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. The majority of patients with SIBO present with bloating, flatulence, abdominal discomfort, or diarrhea or constipation in the case of intestinal methanogen overgrowth (IMO). 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 after confirming SIBO by breath test. 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'.)

- **Small intestinal bacterial overgrowth** – In patients with small intestinal bacterial overgrowth, we use rifaximin (1650 mg per 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.

- **Intestinal methanogen overgrowth (IMO)** – In patients with IMO, we use a combination of neomycin 500 mg twice daily and rifaximin 550 mg 3 times daily for 14 days [9,10]. (See "Small intestinal bacterial overgrowth: Clinical manifestations and diagnosis", section on 'Carbohydrate breath test'.)

Alternative antibiotics for treatment of SIBO include trimethoprim-sulfamethoxazole, norfloxacin, ciprofloxacin, metronidazole, tetracycline, or amoxicillin-clavulanic acid [10]. 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 per day) or metronidazole (750 mg per day), glucose breath test normalization rates at one month were significantly higher in patients treated with rifaximin compared with metronidazole (63 versus 44 percent). Treatment of SIBO with high hydrogen sulfide is still under study. (See 'Society guideline links' below.)

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 replacement' 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 [11]. (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 [12]. 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 [12]. 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-abundant 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 course of rifaximin or an alternative antibiotic [13]. 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 [14]. 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, opioids, 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 fermentation eating or a low fermentable oligo-, di-, and monosaccharides and polyols (FODMAP) diet** – 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. Other low fermentation diets are less restrictive and can be used more long term. (See "Obesity in adults: Dietary therapy".)

- **Probiotics –** There are limited data to support probiotics in the treatment of SIBO [11,15-18]. 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 [18]. 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 [19]. However, studies in patients with intestinal methanogen overgrowth 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

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

- **Initial management** – We suggest antibiotic treatment for SIBO with rifaximin (**Grade 2C**). In patients with intestinal methanogen overgrowth, we use a combination of neomycin and rifaximin (table 1). Adequate antimicrobial coverage can also be achieved with other antibiotic combinations. 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.)

- **Patients with persistent or recurrent symptoms**

  - 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.)

- **Evaluation of the underlying etiology and recurrence prevention** – 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[1]	Pediatric dose*[2,3]	Notes
Rifaximin¶	550 mg three times daily	Children and adolescents ≥12 years: Refer to adult dosing Children 3 to 11 years: 200 mg three times daily[4]	Preferred by UpToDate author Efficacy 61 to 78% Low systemic absorption High cost relative to other options
Alternative antibiotics			
Trimethoprim-sulfamethoxazole (TMP-SMX)	160/800 mg twice daily	4 to 5 mg/kg of trimethoprim component per dose twice daily[5]	
Ciprofloxacin	500 mg twice daily	10 to 20 mg/kg per dose twice daily	Routine use in children avoided due to potential risk of musculoskeletal toxicity (usually mild)
Amoxicillin-clavulanate	875 mg twice per day	25 to 30 mg/kg per day (amoxicillin component) in two or three divided doses	
Metronidazole	250 mg three times per day	10 mg/kg per dose twice daily	
Doxycycline	100 mg once daily to twice per day	Children ≥8 years and >45 kg: Refer to adult dosing Children <8 years: Not recommended	Less risk of dental staining in children with short course Use and dosing extrapolated from data with tetracycline
Tetracycline	250 mg four times per day	Children ≥8 years: 10 to 15 mg/kg per dose three times daily Children <8 years: Not recommended	Use in children <8 years old avoided due to risk of permanent tooth discoloration

Suggested antibiotic regimens for reduction of gut flora overgrowth and symptomatic improvement. The author usually treats for 10 days per course with the exception of rifaximin a 14-day course is given. Doses listed are for patients with normal renal function. For indications and administration of antibiotic therapy in SIBO, refer to the UpToDate clinical topic review.

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* Optimal antibiotic regimen(s) in children have not been established. Antimicrobial choices and doses shown are those used by the UpToDate author and some other experts when antibiotic therapy of SIBO is indicated in children[2,3]. The pediatric daily dose should not exceed the usual daily dose for adult patients. Pediatric doses listed in this table are for children ≥6 years except as noted.

¶ In patients with intestinal methane overgrowth (IMO) the author uses a combination regimen of oral rifaximin 550 mg three times daily with oral neomycin 500 mg twice daily for 14 days.

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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 kidney disease
Advanced age
Total parenteral nutrition (TPN) in children

Graphic 81285 Version 6.0

Contributor Disclosures

Nicholas J Talley, MD, PhD Patent Holder: Australian Provisional Patent [Diagnostic marker for functional gastrointestinal disorders]; Biomarkers of irritable bowel syndrome [Irritable bowel syndrome]; Mayo Clinic [Dysphagia questionnaire]; Mayo Clinic [Bowel Disease questionnaire]; Nepean Dyspepsia Index [Dyspepsia]; Nestec [Irritable bowel syndrome]; Singapore Provisional Patent [BDNF Tissue Repair Pathway]. Grant/Research/Clinical Trial Support: Alimetry [Gastric mapping device research collaboration]; Allakos [Gastric eosinophilic disease]; AstraZeneca [Eosinophilic gastritis, eosinophilic gastroenteritis]; Intrinsic Medicine [Bowel syndrome with constipation]; NHMRC Centre for Research Excellence in Digestive Health [NHMRC Investigator grant]. Consultant/Advisory Boards: Adelphi Values [Functional dyspepsia]; Allakos [Gastric eosinophilic disease, AK002]; AstraZeneca [Eosinophilic gastritis, eosinophilic gastroenteritis]; AusEE [Eosinophilic gut diseases]; Bayer [Inflammatory bowel syndrome]; BluMaiden [Microbiome Ad Board]; Comvita Mānuka Honey [Digestive health]; Dr Falk Pharma [Eosinophilia]; GlaxoSmithKline Australia [Educational speaker eosinophilic gut disease]; Glutagen [Celiac disease]; International Foundation for Functional Gastrointestinal Disorders [Advisory board, functional GI disorders]; Intrinsic Medicine [Human milk oligosaccharide]; IsoThrive [Esophageal microbiome]; Planet Innovation [Gas capsule, inflammatory bowel syndrome]; Progenity Inc [Intestinal capsule]; Rose Pharma [IBS]; Viscera Labs [Inflammatory bowel syndrome, diarrhea]. Other Financial Interest: Elsevier textbook royalties [Medical education]. All of the relevant financial relationships listed have been mitigated. **J Thomas Lamont, MD** Equity Ownership/Stock Options: Allurion [Weight loss]. Consultant/Advisory Boards: Teledoc [Gastrointestinal diseases]. All of the relevant financial relationships listed have been mitigated. **Shilpa Grover, MD, MPH, AGAF** No relevant financial relationship(s) with ineligible companies to disclose.

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