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**Proceedings of UCLA Health**

**Title**

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**Journal**

Proceedings of UCLA Health, 24(1)

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**Publication Date**

2020-03-25

## CLINICAL VIGNETTE

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# Small Intestinal Bacterial Overgrowth

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A 52-year-old female presents with two months of bloating, abdomen discomfort, and constipation. Her symptoms began insidiously and increased in severity over time. She tried over the counter products including as gas-X, laxatives, and psyllium without improvement. Her past history included only hypothyroidism, depression and allergic rhinitis. Medications include levothyroxine 100 mcg daily, escitalopram 10 mg daily, and risperidone 0.5 mg qhs. The escitalopram was started six months ago and the risperidone was started two years ago. She does not take supplements. The patient works in retail, rarely drinks alcohol and does not smoke.

Family History was significant for breast cancer, irritable bowel syndrome, depression, and coronary artery disease.

Physical Examination revealed a slender female in no distress. VS: BP 112/66, pulse 66, temperature 98.8, height 5 feet 3 inches, 95 pounds. Her physical exam was unremarkable other than her abdomen, which was non-distended, with hypoactive bowel sounds, but was diffusely tender to deep palpation, without rebound or organomegaly. Labs included normal CBC, comprehensive metabolic panel, TSH, ESR, lipase, amylase, and urinalysis. Stool calprotectin level was slightly above the upper limits of normal range.

### **General Discussion, Epidemiology, and Etiology**

Small intestinal bacterial overgrowth (also known as SIBO) is a condition where commensal bacteria from the colonic biome migrate into the small intestine causing symptoms such as pain, bloating, flatulence, bowel irregularities, and, in rare cases, malabsorption.<sup>1</sup> SIBO is believed to cause 60-70% irritable bowel disease cases.<sup>2</sup> Many etiologies cause SIBO.<sup>1</sup>

Medications linked to SIBO include opioids, anti-spasmodics, anti-psychotics, antibiotics, and proton pump inhibitors.<sup>1</sup> SIBO has also been linked to disorders including scleroderma, systemic lupus erythematosus, amyloidosis, radiation effects, neuropathies, chronic pancreatitis, inflammatory bowel disease, diverticular disease, intestinal tumors, and post-surgical changes impacting gut motility.<sup>3</sup> Small intestinal bacterial overgrowth is also associated with immunodeficiencies such as IgA deficiency and combined variable immunodeficiency, although it is unclear whether this is a causal or associative relationship.<sup>4</sup> SIBO can also be caused by altered ileo-cecal valve function or by the absence of the ileo-cecal valve.<sup>5</sup> Another common cause of SIBO is post-infectious autonomic

dysregulation where an episode of gastroenteritis appears to cause damage to the neural apparatus of the small intestine.<sup>4</sup>

### **Pathophysiology**

One common factor in each of these conditions is failure or dysfunction of the migrating motor complex whose cleaning waves are responsible for shifting digestive contents including healthy components of the gut biome from the small intestine to the large intestine.<sup>6</sup> In normal gut, the migrating motor complex activates approximately every 2-4 hours, but becomes dysfunctional in patients with SIBO.<sup>1</sup> The disrupted migrating motor process results in accumulation of colonic bacteria in the upper digestive tract.<sup>6</sup> The accumulation of colonic bacteria in the small intestine appears to cause bloating and discomfort.<sup>2</sup> Pathogenic bacteria rarely cause SIBO,<sup>6</sup> rather the accumulation of non-pathogenic bacteria in the upper digestive track results in significant alternations in digestive function.<sup>6</sup> Extreme cases can result in clinically significant malabsorption of carbohydrates, fats, and protein and ultimately malnutrition.<sup>7</sup> Fat malabsorption can produce steatorrhea and deficiencies in fat soluble vitamins (A, D, E, and K).<sup>8</sup> Irregularities in carbohydrate and protein absorption may also develop.<sup>8</sup> Patients may have vitamin B12 deficiency, although folic acid deficiencies are rare, as folic acid is synthesized by commensal gut bacteria.<sup>7</sup> In extreme cases, patients may have mental status changes and hepatic encephalopathy related to ammonia buildup or lactic acidosis related to prior bowel surgery.<sup>8</sup>

### **Diagnosis and Testing**

Diagnosis initially involves excluding potentially more serious conditions such as inflammatory bowel disease, celiac disease or infectious gastroenteritis.<sup>9</sup> Diagnosis of SIBO is confirmed with a clinical history consistent with SIBO and a positive carbohydrate breath test or a positive jejunal aspiration.<sup>9</sup> Colonoscopy with upper endoscopy including duodenal biopsies to rule out other etiologies may be needed.<sup>9</sup> The carbohydrate breath test is performed with a non-absorbable carbohydrate such as lactulose.<sup>10</sup> The lactulose is metabolized by the gut flora resulting in the production of hydrogen and methane which are excreted in the breath and measured with specialized equipment.<sup>10</sup> The test is considered positive if an early peak in hydrogen or methane is noted.<sup>10</sup> Most testing centers prefer that prokinetic agents, antibiotics, and complex carbohydrates are avoided prior to breath testing.<sup>10</sup> False positive results can be seen in patients with rapid transfer through the GI tract.<sup>11</sup> False negative results can be seen in

patients with very slow GI transit time or low bacterial counts in the small intestine.<sup>11</sup> Methane positive test results tend to correlate with constipation-predominant SIBO, while hydrogen positive test results tend to correlate with diarrhea-predominant SIBO.<sup>12</sup> Although the breath test is the most commonly used diagnostic tool for SIBO, jejunal aspiration during endoscopy can also be helpful in certain cases.<sup>12</sup> The breath test is preferred as jejunal aspiration requires an invasive procedure and is more operator dependent.<sup>12</sup> In addition, the location of small intestinal bacteria can vary, and contamination can also be an issue.<sup>11</sup>

### Treatment

The treatment of SIBO involves determining the cause of the bacterial overgrowth and eliminating that cause by reducing the amount of small intestinal bacteria through antibiotics and prokinetic agents.<sup>13</sup> For hydrogen-predominant SIBO, rifaximin (a non-absorbable antibiotic) is the preferred agent.<sup>12</sup> Rifaximin is generally effective, but costly.<sup>12</sup> Methane-predominant SIBO is usually more difficult to treat and usually requires rifaximin, along with neomycin or metronidazole.<sup>13</sup> In addition to antibiotics, prokinetic agents are very important to stimulate the intestinal cleaning waves of the migrating motor complex facilitating movement of the bacteria from the small bowel to the large bowel.<sup>12</sup> Low dose erythromycin, prucalopride, and low-dose naltrexone are the most commonly used prokinetics.<sup>13</sup> Despite treatment, approximately half of SIBO patients will have persistent symptoms after the first round of treatment, requiring further treatments.<sup>13</sup> Treatment for recurrent cases depends on many variables including the age of the patient, duration of symptom-free period, and specific side effects with prior treatments.<sup>14</sup> Recurrences are often seen in patients on proton-pump inhibitors, a history of prior GI surgeries, and in older patients.<sup>14</sup> Patient who recur within three months usually receive a second round of antibiotics, while those who recur after three months are usually sent for a repeat breath test.<sup>4</sup> Most patients will respond after a second round of antibiotics.<sup>14</sup> Those with persistent symptoms should be considered for more extensive testing for other disorders.<sup>13</sup>

Dietary measures are also important in treatment of SIBO.<sup>15</sup> An elemental diet can be very effective in the treatment of SIBO especially in patients who have failed multiple rounds of antibiotics.<sup>15</sup> Unfortunately, the elemental diet is limited by cost and poor-compliance.<sup>15</sup> Other diets have been studied in SIBO patients.<sup>15</sup> The low FODMAP diet has studies supporting its effectiveness, at least for short term use.<sup>15</sup> The low FODMAP diet eliminates most of the carbohydrates that aggravate SIBO, improving short term flatulence, bloating, and pain.<sup>4</sup> Unfortunately, long term effectiveness of the low FODMAP diet is unclear.<sup>4</sup> Probiotics do not appear to have a role in the treatment of SIBO.<sup>16</sup> Interestingly, statins may have a role in the treatment of small intestinal bacterial overgrowth in ongoing studies.<sup>17</sup>

### Prognosis

The prognosis for patients with small intestinal bacterial overgrowth is variable with some patients having complete resolution of symptoms after one round of treatment and other patients having a chronic course with many relapses.<sup>4</sup>

### Clinical Course and Follow-Up

The patient underwent upper endoscopy and colonoscopy which were normal and completed lactulose breath test that was hydrogen positive. She was treated with rifaximin, but suffered a relapse requiring a second round of rifaximin. Nine months later, she remains symptom-free.

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