SIBO. (See 'Inadequate response to initial therapy or recurrence' above and 'Evaluation' above and "Small intestinal bacterial overgrowth: Clinical manifestations and diagnosis", section on 'Carbohydrate breath test'.)

- Patients with persistent symptoms after two courses of antibiotic therapy or progressive symptoms should be evaluated for alternative diagnoses. We reserve the use of an elemental diet to patients who cannot tolerate antibiotics or have failed to respond to antibiotic therapy for SIBO. (See 'Evaluation' above.)

- All patients should receive therapy directed against the underlying etiology of SIBO (table 2). We reserve antibiotic prophylaxis for SIBO for selected patients with multiple recurrences of SIBO and risk factors for recurrence (eg, short bowel syndrome, jejunal diverticulosis). (See 'Prevention of recurrence' above.)

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GRAPHICS

Oral antibiotic therapy for small intestinal bacterial overgrowth (SIBO)

Antibiotic	Adult dose	Pediatric dose*	Notes
Single-agent regimens (7 to 10 days)¶			
Amoxicillin-clavulanate	500 mg three times per day[1] or 875 mg twice per day	25 mg/kg per day (amoxicillin component) in two or three divided doses	
Norfloxacin (no longer available in United States)Δ	400 mg twice per day[1]	Not adequately evaluated	Not recommended in children, older adults, pregnancy, patients at risk for tendinopathy or abnormal cardiac rhythmΔ
Rifaximin	550 mg three times per day[2]	Children ≥12 years: Refer to adult dosing Children 3 to 11 years: 200 mg three times per day[3]	Less clinical resistance observed relative to other choices Low systemic exposure
Combination regimens (7 to 10 days)¶			
Metronidazole with a cephalosporin	Metronidazole 500 mg three times per day; **plus** Cephalexin 500 mg three or four times per day	Metronidazole 20 mg/kg per day in two or three divided doses; **plus** Cephalexin 30 mg/kg per day in three or four divided doses	
Metronidazole with trimethoprim-sulfamethoxazole (co-trimoxazole)	Metronidazole 500 mg three times per day; **plus** Trimethoprim-sulfamethoxazole 1 double-strength tablet twice per day◇	Metronidazole 20 mg/kg per day in two or three divided doses; **plus** Trimethoprim-sulfamethoxazole 10 to 12 mg/kg per day (trimethoprim component) in two divided doses[4]	Rare serious cutaneous allergic reactions

Suggested antibiotic regimens for reduction of gut flora overgrowth and symptomatic improvement. Doses listed are for patients with normal renal function. Dose adjustment of norfloxacin and trimethoprim-sulfamethoxazole may be needed in renal impairment. For specific adjustments and additional detail, refer to the Lexicomp drug-specific monographs included within UpToDate.

* The pediatric daily dose should not exceed the usual daily dose for adult patients. Pediatric doses listed in this table are for children six years and older except as noted.
¶ A single course of 7 to 10 days will often improve symptoms. However, some patients require prolonged therapy before a response is seen and recurrence after treatment is common; refer to accompanying text.
Δ Ciprofloxacin 500 mg orally twice per day in adults (or in children 20 to 30 mg/kg per day in two divided doses) is a reasonable alternative where norfloxacin is unavailable and use of a fluoroquinolone is appropriate. Additional information on fluoroquinolone use in children and other populations is provided separately; refer to the UpToDate topic review of fluoroquinolones.
◇ One double-strength (DS) tablet contains trimethoprim 320 mg with sulfamethoxazole 800 mg.

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Disorders associated with bacterial overgrowth

Small intestinal stasis
Anatomic abnormalities
Small intestinal diverticulosis
Surgically created blind loops (end-to-side anastomosis)
Strictures (Crohn disease, radiation, surgery)
Abnormal small intestinal motility
Diabetes mellitus
Scleroderma
Idiopathic intestinal pseudo-obstruction
Radiation enteritis
Crohn disease
Abnormal communication between the proximal and distal gastrointestinal tract
Gastrocolic or jejunocolic fistula
Resection of the ileocecal valve
Associations usually with multifactorial causes
Hypochlorhydria due to atrophic gastritis or medications. These are usually not clinically significant unless they coexist with concomitant motility disturbances of the small bowel.
Immunodeficiency states (common variable immunodeficiency, AIDS, severe malnutrition)
Chronic pancreatitis
Cirrhosis
Alcoholism
End-stage renal disease
Advanced age
Total parenteral nutrition (TPN) in children

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