PROC (BAYL UNIV MED CENT)
2022;35(6):790–793

https://doi.org/10.1080/08998280.2022.2114070

Taylor & Francis
Taylor & Francis Group

Sucrose intolerance in adults with common functional gastrointestinal symptoms

Christine L. Frissora, MD[a] and Satish S. C. Rao, MD, PhD[b]

[a]Division of Gastroenterology and Hepatology, Weill Cornell Medical College, New York, New York; [b]Division of Gastroenterology/Hepatology, Medical College of Georgia, Augusta, Georgia

ABSTRACT

Sucrose intolerance is a form of carbohydrate malabsorption caused by sucrase-isomaltase deficiency that is more common than recognized. Its symptoms include postprandial cramping, bloating, gas, and diarrhea, which are difficult to distinguish from irritable bowel syndrome. The gold standard test for diagnosing sucrase deficiency is a sucrase enzyme assay of duodenal biopsies obtained by endoscopy. Hydrogen-methane or ^{13}C-sucrose breath tests are noninvasive methods to screen for sucrose malabsorption. This chart review included 258 consecutive adults (47 men and 211 women) with chronic unexplained gastrointestinal symptoms and suspected sucrose intolerance who were screened with a hydrogen-methane or ^{13}C-sucrose breath test. The incidence of sucrose malabsorption with two different hydrogen-methane breath tests was 34.4% (21/61) (Commonwealth Diagnostics International, Inc., Salem, MA) and 40% (20/50) (Aerodiagnostics, Concord, MA). The incidence of sucrose malabsorption with the ^{13}C-sucrose breath test was 26.5% (39/147). In a subgroup of patients with positive breath tests and clinical follow-up, counseling regarding diet and/or enzyme replacement led to symptomatic improvement in 26/43 (60%). In conclusion, sucrose malabsorption may present with irritable bowel syndrome symptoms in a proportion of adult patients, and breath tests may be useful in identifying sucrose malabsorption and differentiating it from other gastrointestinal disorders.

KEYWORDS Breath test; functional gastrointestinal symptoms; intestinal malabsorption; irritable bowel syndrome; sucrose intolerance

About 70% of the adult population is affected by some form of carbohydrate malabsorption. Sucrose malabsorption may be more prevalent than previously recognized.[1] Sucrose intolerance, caused by a deficiency in sucrase enzyme activity in the small intestine, presents with postprandial cramping, bloating, gas, and diarrhea. These are common symptoms that are often attributed to functional gastrointestinal (GI) disorders, such as irritable bowel syndrome (IBS). There are increasing reports of patients diagnosed with IBS whose symptoms are actually due, at least in part, to carbohydrate malabsorption, including sucrose.[2–5] Sucrose intolerance due to congenital sucrase-isomaltase deficiency (CSID) is rare. Secondary or acquired sucrose intolerance is more common and caused by intestinal brush border injury. The gold standard test for sucrase deficiency is the sucrase enzyme activity assay from duodenal biopsies. Alternatively, the sucrose breath test is a noninvasive way to diagnose sucrose malabsorption.[6] When sucrase deficiency is detected, a trial therapy of dietary modification and enzyme replacement therapy can be initiated. Our objective was to describe our clinical experience with a large group of adult patients presenting with chronic GI symptoms who were screened for sucrose malabsorption using breath testing and to discuss clinical outcomes in a subgroup who were followed up in our clinic.

METHODS

We conducted a chart review of 258 adult patients who sought care at an academic medical center with chronic, undiagnosed GI symptoms from October 19, 2016, to September 28, 2021. Patients whose symptoms were consistent with carbohydrate maldigestion were tested for sucrose malabsorption with one of two hydrogen-methane breath tests (Commonwealth Diagnostics International, Inc., Salem, MA, or Aerodiagnostics, Concord, MA). After January 2, 2018, screening was conducted with the ^{13}C-sucrose breath

Corresponding author: Christine L. Frissora, MD, 1283 York Avenue, Floor 9, New York, NY 10021 (e-mail: cfrissor@med.cornell.edu)
The authors report no funding or conflicts of interest.
Received July 22, 2022; Revised August 8, 2022; Accepted August 11, 2022.

test (Metabolic Solutions, Inc., Nashua, NH). Patients with breath test results and a record of their diagnoses at the time of breath testing were included in the review.

Study patients were given detailed instructions on how to prepare for the breath tests. Prior to taking one of the two hydrogen-methane breath tests, patients were instructed to suspend any oral antibiotic therapy for up to 4 weeks; suspend use of any laxatives and/or promotility drugs for 1 week; for 24 hours limit diet to baked or broiled chicken, turkey, or fish with salt and pepper only, plain steamed white rice, eggs, and clear chicken or beef broth; suspend smoking or vaping for 24 hours before and during the test; drink only water for 12 hours before and during the test; and avoid sleep or vigorous exercise for at least 1 hour before and during the test.[7,8]

Patients were instructed to blow exhaled air into the test tube (Commonwealth Diagnostics International) or the breath-gas analysis bag (Aerodiagnostics) labeled "baseline" in the test kit. After exhalation, patients were instructed to immediately secure the cap on the tube or immediately close the breath-gas analysis bag. Patients were instructed to thoroughly mix the contents of the sucrose packet in 8 ounces of room temperature water and drink the entire 8 ounces. The interval between collection of subsequent breath samples was 30 minutes for a total of four or six samples collected after the baseline sample. The labeled test tubes containing the breath samples were mailed directly to the diagnostic laboratory by the patient in a prepaid, labeled box. Any level of exhaled hydrogen or methane gas is considered abnormal, but a disruption in sucrose metabolism and absorption is only one of several possible causes for a patient to exhale these gases.[7,8]

For the ^{13}C-sucrose breath test, patients were instructed to discontinue any oral antibiotic for at least 1 week prior to taking the test and to avoid the use of any oral nonsteroidal antiinflammatory drug or antihistamine for at least 12 hours. They were instructed to fast for at least 8 hours prior to taking the test and to not sleep or exercise vigorously for at least 30 minutes before and during the test. Patients were to not chew gum or smoke on the morning of or during the test.[9] Patients were instructed to mix the packet of ^{13}C-labeled sucrose in 8 ounces of room temperature water. The baseline breath sample was collected prior to drinking the ^{13}C-sucrose solution, and three subsequent breath samples were collected every 30 minutes. Collected breath samples were mailed directly to the diagnostic laboratory.[10] A normal level of sucrose digestion is indicated when the 90-minute breath sample reading of exhaled $^{13}CO_2$ is $\geq$5.10% for women and $\geq$3.91% for men.[11]

RESULTS

We analyzed data from 258 patients, 47 who identified themselves as men and 211 who identified themselves as women, who presented with chronic undiagnosed functional GI symptoms. Sucrose malabsorption was detected by a hydrogen-methane breath test (Commonwealth Diagnostics) in 34.4% (21/61) of patients, including 10% of men and 39.2% of the women. The Aerodiagnostics hydrogen-methane breath test method was positive in 40% (20/50) overall, including 62.5% of men and 35.7% of women. Using the ^{13}C-sucrose breath test, sucrase deficiency was observed in 26.5% (39/147), with a positivity rate of 20.6% in men and 28% in women *(Table 1)*. Combining all breath tests in adult patients with chronic undiagnosed GI symptoms consistent with symptoms of malabsorption, 31% (80/258) were consistent with sucrose intolerance (men: 12/47, 25.5%; women: 47/211, 22%). Gender was not a discriminating factor *(Table 1)*. *Tables 2–4* list breath test outcomes for each test based on the primary ICD-10 diagnosis assigned prior to testing.

Table 1. Demographic and testing results of breath tests for sucrose malabsorption in patients presenting with "functional" gastrointestinal symptoms

Breath test	Patients tested (n)	Average age years (range)	Positive result
Hydrogen-methane for sucrose malabsorption (Commonwealth Diagnostics)	61	45.8 (21–82)	21 (34.4%)
Male	10	50 (33–66)	1 (10%)
Female	51	45 (21–82)	20 (39.2%)
Hydrogen-methane for sucrose intolerance (Aerodiagnostics)	50	47.2 (22–79)	20 (40%)
Male	8	45 (23–76)	5 (62.5%)
Female	42	48 (22–79)	15 (35.7%)
^{13}C-sucrose breath test (Metabolic Solutions)	147	40.3 (18–83)	39 (26.5%)
Male	29	41 (19–71)	6 (20.6%)
Female	118	40 (18-83)	33 (28%)

We attempted to reach every patient to provide test results and educate them regarding diet and enzyme replacement. Subsequently, the charts were reviewed to determine if there was a response to this intervention. In patients with a positive breath test who followed up and received counseling regarding diet and/or enzyme replacement, 26/43 patients (60%) reported improvement of symptoms.

DISCUSSION

In our study of 258 patients who presented with undiagnosed chronic GI symptoms suspicious for malabsorption, 80 patients (31%) had a positive breath test suggesting sucrose malabsorption. Of the patients with documented follow-up, 60% had a clinical response to a plan that included dietary modification or enzymatic treatment. Hydrogen-methane breath tests lack specificity, as a positive finding can be attributed to a number of causes including SIBO and rapid intestinal transit.[12] The ^{13}C-sucrose breath test, which

Table 2. Results of hydrogen-methane breath test analyzed by Commonwealth Diagnostics, by ICD-10 diagnosis (N = 61)

Primary ICD-10 diagnosis	Positive n/21 (%)	Negative n/40 (%)	Total n/61 (%)
Functional diarrhea	5 (23.8%)	9 (22.5%)	14 (22.9%)
Abdominal distension	3 (14.3%)	6 (15.0%)	9 (14.8%)
Abdominal pain	1 (4.8%)	9 (22.5%)	10 (16.4%)
IBS-diarrhea	3 (14.3%)	3 (7.5%)	6 (9.8%)
IBS-constipation	2 (9.5%)	1 (2.5%)	3 (4.9%)
IBS	–	1 (2.5%)	1 (1.6%)
Constipation	2 (9.5%)	2 (5.0%)	4 (6.6%)
Bacterial intestinal infection	2 (9.5%)	–	2 (3.3%)
Flatulence	1 (4.8%)	3 (7.5%)	4 (6.6%)
Iron deficiency anemia	1 (4.8%)	–	1 (1.6%)
Cyst of pancreas	1 (4.8%)	–	1 (1.6%)
Abnormal weight loss	–	1 (2.5%)	1 (1.6%)
GERD without esophagitis	–	1 (2.5%)	1 (1.6%)
Lactose intolerance, unspecified	–	1 (2.5%)	1 (1.6%)
Intestinal adhesions	–	1 (2.5%)	1 (1.6%)
Functional dyspepsia	–	1 (2.5%)	1 (1.6%)
Paralysis of diaphragm	–	1 (2.5%)	1 (1.6%)

GERD indicates gastroesophageal reflux disease; IBS, irritable bowel syndrome.

Table 3. Results of hydrogen-methane breath test analyzed by Aerodiagnostics, by ICD-10 diagnosis (N = 50)

Primary ICD-10 diagnosis	Positive n/20 (%)	Negative n/30 (%)	Total n/50 (%)
Abdominal distension	5 (25%)	5 (16.7%)	10 (20%)
Functional diarrhea	2 (10%)	2 (6.7%)	4 (8%)
Abdominal pain	2 (10%)	3 (10.0%)	5 (10%)
IBS-diarrhea	2 (10%)	5 (16.7%)	7 (14%)
Change in bowel habit	2 (10%)	–	2 (4%)
IBS-mixed	1 (5%)	4 (13.3%)	5 (10%)
IBS-constipation	1 (5%)	1 (3.3%)	2 (4%)
Functional dyspepsia	1 (5%)	1 (3.3%)	2 (4%)
Nausea	1 (5%)	–	1 (2%)
Right upper quadrant pain	1 (5%)	–	1 (2%)
Bacterial intestinal infection (*Clostridium difficile*)	1 (5%)	–	1 (2%)
Glucose intolerance	1 (5%)	–	1 (2%)
Flatulence	–	5 (16.7%)	5 (10%)
Abnormal weight loss	–	1 (3.3%)	1 (2%)
Eructation	–	1 (3.3%)	1 (2%)
Left lower quadrant pain	–	1 (3.3%)	1 (2%)
Constipation	–	1 (3.3%)	1 (2%)

IBS indicates irritable bowel syndrome.

tracks the $^{13}CO_2$ metabolic byproduct of ^{13}C-sucrose, may be a more specific measure of sucrase activity. Using the commercially available ^{13}C-sucrose breath test, the positive test yield was 26.5%.

Sucrase deficiency presents with abdominal symptoms related to the malabsorption of dietary sucrose that are confused with IBS. In our study, the most common diagnoses in the positive breath test group were functional diarrhea, flatulence, abdominal distention, IBS-diarrhea, IBS-mixed, IBS-constipation, and abdominal pain. In certain patients, carbohydrate intolerance coexists with IBS symptoms, so by addressing the malabsorption, at least part of the problem is solved.

Some patients diagnosed with IBS may be predisposed to sucrase deficiency caused by CSID. Two large studies reported that while relatively rare, sucrase-isomaltase (*SI*) variants are more common among adults diagnosed with IBS.[2,5] The first study, which compared 2146 IBS-diagnosed patients with a large, ethnically-matched reference population, found evidence linking *SI* variants with IBS susceptibility.[2] The second study compared the incidence of *SI* variants in 1031 IBS cases with 856 asymptomatic controls. Based on their findings, the investigators suggested *SI* variants may predispose patients to IBS.[5]

CSID, or primary sucrose malabsorption, is a rare genetic disorder associated with one or more mutations in the *SI* gene.[13] Secondary or acquired sucrose intolerance is more common and occurs as a result of mucosal damage and brush border injury from organic causes. The gold standard for diagnosing sucrase deficiency is disaccharidase testing of duodenal biopsies obtained during an upper endoscopy.[14] One recent study reported a 9.3% incidence of sucrase deficiency among 27,875 pediatric GI patients.[15] In a smaller pilot study, the incidence of sucrase deficiency was 14.3% in 28 pediatric GI patients.[16] A recent retrospective study of duodenal biopsies with normal histology from adults with unexplained GI symptoms found that 9.2% (11/120) had pan-disaccharidase deficiency, including sucrase deficiency.[17]

In a study of 46 adult patients diagnosed with IBS-diarrhea, only 52.2% obtained symptomatic relief with a low fermentable oligo-, di-, mono-saccharides and polyols (FODMAP) diet. The low FODMAP diet does not restrict sucrose. When analyzed for the presence of a hypomorphic *SI* variant, 23 patients were carriers of an *SI* variant, which contributed to the diminished response to a low FODMAP diet.[18] Therefore, IBS patients who do not respond to the low FODMAP diet should be tested for sucrose intolerance.

In this review, using the ^{13}C sucrose breath test, the four most common ICD-10 diagnostic codes in patients with a

Table 4. Results of ^{13}C-sucrose breath test by primary ICD-10 diagnosis (N = 147)

Primary ICD-10 diagnosis	Positive n/39 (%)	Negative n/111 (%)	Total n/150 (%)
Functional diarrhea	8 (20.0%)	16 (14.8%)	24 (16.2%)
Flatulence	7 (17.5%)	10 (9.3%)	17 (11.5%)
Abdominal distension	5 (12.5%)	10 (9.3%)	15 (10.1%)
IBS-mixed	4 (10.0%)	1 (0.9%)	5 (3.4%)
Functional dyspepsia	3 (7.5%)	4 (3.7%)	7 (4.7%)
IBS-constipation	3 (7.5%)	16 (14.8%)	19 (12.8%)
Constipation	2 (5.0%)	2 (1.9%)	4 (2.7%)
GERD without esophagitis	2 (5.0%)	2 (1.9%)	4 (2.7%)
Abdominal pain	1 (2.5%)	9 (8.3%)	10 (6.8%)
IBS-diarrhea	1 (2.5%)	17 (15.7%)	18 (12.2%)
Regurgitation	1 (2.5%)	–	1 (0.7%)
Right upper quadrant pain	1 (2.5%)	–	1 (0.7%)
Vitamin D deficiency	1 (2.5%)	–	1 (0.7%)
Hematochezia	1 (2.5%)	–	1 (0.7%)
IBS	–	2 (1.9%)	2 (1.4%)
Nausea	–	7 (6.5%)	7 (4.7%)
Vomiting	–	1 (0.9%)	1 (0.7%)
Change in bowel habit	–	1 (0.9%)	1 (0.7%)
Polyp of colon	–	2 (1.9%)	2 (1.4%)
Upper left quadrant tenderness	–	2 (1.9%)	2 (1.4%)
Celiac disease	–	1 (0.9%)	1 (0.7%)
Anal/rectal pain	–	1 (0.9%)	1 (0.7%)
Bacterial intestinal infection	–	2 (1.9%)	2 (1.4%)
Abnormal weight loss	–	1 (0.9%)	1 (0.7%)
Pelvic somatic dysfunction	–	1 (0.9%)	1 (0.7%)
Lactose intolerance, unspecified	–	1 (0.9%)	1 (0.7%)

GERD indicates gastroesophageal reflux disease; IBS, irritable bowel syndrome.

breath test indicative of sucrose malabsorption were functional diarrhea, flatulence, abdominal distention, and IBS-mixed. Sucrose intolerance can easily be diagnosed with a noninvasive breath test which is home administered and has acceptable test specificity. Our findings reinforce the recommendation that breath testing for sucrose intolerance should be considered in patients who present with unexplained symptoms of carbohydrate malabsorption, especially in patients who are not responding to traditional IBS therapies and diets.

ACKNOWLEDGMENTS

The authors thank QOL Medical, LLC for editorial assistance and Eric Medalla, RN for superb clinical support.

ORCID

Christine L. Frissora http://orcid.org/0000-0003-1742-4769

1. Gericke B, Amiri M, Scott CR, Naim HY. Molecular pathogenicity of novel sucrase-isomaltase mutations found in congenital sucrase-isomaltase deficiency patients. *Biochim Biophys Acta Mol Basis Dis*. 2017;1863(3):817–826. doi:10.1016/j.bbadis.2016.12.017.
2. Garcia-Etxebarria K, Zheng T, Bonfiglio F, et al. Increased prevalence of rare sucrase-isomaltase pathogenic variants in irritable bowel syndrome patients. *Clin Gastroenterol Hepatol*. 2018;16(10):1673–1676. doi:10.1016/j.cgh.2018.01.047.
3. Fedewa A, Rao SS. Dietary fructose intolerance, fructan intolerance and FODMAPs. *Cur Gastroenterol Rep*. 2014;16(1):370. doi:10.1007/s11894-013-0370-0.
4. Gibson P, Halmos E. FODMAPs and carbohydrate intolerance. clinical and basic neurogastroenterology and motility. In Rao SSC, Lee YY, Ghoshal UC, eds. *Clinical and Basic Neurogastroenterology Motility*. London: Academic Press; 2020:371–386. doi:10.1016/B978-0-12-813037-7.00026-1.
5. Henström M, Diekmann L, Bonfiglio F, et al. Functional variants in the sucrase-isomaltase gene associate with increased risk of irritable bowel syndrome. *Gut*. 2018;67(2):263–270. doi:10.1136/gutjnl-2016-312456.
6. Rezaie A, Buresi M, Lembo A, et al. Hydrogen and methane-based breath testing in gastrointestinal disorders: the North American consensus. *Am J Gastroenterol*. 2017;112(5):775–784. doi:10.1038/ajg.2017.46.
7. Aerodiagnostics/QuinTron. Breath-tests and digestive problems. 2015. https://aerodiagnostics.com/docs/Sucroseinst_Version2.pdf.
8. Commonwealth Diagnostics International. 7 simple steps: hydrogen & methane breath test for sucrose malabsorption. September 9, 2020. https://commdx.com/wp-content/uploads/2020/12/CDI-Instructional-Guide-Sucrose.pdf.
9. YouTube. Sucrose intolerance C13 breath test—how-to instructional video. February 21 2019. www.youtube.com/watch?v=lE43P7nlgoU.
10. Metabolic Solutions. Sucrose breath test. 2014. www.metsol.com/wp-content/uploads/2014/04/Sucrose-Breath-Test.pdf.
11. Pelton N, Tran C, Leo A, et al. The reproducibility of the 13C-sucrose breath test in children and adults [White paper]. QOL Medical; 2009.
12. Ghoshal UC. How to interpret hydrogen breath tests. *J Neurogastroenterol Motil*. 2011;17(3):312–317. doi:10.5056/jnm.2011.17.3.312.
13. Gericke B, Amiri M, Naim HY. The multiple roles of sucrase-isomaltase in the intestinal physiology. *Mol Cell Pediatr*. 2016;3(1):2. doi:10.1186/s40348-016-0033-y.
14. Robayo-Torres CC, Quezada-Calvillo R, Nichols BL. Disaccharide digestion: clinical and molecular aspects. *Clin Gastroenterol Hepatol*. 2006;4(3):276–287. doi:10.1016/j.cgh.2005.12.023.
15. Nichols BL Jr, Adams B, Roach CM, Ma CX, Baker SS. Frequency of sucrase deficiency in mucosal biopsies. *J Pediatr Gastroenterol Nutr*. 2012;55(Supplement 2):S28–S30. doi:10.1097/01.mpg.0000421405.42386.64.
16. Chumpitazi BP, Robayo-Torres CC, Tsai CM, et al. Yield of prospective disaccharidase testing in children with recurrent abdominal pain. *Gastroenterology*. 2013;144(5):S401–S402. doi:10.1016/S0016-5085(13)61477-8.
17. Viswanathan L, Kennedy K, Sharma A, Yan Y, Jimenez E, Rao SSC. Prevalence of disaccharidase deficiency in adults with unexplained gastrointestinal symptoms. *J Neurogastroenterol Motil*. 2020;26(3):384–390. doi:10.5056/jnm19167.
18. Zheng T, Eswaran S, Photenhauer AL, Merchant JL, Chey WD, D'Amato M. Reduced efficacy of low FODMAPs diet in patients with IBS-D carrying sucrase-isomaltase (*SI*) hypomorphic variants. *Gut*. 2020;69(2):397–398. doi:10.1136/gutjnl-2018-318036.