Small Intestinal Bacterial Overgrowth: Updates and Clinical Implications

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• We will be compiling your clinical questions and answering as many as we can the final 15 minutes of the webinar.

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Small Intestinal Bacterial Overgrowth: Updates and Clinical Implications

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Learning Objectives

• Overview of SIBO
• Learn when to consider testing for SIBO
• Review the test in detail
• Discuss treatment recommendations
• Case examples
• GI and other test considerations
What is Small Intestinal Bacterial Overgrowth?

- “Small Intestinal Bacterial Overgrowth is a heterogeneous syndrome characterized by an increased number and/or abnormal type of bacteria in the small bowel.”
- “SIBO is a condition in which the small bowel is colonized by excessive numbers of aerobic and anaerobic microbes that are normally found in the large intestine.”
- “Currently a bacterial concentration of $>10^3$ c.f.u./ml is generally considered significant.”

Bacterial Concentrations Throughout the GI Tract
Ways the Body Innately Prevents the Overgrowth of Bacteria in the Small Intestine

- Gastric acid
- Pancreatic and biliary secretions
- Peristalsis and the migrating motor complex (MMC) – stasis promotes bacterial growth
- Ileoceleal valve – prevents reflux of colonic bacteria into the small intestine

The compromise of any of these processes can lead to the development of SIBO

References:
When to Consider SIBO?

Signs and Symptoms
Associated Conditions and Risk Factors
What are the Common Signs and Symptoms of SIBO?

- Abdominal bloating
- Excessive gas or belching
- Abdominal cramps
- Diarrhea
- Constipation
- Nausea
- Heartburn

- Steatorrhea
- Nutrient deficiencies
  - Vitamin B12
  - Iron
  - Macronutrient malabsorption
  - Fat-soluble vitamins
  - RBC folate
Conditions with a High Prevalence of Overgrowth

- Functional GI and motility disorders (such as IBS & gastroparesis)
- Neuromuscular Diseases (such as restless leg syndrome)
- Inflammatory Bowel Disease (IBD)
- Pancreatic disease
- Celiac disease
- Hypothyroidism
- Liver disease
- Diabetes
- Fibromyalgia
- Rosacea
- Parkinson’s disease
- Obesity
- Plus many other conditions

Prevalence of SIBO in Common Conditions

• IBS
  – 78% of patients positive
  – 48% of patients treated successfully for SIBO no longer met Rome criteria

• Fibromyalgia and Chronic Fatigue Syndrome
  – 42/42 patients with fibromyalgia had an abnormal lactulose breath test with significantly greater hydrogen production; significant correlation between degree of pain and peak hydrogen level
  – 77% of CFS patients were found to have SIBO

• Hypothyroidism
  – 54% of patients with hypothyroidism have SIBO compared with 5% of controls
  – “Hypo- and hyperthyroidism, often of autoimmune origin, are respectively associated to small intestinal bacterial overgrowth and to changes in microbiota composition.”
What are Risk Factors for the Development of SIBO?

- Mechanical Stasis
  - Structural/Anatomic: Small intestine diverticula, strictures, surgery
  - Motility Disorders: Gastroparesis, Medications (i.e. opioid analgesics)
- Irritable Bowel Syndrome
- Hypothyroidism
- Metabolic Disorders: Diabetes
- Elderly Age
- Organ System Dysfunction: Liver, kidney, pancreatic dysfunction, Crohn’s, Celiac
- Immunodeficiency states
- Hypochlorhydria
- Medications: Recurrent antibiotics and gastric acid suppressors
- GI Infection

An overgrowth of bacteria in the small intestine can cause:

- Blunting of the villi
- Thinning of the mucosa and crypts
- Increased intraepithelial lymphocytes
- Microscopic inflammatory changes

Testing for SIBO

Gold Standard: Aspirate and Culture
Breath Testing
Gold Standard

Aspirate of small bowel fluid followed by culture and bacterial count

Disadvantages

• Invasive procedure as the small intestine must be intubated so that aspirates can be collected
• Culture-based techniques do not allow for growth of all organisms, thus may underestimate the bacterial population
• Potential for contamination of instrumentation and inaccurate sampling due to technical problems
• Endoscopy can only reach the upper portion of the small intestine and colonoscopy can only reach the lower, thus the substantial middle section of the small intestine is not accessible by this method
Breath Testing versus Small Bowel Aspiration

• “Unlike breath testing, small bowel aspiration is invasive, time-consuming and costly.”

• “Breath Testing is a useful, inexpensive, simple and safe diagnostic test in the evaluation of common gastroenterology problems.”
Breath Testing for SIBO

- Baseline breath measurement
- Drink substrate (lactulose)
- Lactulose transits through small intestine - if bacteria are present, H2 (hydrogen) or CH4 (methane) gas is produced
- H2 and CH4 absorbed through intestines into bloodstream
- Gases carried to lungs through bloodstream and expired
- Breath collected at timed points

Testing Substances for SIBO Breath Test

**Lactulose**
- Cannot be digested or absorbed by humans, thus passes through entire length of small intestine
- *Advantage*: Can diagnose distal overgrowth which is thought to be more common
- Not as sensitive as glucose

**Glucose**
- Glucose is absorbed within first few feet of small intestine, thus can only diagnose proximal overgrowth
- *Disadvantage*: Cannot diagnose distal overgrowth
- Accurate diagnosis of proximal overgrowth
Collection Pack Instructions

• Very important to review the instructions with the patient as they are detailed and specific
• Improper collection can lead to ambiguous results
• Key instructions:
  – 4 weeks prior: No antibiotics, colonoscopy or barium enema
  – 7 days prior: No laxatives, stool softeners, stool bulking agents or antacids
  – 24 hours prior: Diet limited to a few foods and no probiotics
  – 12 hours prior (fasting with only water): No non-essential medications/supplements, toothpaste, gum, candies or mouthwash
  – 1 hour prior and during testing (fasting with only water): No smoking, sleeping, vigorous exercise or toothpaste
Collection Pack Instructions Continued...

• Collection technique with timing and breathing into the tube may need to be reviewed with the patient
  – Breathe normally, inhale and hold 5 seconds
  – Exhale normally into mouthpiece (do not blow hard)
  – Insert tube and remove after 2 seconds
  – Record times on labels and requisition form

Great demonstration video for patients to watch can be found on the SIBO page on www.gdx.net:
www.gdx.net/product/bacterial-overgrowth-of-the-small-intestine-sibo-test
Test Interpretation

- Standardization was lacking regarding indications for testing, test methodology and interpretation of results
- Who formed the consensus group?
- Consensus was reached on 26 statements in the areas of indications, preparation, performance, interpretation of results and knowledge gaps
Breath Tests: 3-Hour versus 2-Hour

3-Hour SIBO Breath Test

2-Hour SIBO Breath Test
Test Components

- Graph of hydrogen (H2) and methane (CH4)
- Chart of breath gases at the timed points
- Carbon dioxide (CO2) evaluation for quality control
- Actual collection times
- Evaluation for hydrogen
- Evaluation for methane
Evaluation for Hydrogen (H2)

• A rise of H2 of >20 ppm over baseline in the first 90 minutes of testing is positive for SIBO

• Genova’s Evaluation for hydrogen based on consensus paper; this cut point is seen widely throughout the literature
Evaluation for Hydrogen

• Significance of elevated baseline H2 levels in patients reporting adherence to fasting and dietary guidelines is not known
  – In a symptomatic patient, some clinical groups with expertise in SIBO management may consider an elevated hydrogen baseline a positive test

• Approximately 8 to 27% of individuals do not produce H2 due to the presence of methanogenic microbiota which consume hydrogen molecules to produce methane gas
  – Low H2 findings through all time points in a symptomatic patient may reflect a false negative result
  – Clinical attention should be shifted to evaluation of CH4
Evaluation for Methane (CH4)

• The consensus group and other papers refer to an absolute value of 10 or greater at any point during the test as a “methane positive” result
  – Results 10+ will be outlined in red and flagged with an “H”

• Peer-reviewed literature suggests an association with certain clinical conditions and methanogen overgrowth at levels as low as 3 ppm, CH4 values between 3 and 9 may indicate the need for clinical intervention in the symptomatic patient
  – Results 3-9 will be outlined in yellow

• Emerging literature suggests that unlike H2, an elevated CH4 level at baseline is common
Evaluation for Methane

• Utilization of breath methane levels for SIBO assessment is controversial largely due to a lack of validation related to diagnostic specifics such as timing and magnitude of increase
  – The rise of CH4 during breath testing appears to not be as sharp as H2

• However, CH4 measurements are increasingly obtained to address other clinical questions such as:
  – Constipation
    • Methane gas itself may slow intestinal transit, and patients with CH4-predominant bacterial overgrowth have been found to be five times more likely to have constipation compared to individuals with H2-predominant overgrowth
    • The severity of constipation has been found to directly correlate with the CH4 level
  – Irritable Bowel Syndrome (IBS)
  – Obesity
Carbon Dioxide (CO2) is measured in every sample. CO2 levels exceeding acceptable limits indicate room air contamination likely at the time of sample collection. If CO2 levels exceed acceptable limits, sample integrity is questionable and results are designated as non-reportable (NR).
Actual Collection Times

On the report

On the requisition form
Actual Collection Times

Actual Time

• The actual time of collection of samples is provided to enhance clinical interpretation
• The actual times reported are utilized to determine the actual interval for comparison to the recommended interval

Actual Interval

• The actual interval can be compared to the recommended collection interval. If the recommended collection interval is not followed correctly, interpretation should be made within the context of the altered collection schedule. Generally, deviations of a few minutes will not significantly alter the interpretation.
• If the 90-minute interval is missed, evaluation for hydrogen may be affected, since the criteria for diagnosis of hydrogen-producing bacterial overgrowth is by 90-minutes
Treating SIBO
Treat the overgrowth
Provide nutritional support
Correct the underlying cause
Treating SIBO

• For the majority of patients diagnosed with a positive breath test, SIBO will likely be a chronic and relapsing condition
  – For example, one study found that 44% of patients treated successfully with antibiotics relapse within 9 months

• Goals of treatment are threefold:
  – Treat the overgrowth
  – Provide nutritional support
  – Correct the underlying cause
Treating SIBO – Treat the Overgrowth

- Rifaximin
- Rifaximin plus Neomycin (or Metronidazole)
- Botanicals
  - Berberine
  - Allicin (component of garlic)
  - Oregano oil
  - Neem
  - Others
Treating SIBO – Provide Nutritional Support

- **Nutritional consequences include:**
  - Weight loss
  - Fat soluble vitamin deficiency
  - Vitamin B12 deficiency
  - Iron deficiency
  - Low serum bile acids
  - Low RBC folate levels

- **Common diets prescribed for SIBO**
  - Specific Carbohydrate Diet (SCD)
  - Low FODMAPs
  - Elemental Diet
The migrating motor complex (MMC) describes the waves of electromechanical activity that sweep through the intestines in a regular cycle.

The MMC is responsible for moving bacteria from the small intestine to the large intestine, as well as for inhibiting migration of colonic bacteria into the terminal ileum.

Supporting optimal function of the MMC includes:

– Meal spacing every 4-5 hours with overnight 12 hour fast
– Use of prokinetic agents
  • Pharmaceutical agents such as low-dose erythromycin, Tegaserod, low-dose naltrexone, and Prucalopride
  • Natural agents such as ginger, herbal bitters and the botanical product Iberogast

Treating SIBO – Address the Cause
Treating SIBO – Address the Cause

• Revisit the slide on risk factors and associated conditions. A few examples of addressing the cause may include:
  – Discontinuation of medications: To be discussed between patient and clinician (acid-blocking medications, meds that slow transit- opioid analgesics, etc.)
  – Treat Hypothyroidism
    • Treatment with Levothyroxine associated with greater incidence of SIBO
    • What is causing the hypothyroidism?
  – Hypochlorhydria
    • Bitters, Betaine HCl, etc.
    • What is causing the hypochlorhydria?
  – Some causes cannot be reversed (i.e. surgical alterations); ongoing management may be necessary.
    • Consider visceral manipulation for adhesions

[www.siboinfo.com is an informative website maintained by Dr. Allison Siebecker, ND, and includes treatment considerations]
Retesting

• In a patient treated for SIBO, many variables affect the decision of when to retest — including the patient’s underlying condition and its severity, length of treatment, etc...

• The NA Consensus Group recommends that antibiotics should be avoided for 4 weeks prior to testing — this recommendation usually applies to initial testing for SIBO

• However, there are emerging clinical recommendations which suggest retesting patients within a few days of antimicrobial course completion to ensure efficacy of the treatment. The North American Consensus group as well as others suggest that ‘breath tests may be performed shortly after cessation of antibiotic therapy to confirm eradication’

Case Examples
Case Example #1 Hydrogen positive, mild methane positive
Case Example #2 Methane positive
Additional Scenario
Case Example #1

- 34 yo female with bloating and alternating diarrhea with constipation
- Symptoms ongoing since she caught a GI bug while traveling in Central America 9 months ago; did not experience these symptoms previously
- Certain foods are problematic and she finds herself eating more paleo to try to control symptoms
- Patient is very active and keeps busy with work and travel; the IBS symptoms have interfered with daily living
Case Example #1

- Hydrogen positive results
- Methane yellow – moderate
- Collection schedule followed correctly
Case Example #1

• Treatment: Since the patient did have a mixed IBS-type picture with alternating diarrhea and constipation, the clinician chose to treat both methane and hydrogen-producing bacteria
  – Botanical regimen including Candibactin AR and BR plus Allimed (for methane) x 6 weeks
  – Begin low FODMAPs diet
  – Meal spacing every 4-5 hours

• Follow up: After 2 months, the patient symptoms had improved, so there was no follow up testing. The patient continued with the meal spacing and modified FODMAPs
  – The goal is not continuous FODMAPs, since fermentable carbohydrate is important to the health of the commensal bacteria of the large intestine. The goal would be to introduce fermentable carbohydrates/resistant starches over time
Case Example #2

• 66 yo male with bloating and excessive belching and flatulence
• Severe constipation for as long as he can remember
• Has up to 2 bowel movements per week that are difficult to pass, he considers this pattern normal for him
• Obese, hypertension, hypothyroid, diabetic
• Takes oxycodone daily for a back injury 3 years ago
• Eats a standard American diet
Case Example #2

- Methane-positive test
- Hydrogen normal
- Collection schedule followed correctly
Case Example #2

• Treatment:
  – The clinician chose to treat methane-producing organisms with Rifaximin plus Neomycin x 14 days
  – A prokinetic was prescribed – MotilPro (combination of ginger and 5HTP) indefinitely until chronic constipation resolves
  – Magnesium was prescribed daily to assist with regularity
  – Levothyroxine Rx was switched to Armour Thyroid
  – Recommended increasing water intake from 1 cup daily to at least 1-2 L daily
  – While fiber is important for constipation, it was avoided initially to address SIBO
  – Low carbohydrate diet recommended (for diabetes, obesity, and SIBO)
Case Example #2

- The long-term focus with this patient would be to work on his overall health conditions and habits that may predispose to SIBO (diabetes, hypothyroid, Standard American Diet, oxycodone use)
  - The recurrence of SIBO is common especially if underlying conditions are not addressed
  - This patient’s lifestyle and health conditions are inflammation-promoting, so transitioning to anti-inflammatory diet/lifestyle may take time, in order to come off oxycodone

- A GI Effects Comprehensive stool analysis was also ordered for this patient
  - If there are other GI abnormalities, for example pancreatic insufficiency, then pancreatic enzymes can be given to help with digestion (pancreatic insufficiency is common with diabetes)
Additional Scenario: “Flatline Test”

• Low H2 and CH4 throughout the test could indicate:
  – It is a negative test for SIBO; consider other testing to assess etiology of patient symptoms
  – If both H2 and CH4 are low all 3 hours, it may suggest the presence of H2S-producing bacteria
    • The H2S-producing bacteria consume the H that would otherwise have gone to the bacteria that make H2 or CH4
    • H2S smells like rotten eggs, so if this is what the patient experiences, this may be the case
  – The patient may not have followed collection pack instructions correctly
    • The breath didn’t make it into the tube
    • They may have just completed antibiotics
      – Instructions say wait 4 weeks after discontinuing antibiotics
      – Some clinicians may advise their patient to collect immediately after finishing antibiotics to ensure efficacy of treatment
GI Test Considerations

SIBO
Other tests
Review: When to Order SIBO Testing

- IBS
- GI symptoms
- Bloating
- Intolerance to carbohydrates or FODMAPs
- Symptoms after eating
- Unexplained abdominal symptoms
- Predisposing conditions (see list)

It is important to designate someone in the office to go over collection package instructions with each patient to ensure optimal results.
Other GI Test Considerations for Similar Symptoms

- GI Effects is comprehensive and can identify:
  - Pancreatic insufficiency
  - Inflammation
  - Dysbiosis
  - Yeast overgrowth
  - Parasitic infection

- Food Antibody panel
- Celiac and Gluten Sensitivity panel
GI Effects profile can not diagnose Small Intestinal Bacterial Overgrowth

• There are markers on this profile that can be suggestive of SIBO in the right patient population:
  – Elevations in Products of Protein Breakdown
  – Elevations in Fecal Fats
  – Unexpected or extreme elevations in Total SCFAs and n-butyrate
Nutritional Insufficiencies

- B vitamins
- Macronutrients
- Fat-soluble vitamins

The NutrEval assesses urine organic acids including malabsorption and dysbiosis biomarkers.
Additional Questions?

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UK Client Services: 020-8336-7750

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- How Genova’s profiles might support patients in your clinical practice
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