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Making Sense of Patients with Gas and Bloating of Undetermined Origin

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Unexplained bloating is one of the most common and bothersome gastroenterology complaints in gastrointestinal (GI) specialty and primary care clinics. Abdominal bloating is likely to present in association with other complaints including belching, flatulence, post-prandial distension, borborygmi, abdominal pain and diarrhea. Given the lack of a systematic approach to these complaints, symptomatic patients are often asked to keep a food diary and dietary modifications are suggested. If symptom resolution does not occur, further testing (blood and stool tests, imaging studies, endoscopic procedures) to rule out organic disorders is initiated. A "negative" or unremarkable work up often places patients into the "functional" GI disorder compartment. This article attempts to provide physicians with a simple and rational approach to unexplained abdominal bloating and to identify underdiagnosed entities that could be responsible for this symptom.

INTRODUCTION

Abdominal bloating is a nonspecific term whose definition varies among gastroenterologists with an even broader meaning for patients in general. Bloating can be defined as the objective abdominal distention originating from gas or as a subjective feeling of abdominal distention or abdominal wall tension without objective distension. These symptoms have been linked with different pathophysiologic mechanisms that are not fully understood. Several functional gastrointestinal disorders (functional dyspepsia,[1,2] irritable bowel syndrome (IBS),[1,2,3] functional constipation[1,2,4,5] and functional bloating[6]) have bloating as a manifestation despite the absence of a somatic abnormality.

Bloating is likely to present in association with other nonspecific GI complains including belching, flatulence, borborygmi, abdominal pain, nausea and diarrhea. Patients with such gastrointestinal (GI) symptoms, especially those with alarm symptoms, usually undergo multiple studies to rule out organic disorders. Testing includes but is not limited to blood work, stool tests, imaging studies and endoscopic procedures. When these tests fail to expose any abnormality, patients are diagnosed with functional GI disorders.

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Table 1. Main Risk Factors of SIBO

Cystic Fibrosis
Scleroderma
Vagotomy
Billroth II and Roux-ENY Surgeries
Right Colon or Distal Ileal Resections
Diabetes mellitus
Bariatric Surgery
Small Bowel Diverticulosis
Radiation Injury to Bowel
Celiac Sprue
Crohn's Disease
Hypo or Achlorhydria

Carbohydrate intolerance or malabsorption and small bowel bacterial overgrowth (SIBO) are common problems frequently encountered in the GI and primary care clinics. These disorders are responsible for bloating as well as other unspecific symptoms. Their exact prevalence is unknown because they are poorly recognized and, as a consequence, are poorly managed. The current report attempts to provide physicians with a rational approach to address these GI symptoms and to identify underdiagnosed or underappreciated entities before patients are placed into the GI functional disorders compartment where further investigations may be limited.

Small Intestinal Bacterial Overgrowth

SIBO is the presence of excessive bacteria in the small intestine, defined as a bacterial population, possibly colonic-type species, exceeding 10^5–10^6 organisms/ml in jejunal fluid.[7,8] Symptoms of SIBO are nonspecific and include bloating, abdominal distension, abdominal pain or discomfort, diarrhea, constipation, fatigue and weakness. The severity of symptoms likely reflects the degree of bacterial overgrowth and the extent of mucosal inflammation.

Risk factors for SIBO include GI tract structural or anatomic abnormalities (e.g. small bowel diverticulosis, strictures), post-surgical changes (e.g. vagotomy, Bilroth I and II anastomoses, bariatric surgery, gastro-jejunostomy, colectomy with ileocecal valve resection), radiation damage to the small bowel, motility disorders (e.g. gastroparesis, small bowel dysmoltility), systemic diseases that affect bowel motility (e.g. diabetes, scleroderma, amyloidosis), IBS, cirrhosis, pancreatitis, immunodeficient states, hypochlorhydria (e.g. atrophic gastritis, proton pump inhibitor (PPI) use), advanced age which may overlap with hypochlorhydria, recurrent antibiotic use and medications that decrease motility (e.g. narcotics, anticholinergics) (Table 1).

The presenting symptoms of SIBO can sometimes also reflect the underlying cause (e.g. abdominal pain, early satiety and vomiting may point towards gastroparesis or small bowel dysmotility). Other symptoms can reflect complications of SIBO, including malabsorption, nutritional deficiencies (e.g. B12 related anemia) and metabolic bone disorders.[9] The nonspecific nature of these complaints makes SIBO difficult to distinguish clinically from other disease entities, such as IBS, lactose intolerance and fructose intolerance.

Fructose Malabsorption

Dietary fructose intolerance (DFI), although its role is somewhat controversial, is often implicated in the causation of GI symptoms. Several studies reported a prevalence of fructose malabsorption in patients with the diagnosis of functional dyspepsia or unexplained GI symptoms between 40 and 73%.[10,11] Another study has estimated that up to one third of patients with suspected IBS had DFI.[12]

Undigested or poorly digested fructose generates an osmotic force driving water into the lumen of the small bowel and leading to decrease transit times of bowel contents which then reach the colonic flora producing fermentation of this carbohydrate.[13] This may result in symptoms including abdominal pain, excessive gas, bloating and variable diarrhea, especially in patients with visceral hypersensitivity.[14]

Symptoms, and self-rated health, improve if patients are willing to adhere to a low fructose diet.[15] Fructose is present in a variety of fruits, vegetables and honey but it is also produced from the digestion of high fructose

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corn syrup, commonly found in processed food. The amount of fructose in the diet of the average American has definitely increased during the last 50 years when high fructose corn syrup was introduced to the food industry in the late 1960s. GI symptoms might develop after the consumption of 37.5 gm of fructose per day[16] (for reference, an 8 ounce can of Coca-Cola contains 25 gm of fructose). It is possible that a rise in fructose consumption in the United States (US) population has resulted in a rise in fructose malabsorption and intolerance.[10]

Breath Testing

Hydrogen breath tests are currently utilized as diagnostic tests to confirm or eliminate the possibility of carbohydrate malabsorption or SIBO in such patients. Currently available breath tests include: lactose, fructose (FBT), lactulose and glucose.

Lack of standardization has led to subjectivity of these tests and institutional comparisons are difficult given the variability of parameters such as the dose of substrate administered, duration of the test, the interval of breath testing and cut-off values.[17]

The breath tests measure hydrogen (H_2), methane (CH_4) and CO_2 present in the exhaled air. H_2 is a common gas produced by bacteria during the metabolism of these carbohydrates; conversely, methanogenic flora is far less common and has been described to be present in up to 30% of patients with Scandinavian descent and in less than 10% of US population. By adding methane measurements the sensitivity of the tests is increased. CO_2 level is determined to ensure that the sample measures actual alveolar air to assure accuracy of breath samples.

The glucose hydrogen breath test (GBT) is more acceptable for diagnosis of SIBO whereas lactose and fructose hydrogen breath tests are used for detection of lactose and fructose maldigestion respectively. Lactulose hydrogen breath test has been used for SIBO as well but glucose breath test has greater advantages over lactulose because of its higher specificity. Lactulose breath test is also used in GI motility to measure the orocecal transit time. These methods are noninvasive and inexpensive. Breath tests, though valuable tools, are underutilized in evaluating dyspepsia, functional bloating and diarrhea as well as suspected malabsorption.

Our extensive experience with glucose breath testing to rule out SIBO has indicated us that the optimal protocol should include the administration of a 100 gm oral glucose challenge with collection of breath samples every 20 minutes for 3 hours to measure hydrogen and methane concentrations. Over the last 2 two years we have performed this study in 188 patients presenting with unexplained abdominal bloating to our motility Center at University Medical Center at Texas Tech Health and Sciences, El Paso. We found that 85 of these patients were positive for SIBO representing 45% of the total of patients tested. A glucose breath test was considered to be positive if there was an increase in hydrogen concentration exceeding 20 parts per million (ppm), an increase over 10 ppm for methane or when the baseline values are >20 ppm. 38 of these patients with negative glucose breath tests and unexplained bloating underwent further testing using fructose breath tests (FBT) performed after 25 gm fructose oral administration with collection of breath samples in the same fashion. 18 out of the total 38 patients were found to be FBT positive. This represents 47% of the FBTs evaluated. The parameters utilized for a positive fructose test include H_2 or CH_4 peaks of more than 20 ppm and 10 ppm respectively. Usually these peaks occur in the range of 90 min to 3 hours after fructose intake when unabsorbed fructose is metabolized by colonic flora.[18]

Approach to Abdominal Bloating, Gas and Distension

Patients with abdominal distension, bloating and excess gas, with or without additional GI symptoms, often have a negative GI work up. Evaluation may include laboratory tests for hypothyroidism, stool tests for bacterial, helminthic and protozoa infections, imaging for bowel obstruction or ascites, endoscopy for common disorder such as celiac disease, H. pylori infection and lactose intolerance exclusion through a dairy free diet.

As a next step in evaluating bloating without a determined etiology, a GBT to assess for SIBO could be performed. A positive GBT may indicate the presence of excess bacteria in the small bowel requiring appropriate antibiotic treatment. Acceptable antibiotic regimes include metronidazole 500 mg PO BID, neomycin 500 mg PO BID, amoxicillin/clavulanic acid 500 mg PO BID, doxycycline 100 mg PO BID or rifaximin 400 mg PO TID (non-standard dosing)[19,20,21] for 2 to 3 weeks. (Table 2) Refractory symptoms in the setting of a repeat positive GBT may require an alternative antibiotic or combination therapy. Patients

Table 2. Available Antibiotic Alternatives for the Treatment of SIBO - Including efficacy of treatments, distribution of the medications, affection of colonic flora and resistance profile.

Antibiotic	Efficacy	Systemic	Colonic Flora	Resistance
Metronidazole 500 mg BID	5%-10%	Yes	Affected	Yes
Neomycin 500 mg BID	20%-25%	Yes	Affected	Yes
Amoxicillin/clavulanic acid 500 mg BID	30%-40%	Yes	Affected	Yes
Doxycycline 100 mg BID	30%-40%	Yes	Affected	Yes
Rifaximin 400 mg BID	60%-70%	No	Not Affected	No

with continued symptomatic or recurrence may benefit from 1) gastric and small bowel prokinetics (eg. low dose erythromycin, metoclopramide or pyridostigmine) in settings of gastric or small bowel motility disorders, 2) treating constipation with linaclotide or lubiprostone, 3) probiotics, specifically containing bifidobacterium infantus, 4) discontinuing PPI to reduce hypochlorhydria which promotes the possibility of bacterial colonization of the small bowel and 5) stopping or decreasing doses of anticholinergic drugs and/or narcotics which reduce gut motility and enhance bacterial colonization. A negative GBT may prompt a FBT. A positive fructose test would indicate the presence of fructose intolerance and should trigger the treatment with a low fructose diet. A patient with a negative FBT on the other hand may be empirically treated with a low FODMAP diet to assess if there is any improvement of symptoms. Hence the algorithm we illustrate can unmask the presence of DFI and see if a less restrictive diet would help before recommending a more demanding low FODMAP diet (Figure 1).

Dietary Management

A low fructose diet is a less restrictive alternative than the low FODMAP diet since it only limits the consumption of fructose from some fruits (e.g. prunes, pears, cherries, peaches, apples, plums, dates, mango, watermelon) vegetables (e.g. sugar snap peas, tomatoes, corn, carrot, sweet potatoes) honey and other processed foods with fructose on the label.

FODMAPs (fermentable oligosaccharides, disaccharides, monosacharides and polyols) are osmoticaly active carbohydrates that are high in fructose (e.g. honey, peaches, dried fruits), fructans (e.g. wheat, rye, onions), sorbitol (e.g. dried fruits, sugar alcohols and sweeteners), and rafinose (e.g. lentils, cabbage, legumens). The high osmolality of FODMAPs leads to increased water in the small bowel, decreasing transit time resulting in increasing gas and colonic distention from bacterial fermentation of poorly absorbed carbohydrates.[13] This diet limits the consumption of high fiber foods such as beans, fruits, vegetables and grains. The low FODMAP diet implementation is flexible and can be tailored to meet individual's lifestyle and preferences.

The low FODMAP diet was developed by a research group in Australia as a new dietary management of IBS and other functional gastrointestinal disorders with bloating and abdominal pain.[22] A pilot study showed that a low FODMAP diet led to sustained improvement in all gut symptoms in 86% of the patients diagnosed with IBS compared to the standard diet group of 49%.[19]

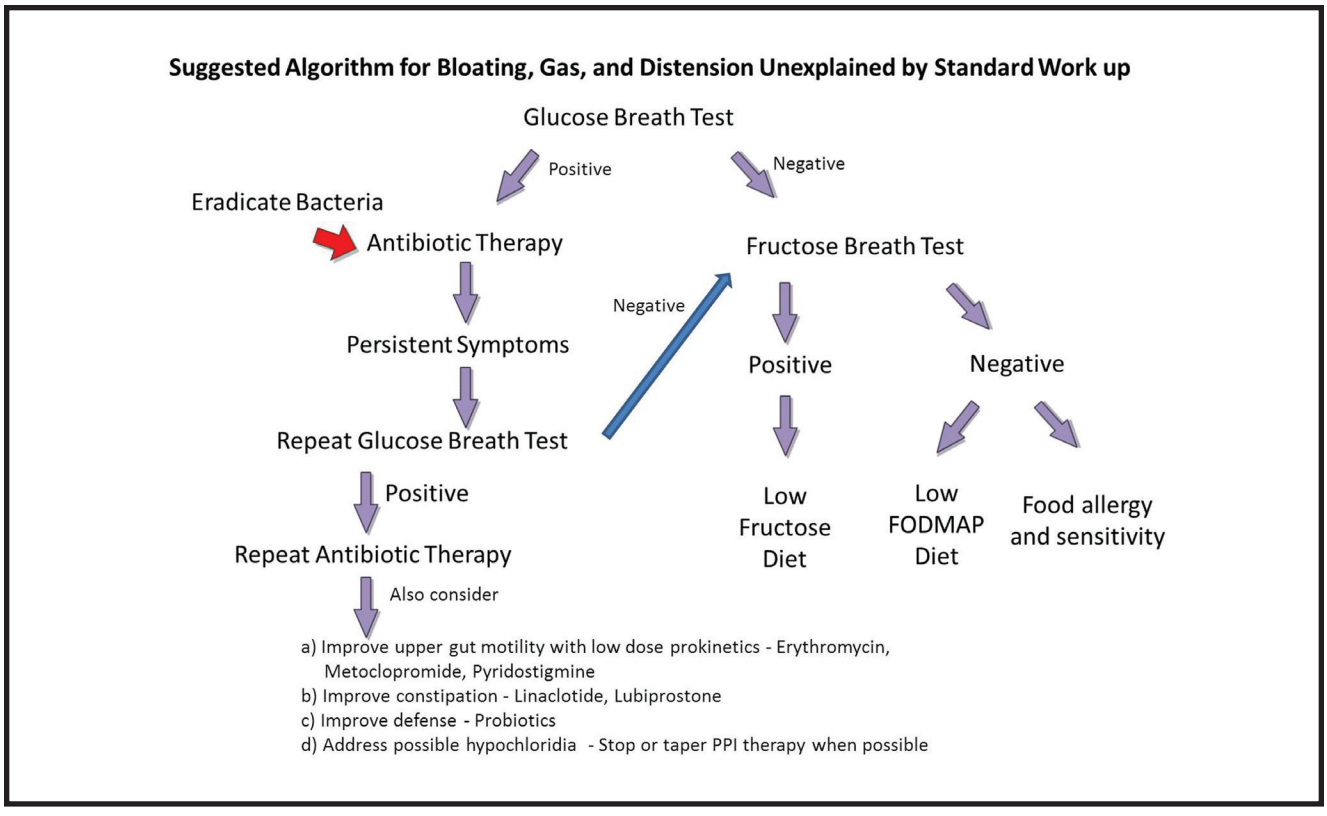

Figure 1. Algorithm Summarizing the Proposed Approach to Bloating of Undetermined Origin

Subsequently several high-quality clinical studies have further confirmed that FODMAP diet allows drug-free symptom relief in many patients with IBS.[23,24,25]

A typical approach in the implementation of the low FODMAP diet would involve restricting problematic (elimination diet) FODMAPs for 6 to 8 weeks, or until symptomatic control is achieved. This is performed by substituting high FODMAP foods with lower options or by reducing the total FODMAP load consumed in each meal or across the day. After this, small amounts of FODMAP-containing foods are reintroduced through challenges. The aim of challenging is to gradually increase to levels well-tolerated by the individual, while widening the diet as much as possible.

Food Sensitivity

Food sensitivity is an evolving science in nutrition, and it is different than food allergy or food intolerance. Food allergy is an IgE mediated immune response that occurs reproducibly on exposure to a given food, with a physiological response usually within 2 hours of exposure. Food intolerance can be due to lack of enzymes or bacterial changes. Food sensitivity is a reaction from an assault to the gut from food irritants, toxins (mold, pesticides), infections (SIBO), pharmacological decreases and increases in gut permeability, malabsorptions and psychological stress. True food sensitivity is a non-IgE adverse food reaction, where the individual may or may not have an initial reaction because it is usually delayed and dose dependent. Symptoms of food sensitivity can be similar to a food allergy resulting in skin changes, but it may also be systemic causing fatigue, asthma, migraines and body aches.

Serum testing for IgG and IgE antibodies to specific food antigens has been performed in the past with some degree of success. In a study in which 20 IBS patients unresponsive to standard therapy where enrolled, IgG and IgE levels to different food and mold panels were obtained. The most frequent positive serologic IgG antigen-antibody complexes in the study were: 4 or more molds, baker's yeast, onion mix, pork and peanut. These patients underwent targeted elimination diet followed by controlled food challenges and were followed at 1 year after trial completion with a questionnaire. This approach resulted in a sustained clinical response and improvement in overall well-being and quality

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of life.[26] These specific testing and treatment for food sensitivities really comes into play where breath testing has not been fruitful and other GI medical diagnoses are excluded. Determination of IgG serum antibodies to food constituents, elimination diets and re-challenge play a role in food sensitivity approaches.

Take Home Pearls

When the standard gastrointestinal work up for bloating of undetermined origin fails to expose any abnormality, providers should consider SIBO and DFI before patients are placed into the functional GI disorder compartment. Glucose and fructose breath tests are specific and sensitive diagnostic tests that can be used to either confirm or eliminate the possibility of SIBO or fructose intolerance in such patients.

For refractory cases of SIBO, the authors recommend to improve GI motility with low dose prokinetics when gastroparesis and/or small bowel dysmotility are present; chronic constipation should be aggressively treated if present; bifidobacterium infantus containing probiotics should be started to augment host defense; PPI should be tapered or stopped when possible to improve hypochlorhydria. Additionally, stop or attempt to decrease dose of anticholinergic drugs and/or narcotics when possible.

A positive fructose test would indicate the presence of fructose intolerance and should result in treatment with a low fructose diet. A negative FBT on the other hand should lead to a trial with the low FODMAP diet to assess if there is any improvement of symptoms. Finally food sensitivity and "food allergy" are a consideration to provide a rational approach for the practitioner.

We hope this article enlightens our readers and most of all we hope it improves the caring treatment and quality of life of your patients with abdominal bloating. ■

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