ejpmr, 2017,4(12), 339-349

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

SMALL INTESTINAL BACTERIAL OVERGROWTH: TOO MUCH OF A GOOD THING CAN BE A BAD THING

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Article Received on 26/09/2017 **Article Revised on 16/10/2017** **Article Accepted on 06/11/2017**

ABSTRACT

Small intestinal bacterial overgrowth (SIBO), defined as excessive bacteria in the small intestine, remains a poorly understood disease. Initially thought to occur in only a small number of patients, it is now apparent that this disorder is more prevalent than previously thought. Patients with SIBO vary in presentation, from being only mildly symptomatic to suffering from chronic diarrhea, weight loss, and malabsorption. A number of diagnostic tests are currently available, although the optimal treatment regimen remains elusive. Recently there has been renewed interest in SIBO and its putative association with irritable bowel syndrome. In this comprehensive review, the discussion will be on the epidemiology, pathogenesis, clinical manifestations, diagnosis and treatment of SIBO.

KEYWORDS: Gut flora, Bacterial overgrowth, small intestinal bacterial overgrowth, diarrhea, bloating, motility disorders, antibiotics, FODMAP.

INTRODUCTION

Gut flora, (gut microbiota, or gastrointestinal microbiota) is the complex community of microorganisms that live in the digestive tracts of humans and other animals, including insects. The gut metagenome is the aggregate of all the genomes of gut microbiota. One of the reasons why the gut has so much influence on your health has to do with the 100 trillion bacteria--about three pounds worth--that line the intestinal tract. This is an extremely complex living system that aggressively protects your body from outside offenders. The gut is one niche that human microbiota inhabit. In humans, the gut microbiota has the largest numbers of bacteria and the greatest number of species compared to other areas of the body. In humans the gut flora is established at one to two years after birth and by that time the intestinal epithelium and the intestinal mucosal barrier that it secretes have co-developed in a way that is tolerant to and even supportive of, the gut flora and that also provides a barrier to pathogenic organisms. The relationship between some gut flora and humans is not merely commensal (a non-harmful coexistence), but rather a mutualistic relationship. Some human gut microorganisms benefit the host by fermenting dietary fiber into short-chain fatty acids (SCFAs), such as acetic acid and butyric acid, which are then absorbed by the host. Intestinal bacteria also play a role in synthesizing vitamin B and vitamin K as well as metabolizing bile acids, sterols and xenobiotics. The systemic importance of the SCFAs and other compounds they produce are like hormones and the gut flora itself appears to function like an endocrine organ and dysregulation of the gut flora has been correlated with a host of inflammatory and autoimmune conditions. The composition of human gut microbiota changes over time, when the diet changes and as overall health changes. A systematic review from 2016 examined the preclinical and small human trials that have been conducted with certain commercially available strains of probiotic bacteria and identified those that had the most potential to be useful for certain central nervous system disorders. The four dominant bacterial phyla in the human gut are ***Firmicutes***, ***Bacteroidetes***, ***Actinobacteria*** and ***Proteobacteria***. Most bacteria belong to the genera *Bacteroides*, *Clostridium*, *Faecalibacterium*, *Eubacterium*, *Ruminococcus*, *Peptococcus*, *Peptostreptococcus* and *Bifidobacterium*. Other genera, such as *Escherichia* and *Lactobacillus*, are present to a lesser extent. Species from the genus *Bacteroides* alone constitute about 30% of all bacteria in the gut, suggesting that this genus is especially important in the functioning of the host. Fungal genera that have been detected in the gut include *Candida*, *Saccharomyces*, *Aspergillus*, *Penicillium*, *Rhodotorula*, *Trametes*, *Pleospora*, *Sclerotinia*, *Bullera* and *Galactomyces*, among others. *Rhodotorula* is most frequently found in individuals with inflammatory bowel disease while Candida is most frequently found in individuals with hepatitis B cirrhosis and chronic

hepatitis B. *Archaea* constitute another large class of gut flora which are important in the metabolism of the bacterial products of fermentation. Small intestinal bacterial overgrowth (SIBO) refers to a condition in which abnormally large numbers of bacteria (usually defined as at least 100,000 bacteria per ml of fluid) are present in the small intestine and the types of bacteria in the small intestine resemble more the bacteria of the colon than the small.[1]

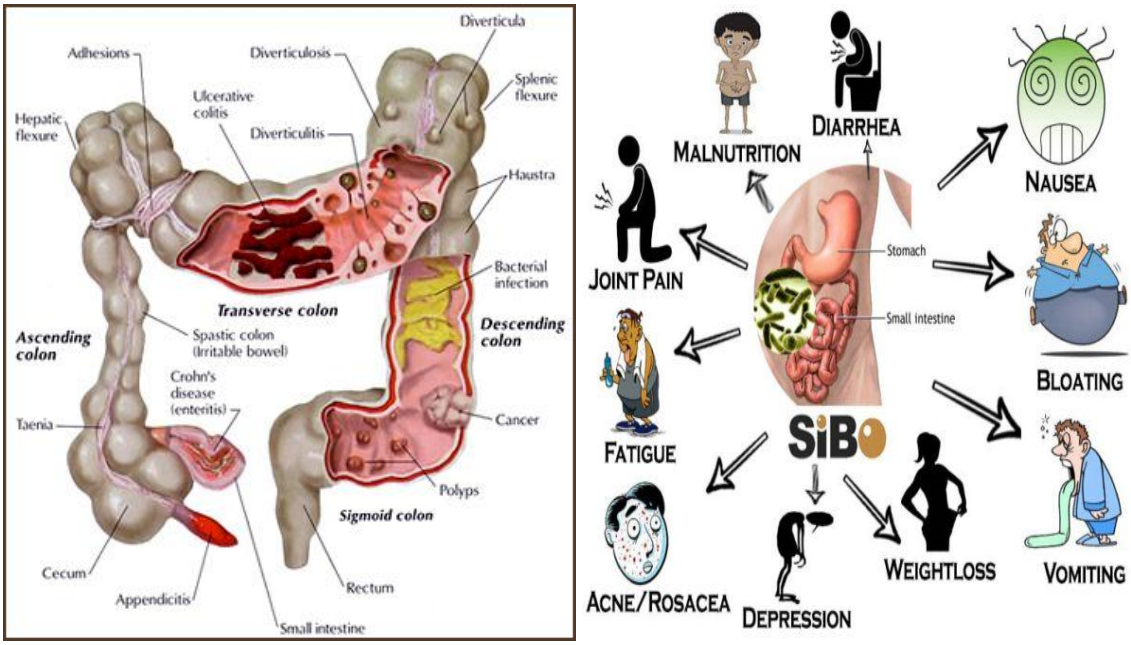


Figure-1: Intestine and SIBO.

SIBO: Have you ever eaten something and within a few hours realized that your stomach is so bloated that you can't button your pants? It's not uncommon for the patients to tell that they wake up with a flat belly and by the end of the day they look six months pregnant. Small intestine bacterial overgrowth (SIBO), also termed bacterial overgrowths, or small bowel bacterial overgrowth syndrome (SBBOS), is a disorder of excessive bacterial growth in the small intestine. Unlike the colon (or large bowel), which is rich with bacteria, the small bowel usually has fewer than 10,000 organisms per millilitre. Patients with bacterial overgrowth typically develop symptoms including **nausea, bloating, vomiting, diarrhea, malnutrition, weight loss and malabsorption**, which is caused by a number of mechanisms.[2]

Even if you haven't experienced abdominal swelling to such an extreme, any amount of bloating is not normal; it's a sign of intestinal inflammation. If you're having gas and/or bloating regularly, you could have food sensitivities and/or a gut infection, such as small intestinal bacterial overgrowth, or SIBO.

What is SIBO? SIBO occurs when the bacteria in our gut get out of balance and overgrow. I often say, "Too much of a good thing can be a bad thing." How do we get too much of some bacteria over others? This can manifest in several different ways and often occurs in those eating a diet high in sugar, alcohol and refined carbohydrates. Certain strains of bacteria feed off of refined carbohydrates and break them down into short-chain fatty acids, creating gas and causing bloating. Another strain of bacteria can break down bile salts before the body has a chance to use them. Bile salts are crucial for the breakdown of fats; without them, the end result is fat malabsorption or diarrhea. Finally, a third type of bacteria can produce toxins that damage the lining of the small intestine. This prevents your body from absorbing the nutrients you need, much like what we see with a leaky gut.[3]

What causes the bacterial overgrowth? Our gut relies on nerves, muscles, enzymes and neurotransmitters to properly digest food. While enzymes mainly break down our food, the nerves, muscles and neurotransmitters physically move the food through our digestive tract from the stomach to the small intestine and to the colon. When this happens in a healthy gut, bacteria get passed through the digestive tract along with the food to its final destination in the colon. Problems arise when something interferes with this process. Damage to the nerves or muscles in the gut can result in leftover bacteria in the small intestine, increasing the risk for SIBO. For example, diabetes mellitus and scleroderma can both affect the muscles in the gut, leaving room for SIBO to develop. Physical obstructions in the gut, like scarring from surgeries or Crohn's disease, can also cause an abnormal buildup of bacteria in the small intestine. Diverticulitis, which is tiny pouches that can form in the wall of the small intestine, can also collect bacteria instead of passing it on to the colon, where it belongs.

There are also medications that influence or disrupt the normal gut flora, such as antibiotics, acid-blocking drugs and steroids.[4]

10 Signs of Small Intestinal Bacterial Overgrowth (SIBO): Gas, Bloating, Diarrhea, Abdominal pain or cramping, Constipation (much less common than diarrhea), Diagnosis of irritable bowel syndrome or inflammatory bowel disease, Food intolerances such as gluten, casein, lactose, fructose and more, Chronic illnesses such as fibromyalgia, chronic fatigue syndrome, diabetes, neuromuscular disorders and autoimmune diseases, B_{12} deficiency as well as other vitamins and minerals, Fat malabsorption can cause SIBO.

How to test for SIBO?

Breath Test: This is the gold standard, however it's quite cumbersome. Individuals must fast for 12 hours, breathe into a small balloon, ingest a precise amount of sugar and repeat breath samples every 15 minutes for 3 or more hours. Abnormal breath tests can also signify pancreatic insufficiency and celiac disease.

Organix Dysbiosis Test: This functional medicine lab test the urine for by-products of yeast or bacteria in the small intestine. If your small intestine is housing a yeast or bacterial overgrowth, byproducts will appear in your urine, indicating their presence. This test is much easier for patients and only requires one single urine specimen.

Comprehensive Stool Test: This is also a functional medicine lab test looking at the flora of the large intestines.[5]

How to treat SIBO? The standard treatment for SIBO patients is an antibiotic called Xifaxan. Because Xifaxan is not well absorbed throughout the body, it mostly stays in the gut and is very effective against SIBO. The problem with Xifaxan is that most insurance companies have approved it as a treatment for traveler's diarrhea, but not a treatment for SIBO, so it can be very cost-prohibitive for most patients. Similar to Candida overgrowth, those who are susceptible to SIBO may have reoccurrence after treatment. It is advised to adopt a long-term diet that is low in carbohydrates and especially refined carbohydrates. The diagnosis of bacterial overgrowth is made by a number of techniques, with the gold standard being an aspirate from the jejunum that grows in excess of 105 bacteria per millilitre.

Gold standard: In medicine and statistics, gold standard test is usually diagnostic test or benchmark that is the best available under reasonable conditions. Other times, gold standard is the most accurate test possible without restrictions.

Both meanings are different because for example, in medicine, dealing with conditions that would require an autopsy to have a perfect diagnosis, the gold standard test would be the best one that keeps the patient alive instead of the autopsy.

The phrase is therefore ambiguous and its meaning should be deduced from the context in which it appears. Part of the ambiguity stems from its usage in economics where gold standard is a concept within monetary theory.[6]

Figure-2: Intestine and bacterial overgrowth

In medicine: "Gold standard" can refer to the criteria by which scientific evidence is evaluated. For example, in resuscitation research, the "gold standard" test of a medication or procedure is whether or not it leads to an increase in the number of neurologically intact survivors that walk out of the hospital. Other types of medical research might regard a significant decrease in 30-day mortality as the gold standard. The AMA Style Guide

prefers the phrase Criterion Standard instead of "gold standard", and many medical journals now mandate this usage in their instructions for contributors. For instance, Archives of biological Medicine and Rehabilitation specifies this usage. When the criterion is a whole clinical testing procedure it is usually referred to as clinical definition or clinical case definition. A hypothetical ideal "gold standard" test has a sensitivity of 100% with respect to the presence of the disease (it identifies all individuals with a well defined disease process; it does not have any false-negative results) and a specificity of 100% (it does not falsely identify someone with a condition that does not have the condition; it does not have any false-positive results). In practice, there are sometimes no true "gold standard" tests. These are called "imperfect" or "alloyed" gold standards.

As new diagnostic methods become available, the "gold standard" test may change over time. For instance, for the diagnosis of aortic dissection, the "gold standard" test used to be the aortogram, which had a sensitivity as low as 83% and a specificity as low as 87%. Since the advancements of magnetic resonance imaging, the magnetic resonance angiogram (MRA) has become the new "gold standard" test for aortic dissection, with a sensitivity of 95% and a specificity of 92%. Before widespread acceptance of any new test, the former test retains its status as the "gold standard."

Test calibration: Because tests can be incorrect (yielding a false-negative or a false-positive), results should be interpreted in the context of the history, physical findings, and other test results in the individual being tested. It is within this context that the sensitivity and specificity of the "gold standard" test is determined.[7]

When the gold standard is not a perfect one, its sensitivity and specificity must be calibrated against more accurate tests or against the definition of the condition. This calibration is especially important when a perfect test is available only by autopsy. It is important to emphasize that a test has to meet some interobserver agreement, to avoid some bias induced by the study itself.

Gold standard ambiguity: Sometimes "gold standard test" refers to the best performing test available. In these cases, there is no other criterion against which it can be compared and it is equivalent to a definition. When referring to this meaning, gold standard tests are normally not performed at all. This is because the gold standard test may be difficult to perform or may be impossible to perform on a living person (i.e. the test is performed as part of an autopsy or may take too long for the results of the test to be available to be clinically useful).

Other times, "gold standard" does not refer to the best performing test available, but the best available under reasonable conditions. For example, in this sense, a MRI is the gold standard for brain tumour diagnosis, though it is not as good as a biopsy. In this case the sensitivity and specificity of the gold standard are not 100% and it is said to be an "imperfect gold standard" or "alloyed gold standard". The term ground truth refers to the underlying absolute state of information; the gold standard strives to represent the ground truth as closely as possible. While the gold standard is a best effort to obtain the truth, ground truth is typically collected by direct observations. In machine learning and information retrieval, "ground truth" is the preferred term even when classifications may be imperfect; the gold standard is assumed to be the ground truth. Calibration errors can lead to misdiagnosis. Risk factors for the development of bacterial overgrowth include dysmotility; anatomical disturbances in the bowel, including fistulae, diverticulitis and blind loops created after surgery, and resection of the ileo-cecal valve; gastroenteritis-induced alterations to the small intestine; and the use of certain medications, including proton pump inhibitors. Small bowel bacterial overgrowth syndrome is treated with an elemental diet or antibiotics, which may be given in a cyclic fashion to prevent tolerance to the antibiotics, sometimes followed by prokinetic drugs to prevent recurrence if dysmotility is a suspected cause.[8]

Signs and symptoms: Bacterial overgrowth can cause a variety of symptoms, many of which are also found in other conditions, making the diagnosis challenging at times. Many of the symptoms are due to malabsorption of nutrients due to the effects of bacteria which either metabolize nutrients or cause inflammation of the small bowel, impairing absorption. The symptoms of bacterial overgrowth include nausea, flatus, constipation, bloating, abdominal distension, abdominal pain or discomfort, diarrhea, fatigue, and weakness. SIBO also causes an increased permeability of the small intestine. Some patients may lose weight. Children with bacterial overgrowth may develop malnutrition and have difficulty attaining proper growth. Steatorrhea, a sticky type of diarrhea where fats are not properly absorbed and spill into the stool, may also occur.[9]

Patients with bacterial overgrowth that is longstanding can develop complications of their illness as a result of malabsorption of nutrients. Anemia may occur from a variety of mechanisms, as many of the nutrients involved in production of red blood cells are absorbed in the affected small bowel. Iron is absorbed in the more proximal parts of the small bowel, the duodenum and jejunum, and patients with malabsorption of iron can develop a microcytic anemia, with small red blood cells. Vitamin B_{12} is absorbed in the last part of the small bowel, the ileum, and patients who malabsorb Vitamin B_{12} can develop a megaloblastic anemia with large red blood cells. In older adults, small bowel bacterial overgrowth is associated with a higher frequency of diarrhea, a lower body mass index, and a significantly lower serum albumin concentration.

Risk Factors: Certain people are more predisposed to the development of bacterial overgrowth because of certain risk factors. These factors can be grouped into three categories: (1) disordered motility or movement of the small bowel or anatomical changes that lead to stasis, (2) disorders in the immune system and (3) conditions that cause more bacteria from the colon to enter the small bowel. Problems with motility may either be diffuse, or localized to particular areas. Diseases like scleroderma and possibly celiac disease cause diffuse slowing of the bowel, leading to increased bacterial concentrations. More commonly, the small bowel may have anatomical problems, such as out-pouchings known as diverticula that can cause bacteria to accumulate. After surgery involving the stomach and duodenum (most commonly with Billroth II antrectomy), a blind loop may be formed, leading to stasis of flow of intestinal contents. This can cause overgrowth, and is termed blind loop syndrome.[10]

Disorders of the immune system can cause bacterial overgrowth. Chronic pancreatitis, or inflammation of the pancreas can cause bacterial overgrowth through mechanisms linked to this. The use of immunosuppressant medications to treat other conditions can cause this, as evidenced from animal models. Other causes include inherited immunodeficiency conditions, such as common variable immunodeficiency, IgA deficiency and hypogammaglobulinemia. Finally, abnormal connections between the bacteria-rich colon and the small bowel can increase the bacterial load in the small bowel. Patients with Crohn's disease or other diseases of the ileum may require surgery that removes the ileocecal valve connecting the small and large bowel; this leads to an increased reflux of bacteria into the small bowel. After bariatric surgery for obesity, connections between the stomach and the ileum can be formed, which may increase bacterial load in the small bowel. Proton pump inhibitors, a class of medication that are used to reduce stomach acid, is associated with an increased risk of developing SIBO. In recent years, several proposed links between SIBO and other disorders have been made. However, the usual methodology of these studies involves the use of breath testing as an indirect investigation for SIBO. Breath testing has been criticized by some authors for being an imperfect test for SIBO, with multiple known false positives. Irritable bowel syndrome. Some studies reported up to 80% of patients with irritable bowel syndrome (IBS) have SIBO (using the hydrogen breath test). Subsequent studies demonstrated statistically significant reduction in IBS symptoms following therapy for SIBO.[11]

There is a lack of consensus however, regarding the suggested link between IBS and SIBO. Other authors concluded that the abnormal breath results so common in IBS patients do not suggest SIBO, and state that "abnormal fermentation timing and dynamics of the breath test findings support a role for abnormal intestinal bacterial distribution in IBS." There is general consensus that breath tests are abnormal in IBS; however, the disagreement lies in whether this is representative of SIBO.

Fibromyalgia: Fibromyalgia is a poorly understood pain condition. Lactulose breath testing has shown that patients with fibromyalgia have a more pronounced degree of abnormal results compared to both IBS patients and the general population. This study also demonstrated positive correlation between the amount of pain and the degree of abnormality on the breath test. A subsequent study also demonstrated increased prevalence of intestinal hyperpermeability, which some believe occurs commonly with SIBO.[12]

Rosacea: Intestinal bacteria may play a causal role in the dermatological condition rosacea. A recent study subjected patients to a hydrogen breath test to detect the occurrence of SIBO. It was found that significantly more patients were hydrogen-positive than controls indicating the presence of bacterial overgrowth (47% v. 5%, $p<0.001$).

Hydrogen-positive patients were then given a 10-day course of rifaximin, a non-absorbable antibiotic that does not leave the digestive tract and therefore does not enter the circulation or reach the skin. 96% of patients experienced a complete remission of rosacea symptoms that lasted beyond 9 months. These patients were also negative when retested for bacterial overgrowth. In the 4% of patients that experienced relapse, it was found that bacterial overgrowth had returned. These patients were given a second course of rifaximin which again cleared rosacea symptoms and normalized hydrogen excretion.[13]

In another study, it was found that some rosacea patients that tested hydrogen-negative were still positive for bacterial overgrowth when using a methane breath test instead. These patients showed little improvement with rifaximin, as found in the previous study, but experienced clearance of rosacea symptoms and normalization of methane excretion following administration of the antibiotic metronidazole, which is effective at targeting methanogenic intestinal bacteria. These results suggest that optimal antibiotic therapy may vary between patients and that diverse species of intestinal bacteria appear to be capable of mediating rosacea symptoms. This may also explain the improvement in symptoms experienced by some patients when given a reduced carbohydrate diet. Such a diet would restrict the available material necessary for bacterial fermentation and thereby reduce intestinal bacterial populations.

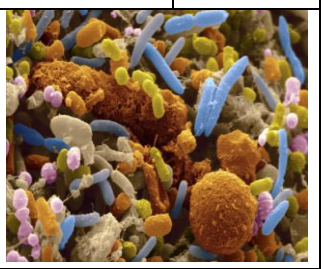
Bacterium	Incidence (%)	Bacterium	Incidence (%)	Bacterium	Incidence (%)	Bacterium	Incidence (%)
Bacteroides fragilis	100	*Escherichia coli*	100	*Staphylococcus aureus*	30–50	*Clostridium tetani*	1–35
Bacteroides melaninogenicus	100	*Enterobacter sp.*	40–80	*Lactobacillus*	20–60	*Clostridium septicum*	5–25
Bacteroides oralis	100	*Klebsiella sp.*	40–80	*Clostridium perfringens*	25–35	*Pseudomonas aeruginosa*	3–11
Enterococcus faecalis	100	*Bifidobacterium bifidum*	30–70	*Proteus mirabilis*	5–55	*Salmonella enterica*	3–7
Faecalibacterium prausnitzii	common	*Peptostreptococcus sp.*	common	*Peptococcus sp.*	common		

Table-1: Bacteria commonly found in the human colon

Pathophysiology: Certain species of bacteria are more commonly found in aspirates of the jejunum taken from patients with bacterial overgrowth. The most common isolates are *Escherichia coli*, *Streptococcus*, *Lactobacillus*, *Bacteroides* and *Enterococcus* species. Soon after birth, the gastrointestinal tract is colonized with bacteria, which, on the basis of models with animals raised in a germ-free environment, have beneficial effects on function of the gastrointestinal tract. There are 500-1000 different species of bacteria that reside in the bowel. However, if the flora of the small bowel is altered, inflammation or altered digestion can occur, leading to symptoms. Many patients with chronic diarrhea have bacterial overgrowth as a cause or a contributor to their symptoms. While the consensus definition of chronic diarrhea varies, in general it is considered to be an alteration in stool consistency or increased frequency, that occurs for over three weeks. Various mechanisms are involved in the development of diarrhea in bacterial overgrowth. First, the excessive bacterial concentrations can cause direct inflammation of the small bowel cells, leading to an inflammatory diarrhea. The malabsorption of lipids, proteins and carbohydrates may cause poorly digestible products to enter into the colon. This can cause diarrhea by the osmotic drive of these molecules, but can also stimulate the secretory mechanisms of colonic cells, leading to a secretory diarrhea.[14]

There is an overlap in findings between tropical sprue, post-infectious irritable bowel syndrome and small intestinal bacterial overgrowth in the pathophysiology of the three conditions and also SIBO can similarly sometimes be triggered by an acute gastrointestinal infection.

Diagnosis: The diagnosis of bacterial overgrowth can be made by physicians in various ways. Malabsorption can be detected by a test called the D-xylose test. Xylose is a sugar that does not require enzymes to be digested. The D-xylose test involves having a patient drink a certain quantity of D-xylose, and measuring levels in the urine and blood; if there is no evidence of D-xylose in the urine and blood, it suggests that the small bowel is not absorbing properly (as opposed to problems with enzymes required for digestion).

The gold standard for detection of bacterial overgrowth is the aspiration of more than 105 bacteria per millilitre from the small bowel. The normal small bowel has less than 104 bacteria per millilitre. Some experts however, consider aspiration of more than 103 positive if the flora is predominately colonic type bacteria as these types of bacteria are considered pathological in excessive numbers in the small intestine. The reliability of aspiration in the diagnosis of SIBO has been questioned as SIBO can be patchy and the reproducibility can be as low as 38 percent. Breath tests have their own reliability problems with a high rate of false positive. Some doctors factor in a patients' response to treatment as part of the diagnosis. Biopsies of the small bowel in bacterial overgrowth can mimic celiac disease, with partial villous atrophy.[15]

Breath tests have been developed to test for bacterial overgrowth, based on bacterial metabolism of carbohydrates to hydrogen and/or methane, or based on the detection of by-products of digestion of carbohydrates that are not usually metabolized. The hydrogen breath test involves having the patient fast for a minimum of 12 hours then having them drink a substrate usually glucose or lactulose, then measuring expired hydrogen and methane concentrations typically over a period of 2–3 hours. It compares well to jejunal aspirates

in making the diagnosis of bacterial overgrowth. 13C and 14C based tests have also been developed based on the bacterial metabolism of D-xylose. Increased bacterial concentrations are also involved in the deconjugation of bile acids. The glycocholic acid breath test involves the administration of the bile acid 14C glychocholic acid, and the detection of $14CO_2$, which would be elevated in bacterial overgrowth.

Some patients with symptoms of bacterial overgrowth will undergo gastroscopy, or visualization of the stomach and duodenum with an endoscopic camera. Biopsies of the small bowel in bacterial overgrowth can mimic those of celiac disease, making the diagnosis more challenging. Findings include blunting of villi, hyperplasia of crypts and an increased number of lymphocytes in the lamina propria. However, some physicians suggest that if the suspicion of bacterial overgrowth is high enough, the best diagnostic test is a trial of treatment. If the symptoms improve, an empiric diagnosis of bacterial overgrowth can be made.[16]

Treatment

Bacterial overgrowth is usually treated with a course of antibiotics although whether antibiotics should be a first line treatment is a matter of debate. Some experts recommend probiotics as first line therapy with antibiotics being reserved as a second line treatment for more severe cases of SIBO. Prokinetic drugs are other options but research in humans is limited. A variety of antibiotics, including tetracycline, amoxicillin-clavulanate, fluoroquinolones, metronidazole, neomycin, cephalexin, trimethoprim-sulfamethoxazole, and nitazoxanide have been used; however, the best evidence is for the use of rifaximin.[17]

A course of one week of antibiotics is usually sufficient to treat the condition. However, if the condition recurs, antibiotics can be given in a cyclical fashion in order to prevent tolerance. For example, antibiotics may be given for a week, followed by three weeks off antibiotics, followed by another week of treatment. Alternatively, the choice of antibiotic used can be cycled. The condition that predisposed the patient to bacterial overgrowth should also be treated. For example, if the bacterial overgrowth is caused by chronic pancreatitis, the patient should be treated with coated pancreatic enzyme supplements. Probiotics are bacterial preparations that alter the bacterial flora in the bowel to cause a beneficial effect. Animal research has demonstrated that probiotics have barrier enhancing, antibacterial, immune modulating and anti-inflammatory effects which may have a positive effect in the management of SIBO in humans. Lactobacillus casei has been found to be effective in improving breath hydrogen scores after 6 weeks of treatment presumably by suppressing levels of a small intestinal bacterial overgrowth of fermenting bacteria. The multi-strain preparation VSL#3 was found to be effective in suppressing SIBO. Lactobacillus plantarum, Lactobacillus acidophilus, and Lactobacillus casei have all demonstrated effectiveness in the treatment and management of SIBO. Conversely, Lactobacillus fermentum and Saccharomyces boulardii have been found to be ineffective. A combination of Lactobacillus plantarum and Lactobacillus rhamnosus has been found to be effective in suppressing bacterial overgrowth of abnormal gas producing organisms in the small intestine.[18]

Probiotics are superior to antibiotics in the treatment of SIBO. A combination of probiotic strains has been found to produce better results than therapy with the antibiotic drug metronidazole and probiotics have been found to be effective in treating and preventing secondary lactase deficiency and small intestinal bacteria overgrowth in individuals suffering from post-infectious irritable bowel syndrome. Probiotics taken in uncomplicated cases of SIBO can usually result in the individual becoming symptom free. Probiotic therapy may need to be taken continuously to prevent the return of overgrowth of gas producing bacteria. A study by the probiotic yogurt producer Nestlé found that probiotic yogurt may also be effective in treating SIBO with evidence of reduced inflammation after 4 weeks of treatment. An elemental diet taken for two weeks is an alternative to antibiotics for eliminating SIBO. An elemental diet works via providing nutrition for the individual while depriving the bacteria of a food source. Additional treatment options include the use of prokinetic drugs such as 5-HT4 receptor agonists or motilin agonists to extend the SIBO free period after treatment with an elemental diet or antibiotics. A diet void of certain foods that feed the bacteria can help alleviate the symptoms. For example, if the symptoms are caused by bacterial overgrowth feeding on indigestible carbohydrate rich foods, following a FODMAP (**F**ermentable, **O**ligo-, **D**i-, **M**ono-saccharides **A**nd **P**olyols) restriction diet may help.[19] FODMAPs are short chain carbohydrates that are poorly absorbed in the small intestine. They include short chain oligo-saccharide polymers of fructose (fructans) and galactooligosaccharides (GOS, stachyose, raffinose), disaccharides (lactose), monosaccharides (fructose), and sugar alcohols (polyols), such as sorbitol, mannitol, xylitol and maltitol. Although FODMAPs are naturally present in food and the human diet, FODMAP restriction has been found to improve symptom control in people with irritable bowel syndrome (IBS) and other Functional Gastro-Intestinal Disorders (FGID). Prior to the formation of the FODMAP concept, diet was seldom used as first line therapy for management of IBS and other FGID. Dose finding studies have achieved up to 91% success in eradicating SIBO (measured by hydrogen breath test) and 94% symptom improvement. The primary antibiotics used are Rifaximin (Xifaxan) and Neomycin.

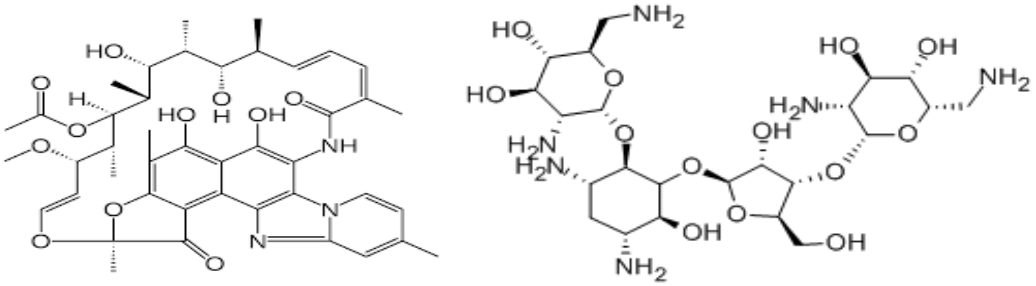


Figure-3: Antibiotics (Rifaximin & Neomycin).

Rifaximin, sold under the trade name Xifaxan among others, is an antibiotic used to treat traveler's diarrhea, irritable bowel syndrome, and hepatic encephalopathy. It has poor absorption when taken by mouth. It is based on rifamycin. Rifaximin was approved for medical use in the United States in 2004.

Antibiotic Treatment

This approach seeks to attack the bacterial overgrowth head on and fairly quickly with antibiotic drugs (Abx). It is the first choice for most gastroenterologists. It must be followed with preventative measures. Dose finding studies have achieved up to 91% success in eradicating SIBO (measured by hydrogen breath test) and 94% symptom improvement.

Which ones are used? The primary antibiotics used are Rifaximin (Xifaxan) and Neomycin. They are almost completely non-absorbable which means they stay in the intestines, having a local action and don't cause systemic side effects, such as urinary tract infections. They are chosen specifically for this property which allows them to act only where they are needed. Metronidazole, a systemic antibiotic, is also used.[20]

SIBO Antibiotic Doses

The following information is provided for physicians, based on the most recent dose finding studies and clinical expertise of Drs Scarpellini, Pimentel, Lombardo, Furnari and their teams. Many thanks for all their excellent, tireless work. Rifaximin may be used for all cases of SIBO. There are 3 excellent dose options currently reported. Neomycin is effective for constipation cases and is used in addition to Rifaximin, as double Abx therapy. Metronidazole is an effective alternative to Neomycin, currently under study at Cedars-Sinai.[21]

If alternating diarrhea is present with constipation, the use of Rifaximin alone has been suggested.

Rifaximin Dose Options

1) 1600 mg per day × 10 days- 70-85% success normalizing LBT, 82% success normalizing GBT (Scarpellini) 1650 mg per day × 14 days (Pimentel), 550 mg t.i.d.
2) 1200 mg per day × 14 days- 87-91% success normalizing GBT, 90-94% symptom improvement (Lombardo).
3) 1200 mg per day × 10 days with 5 g per day Partially Hydrolyzed Guar Gum -87% success normalizing GBT, 91% symptom improvement (Furnari) Rifaximin is available in both 200 mg and 550 mg in the US. T.i.d. study doses are given at 8 am, 2 pm, 8 pm.

Rifaximin Pediatric Dosing

1) 600mg per day × 7 days - 64% success normalizing LBT (Scarpellini).
2) 10-30mg/kg body weight, for IBD. 61% of cases had symptom relief. Higher dose had better pain relief. (Muniyappa).

Rifaximin + Neomycin Dosing

Rifaximin 1600 mg per day + Neomycin 1000 mg per day × 10 days, 87% success normalizing LBT (Pimentel- this study used 1200 mg Rifaximin x 10 days but Dr Pimentel currently uses 1650 mg/day).

Neomycin is available in 500 mg in the US and is given bid (8 am and 8 pm or as fits one's schedule).

Rifaximin + Metronidazole Dosing

Rifaximin 1600 mg per day + Metronidazole 750 mg per day × 10 days.

Metronidazole is available in 3 doses in the US (250 mg, 500 mg and 750 mg) and is usually given at 250 mg t.i.d.[22]

The treatment for SIBO includes controlling and treating any underlying associated illness. The goal is to control the symptoms of small intestine bacterial overgrowth since it may not be possible to "cure" the disease. Antibiotics are one of the treatments that are helpful in controlling the excess bacteria. It is important that not all the bacteria in the intestine are eradicated, since some are required to help with normal digestion. Amoxillin-clavulanate (Augmentin) and rifaxamin (Xifaxan) are the two common first line antibiotics that may be prescribed. Depending upon the situation, other antibiotics may also be considered, including: clindamycin, metronidazole (Flagyl), floxins (ciprofloxacin [Cipro, Cipro XR, Proquin XR], levofloxacin [Levaquin]), trimethoprim-sulfamethoxazole (Bactrim, Septran). While a single course of antibiotics for 1-2 weeks may be sufficient, SIBO has a tendency to relapse, and sometimes repeated courses of antibiotics may be required. In some people, the antibiotics will be routinely cycled, meaning that they will alternate a 1-2 weeks on the antibiotic with 1-2

weeks off. In addition, underlying vitamin and nutrient deficiencies due to malabsorption should be treated.

How can the condition be prevented? Since SIBO usually is a secondary illness that occurs because the intestine has in some way been affected by another disease, it is important to keep chronic diseases properly treated and under control as best as possible.

Does SIBO relapse? What's the prognosis? Small intestine bacterial overgrowth is usually associated with another underlying illness. Even with appropriate treatment, the relapse rate is high and often depends upon how well the underlying illness is managed and controlled.

CONCLUSION

Bacterial overgrowth in the small intestine is thought to be a condition that may be present for years without causing obvious symptoms. A condition that is not recognized in conventional medicine, small intestine bacterial overgrowth is associated with chronic digestive problems such as gas, bloating, diarrhea, and/or constipation. People may be told they have irritable bowel syndrome (IBS). For instance, a study by researchers at Cedars-Sinai Medical Center in California examined 202 people who met the diagnostic criteria for irritable bowel syndrome and gave them a test for bacterial overgrowth called the lactulose hydrogen test. Researchers found that 157 of the 202 people (78 percent) had bacterial overgrowth. When the unwanted intestinal bacteria were eradicated, symptoms of IBS improved in 48 percent of the subjects, particularly diarrhea and abdominal pain. It's not just people with IBS-like symptoms that have bacterial overgrowth. Non-digestive symptoms such as a lack of energy may be the primary concern. Some alternative medicine practitioners believe that it can be involved in chronic fatigue syndrome, fibromyalgia, allergies, arthritis, lupus, autoimmune diseases, diabetes, and other chronic conditions.

Overview: Bacteria in the small intestine may result in impaired absorption of nutrients. Bacteria may lead to fat malabsorption through a process called bile acid deconjugation. Carbohydrate absorption may be affected and result in carbohydrate fermentation in the intestines and gas, bloating, pain, mucous in stools, foul-smelling stools and gas, and diarrhea. According to alternative medicine practitioners, sweets and starchy foods cause the worst symptoms. Toxic metabolic substances produced by the bacteria may injure intestinal cells and impair absorption, resulting in nutrient deficiencies, food allergies and intolerances, and impaired digestive enzyme activity.

Causes: The small intestine normally contains relatively small numbers of bacteria. However, some alternative medicine practitioners believe that certain factors may promote the growth of excess bacteria. Decreased motility in the small intestine: caused by excess dietary sugar, chronic stress, and conditions such as diabetes, hypothyroidism, and scleroderma.

Hypochlorhydria: as people get older, the amount of stomach acid they secrete declines. If there is less stomach acid, bacteria are more likely to proliferate. Overuse of antacids is also thought to lead to bacterial overgrowth.
Structural abnormalities in the small intestine: gastric bypass surgery, small intestinal diverticula, blind loop, intestinal obstruction, and Crohn's disease fistula are some of the structural factors that may be involved in bacterial overgrowth.

Other possible causes include immune deficiency, stress, certain medications such as steroids, antibiotics, and birth control pills, inadequate dietary fiber, and pancreatic enzyme deficiency.
Symptoms: Abdominal bloating and gas after meals, Pain, Constipation, Chronic loose stools or diarrhea: studies have found 48% to 67% of people with chronic diarrhea had bacterial overgrowth, Soft, foul-smelling stools that stick to the bowl, Fatigue: megaloblastic anemia due to vitamin B_{12} malabsorption, Depression, Nutritional deficiency despite taking supplements, Weight loss, Abdominal pain, Mucous in stools, Bloating worse with carbs, fiber, and sugar.

Natural Remedies: Due to a lack of research, fairly little is known about this condition. While antimicrobial drugs may be prescribed, the condition isn't always medically recognized. If you are experiencing symptoms, it's important to talk with your doctor. Self-treating and avoiding or delaying standard care may be harmful to your health. According to alternative medicine practitioners, there are three parts to the natural treatment of bacterial overgrowth:

Diet: Low carbohydrate diet. Eradicate unfriendly bacteria in the small intestine using herbs such as enteric-coated peppermint oil.

Replace: Bacterial overgrowth impairs friendly bacteria ("probiotics") and digestive enzymes.

Herbal Supplements: Enteric-coated peppermint oil is one of the more common supplements for small intestine bacterial overgrowth. The course of treatment is usually 1 to 6 months. A typical dose of enteric-coated peppermint oil is one to two capsules three times a day, taken in between meals with a glass of water. Side effects can include heartburn, rectal burning, and minty burping. Other herbal antimicrobials used to treat bacterial overgrowth may include: Grapefruit seed extract: for people who don't like taking capsules, grapefruit seed extract can be found in liquid form. Add a few drops to a glass of water and drink in between meals, Oregano oil capsules, Garlic, Berberine: goldenseal, Oregon grape, Olive leaf extract, Pau d'arco

tea. Pau D'arco Tea — Fights Candida, Cancer & Inflammation. The bark and wood of the tree are used externally and internally to treat arthritis, pain, inflammation of the prostate gland, fever, dysentery, boils and ulcers, and various cancers.

Diet: During treatment, alternative medicine practitioners usually recommend going on a diet that limits the intake of sweet and starchy foods. One such diet is the specific carbohydrate diet, which restricts grains, starchy vegetables, and some legumes, and was created to address digestive disorders such as bacterial overgrowth, Crohn's disease and ulcerative colitis. Medium Chain Triglycerides: Unlike regular oils, which a person with bacterial overgrowth may not be able to assimilate, medium chain triglycerides are absorbed directly without the need for digestive enzymes. Medium chain triglycerides, such as coconut oil, are often recommended for people with bacterial overgrowth or any type of malabsorption. Digestive enzymes: Digestive enzyme supplements can support the body's digestive enzymes until function is restored. They should be taken before meals. More on digestive enzymes. Vitamins and minerals that may be deficient in people with bacterial overgrowth include vitamin B_{12}, magnesium, calcium, iron, zinc, copper, vitamin A, D, E, K. Probiotics: needed to replace healthy bacteria in the intestines. *Lactobacillus plantarum* (ATCC 8014) and *Lactobacillus rhamnosus* GG (ATCC 53103) are some types that have been used for bacterial overgrowth.

Testing: The "gold standard" test is to take bacterial cultures of small intestine fluid. Lactulose hydrogen breath test: The most common test is the lactulose hydrogen breath test because it is less invasive. Lactulose is a non-absorbable sugar that's fermented if there is intestinal bacteria, resulting in hydrogen production. If there is bacterial overgrowth, fasting hydrogen levels will be high. In addition, after ingesting glucose, there will be a significant rise in hydrogen. Other tests are the schilling test (for a vitamin B_{12} deficiency). A small bowel follow-through may be done to look for structural problems. One of the underlying issues in bacterial overgrowth may be insufficient stomach acid, called hypochlorhydria or achlorhydria. Stomach acid naturally declines with age.

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