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Fructose Intolerance: Cause or Cure of Chronic Functional Constipation

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Abstract

Functional constipation is a common occurrence in the pediatric population. The link between fructose ingestion and constipation is obscure due to a lack of published data. In this article, we discuss the relationship of fructose tolerance and the development of constipation via a literature review and our single-center experience. A literature review of constipation and fructose ingestion was performed using PubMed. A retrospective chart review from the pediatric gastroenterology clinic, January 2012 to December 2015, was completed, with attention to the relationship of fructose intolerance and its clinical presentations. There were 367 patients who underwent the fructose breath hydrogen test (FBHT), out of which 208 patients had fructose intolerance. Clinical presentations included chronic abdominal pain, chronic diarrhea, chronic constipation, emesis, and nausea. Statistical significance was reached for chronic constipation, emesis, and nausea, being less likely to be found in FBHT-positive patients. Thus, fructose intolerance may help resolve symptoms in patients with chronic functional constipation.

Keywords

chronic functional constipation, fructose intolerance, abdominal pain, malabsorption, diet

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Introduction

Constipation, with a prevalence of 3%, is a common occurrence in the pediatric population. With varying reported symptoms, it is important to define constipation and understand what to look for in a child. The Rome IV criteria defines it as having at least 2 of the following present for at least 1 month: 2 or fewer defecations per week, history of excessive stool retention, history of painful or hard bowel movements (BM), history of large-diameter stools, and presence of a large fecal mass in the rectum. In toilet-trained children, the following additional criteria may be used: at least 1 episode/week of incontinence after the acquisition of toileting skills and a history of large-diameter stools that may obstruct the toilet. In children older than 4 years of age, a history of retentive posturing, excessive stool retention, and having at least 1 episode of fecal incontinence/week should be considered.[1-3]

Before we attempt to treat constipation, functional causes have to be differentiated from organic ones. Organic causes of constipation may include neurological conditions (eg, cerebral palsy, mental retardation, or spinal cord problems), hypothyroidism, cystic fibrosis, abnormal neural development of the bowel (eg, Hirschsprung disease), and side effects of medications (eg, antacids, antidepressants, anticonvulsants, chemotherapy medications, or narcotic pain medications). Functional constipation is constipation that appears without objective evidence of an underlying pathological, anatomical, or biochemical condition.[4]

The most common cause of constipation in children is functional constipation. It typically presents as stool retention that may be associated with factors such as toilet training, changes in diet or behavior, stress, illness, painful defection, or stool withholding due to fear of painful defecation.[1] In this article, we will discuss

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chronic functional constipation (CFC) and its relationship to fructose intolerance.

Fructose is a monosaccharide found in our diet as 3 main forms: as free fructose (present in fruits and honey), as a constituent of the disaccharide sucrose, or as fructans, a polymer of fructose usually in oligosaccharide form (present in some vegetables and wheat).[5,6] A failure to completely absorb fructose in the small intestine is classified as fructose malabsorption. This malabsorption presents a solvent drag, pulling fluid into the lumen. This, in turn, leads to luminal distention, oftentimes causing abdominal pain and increased small bowel and colonic motility, resulting in diarrhea.[4,5] The remaining fructose that reaches the colon is then fermented by bacteria into hydrogen, carbon dioxide, and methane. These gases then lead to abdominal pain, bloating, and flatulence.[4] As such, the clinical manifestation of fructose malabsorption is defined as fructose intolerance.[6] Here, we will explore whether we can use fructose intolerance to help relieve gastrointestinal dysfunctions such as CFC.

Loening-Baucke[7] looked at implementing dietary changes such as the use of corn syrup (a form of fructose) versus laxatives in the treatment of CFC via a retrospective chart review. The study was done on 172 infants and toddlers with CFC, younger than the age of 2 years. Parameters that were looked at included the following: duration of constipation, frequency of BM per week, BM consistency (scale: 1 = rock-hard or hard; 2 = formed; 3 = soft; 4 = loose; 5 = watery), the presence of pain (reported by the mother as screaming with BMs), stool withholding, blood with BMs, and the presence of rectal impaction or abdominal fecal mass. The initial treatment in 116 children was dietary changes, such as fruit juices, fruits, and vegetables, corn syrup, or both. Of those who followed-up, 25% had resolution of their constipation.[7] With retrospective chart review, it was found that these were children with mild symptoms or acute constipation. For example, their score within the above-mentioned parameters was found to be significantly milder compared with the children requiring treatment with laxatives, especially in terms of duration of constipation, pain with BMs, blood with BM, fecal impaction, and abdominal fecal mass. Thus, the introduction of fructose may be of benefit in children with mild symptoms of constipation.

Savino et al took a similar approach and studied the effect of introducing both fructooligosaccharides and galactooligosaccharides to partially hydrolyzed infant milk formula to alleviate common feeding problems such as constipation, colic, and regurgitation. This observational prospective study involved introducing this formula to infants for 14 days and observing its effects on the above-mentioned gastrointestinal disorders. Of the 232 infants with constipation, given the formula, 147 (63%) demonstrated an increase in the daily number of stools by 0.42 (95% confidence interval = 0.5-0.3; $P = .005$). Thus, the introduction of fructooligosaccharides to formula may have helped relieve symptoms of constipation in these formula-fed infants.[8]

In fact, the association of fructose ingestion and gastrointestinal symptoms may have a dose-dependent relationship. Esobar et al found that with increasing fructose consumption from 25 to 50 g, there was an increase in prevalence of fructose malabsorption from approximately 20% to 60%[3,5,7,9] in adults.[4] Likewise, Whitfield et al and Gomara et al discussed the role of fructose, in the form of high-fructose corn syrup, in exacerbating gastrointestinal symptoms such as nausea, bloating, and abdominal pain.[10,11] Such symptoms were found to be more frequent at higher doses of fructose.

This trend can be explained by the pathophysiology of how fructose is absorbed in the small intestine. One study by Escobar et al hypothesized the role of fructose malabsorption in chronic abdominal pain as being dependent on the ratio of fructose and glucose. There are 2 transport systems at play in fructose absorption. The first, GLUT (glucose transport protein) 5, is found in the brush border membrane of human small intestine enterocytes, and fructose is transported passively by facilitated diffusion. GLUT 5 is a glucose-independent model of fructose absorption. The second means of absorption involves a paracellular transport system with opening of tight junctions by glucose absorption. Thus, fructose is able to move passively with water via osmotic drag through the channels between the enterocytes. Due to the limited capacity of GLUT 5 to transport fructose via facilitated diffusion, glucose facilitates fructose absorption by the second model. Thus, it is suggested by Escobar et al that fructose malabsorption occurs when there is fructose present in excess of glucose, or in other words, that absorption of fructose is facilitated by foods that have closer to a 1:1 ratio of glucose-fructose. Therefore, in terms of dietary interventions to help relieve CFC, it may be reasonable to consider the glucose-fructose ratio and implement diets where fructose is present in excess to glucose.

As we can see, the relationship between fructose malabsorption and CFC is confounded by an interplay of a multitude of factors such as the quantity/ratio of fructose ingested, the type of dietary foods consumed, as well as degree of constipation. Thus, this relationship requires more clarification in order to appropriately guide clinical practice and the treatment of children with CFC.

Table 1. Characteristics of Patients Undergoing FBHT.

	Negative FBHT (N = 159)	Positive FBHT (N = 208)	*P-Value*[a]
Sex			
Female	113	133	
Male	46	75	
Age (years)	13.05	11.48	
Symptoms			
Abdominal pain	158	206	.726
Diarrhea	65	79	.573
Constipation	50	27	<.001
Emesis	36	27	.015
Nausea	103	101	.002
Foul breath	1	1	.848
Bloating	23	45	.061
Flatulence	7	11	.697

Abbreviation: FBHT, fructose breath hydrogen test.
[a]$P< 0.05$

Single-Center Experience With Fructose Malabsorption

Many studies have explored the relationship of fructose, its malabsorption, and intolerance in particular, to various gastrointestinal symptoms. Thus far, we have learned that fructose malabsorption is not only associated with abdominal pain, bloating, nausea, flatulence, diarrhea, and emesis but may also help relieve symptoms of CFC. Our goal in this study was to further assess the association between fructose intolerance and CFC, in particular looking at whether fructose intolerance may be protective of CFC. To do so, we took a closer look at the patient population at a single-center pediatric gastroenterology clinic.

Methods

Institutional review board approval was granted by SUNY Upstate Medical University after review of the study protocol. A retrospective chart review study was performed. Inclusion criteria was any child younger than 21 years of age who had undergone a breath hydrogen or methane test (CPT code 91065) at the pediatric gastroenterology clinic from March 2012 to September 2015. Exclusion criteria included asymptomatic patients, patients on antibiotics, and patients younger than 6 years of age as they were not able to perform the tests. From the data, we abstracted demographic information, the clinical characteristics on first presentation, and the results of the fructose breath hydrogen test (FBHT). Fructose intolerance was defined as having clinical gastrointestinal symptoms and a positive FBHT. Of note, constipation was defined based on the above-mentioned Rome IV criteria. From there, χ^2 test was performed for statistical analysis of initial presenting symptoms among those patients who tested positive for FBHT and those who tested negative for FBHT; significance was assigned at $P < .05$.

The FBHT test was administered to patients evaluated in clinic with unexplained chronic abdominal pain alone or associated with constipation, gas or bloating, and/or diarrhea. The patients were given a standard dose of 1 g/kg fructose to a maximum of 25 g. Hydrogen and methane were measured at 8 time points. The test was presumed positive if breath hydrogen exceeded 20 ppm above baseline.

Results

Once the retrospective chart review was performed, a total of 367 patients who had undergone the FBHT were identified (246 females and 121 males) with a mean age of 12.2 years. Utilizing the results from the prior FBHTs performed, 208 of the 367 patients (133 females/76 males, mean age of 11.5 years) were identified to have fructose intolerance. The remaining 159 of the 367 patients (113 females/45 males, mean age of 13.1 years) had a negative FBHT (Table 1).

Subsequently, the initial clinical characteristics of these patients were related to their FBHT results, as seen in Table 1. Of the patients with positive FBHT, 206 had abdominal pain, 79 had diarrhea, 27 had constipation, 27 had emesis, 101 had nausea, 1 had foul breath, 45 had bloating, and 11 had flatulence. Of the patients with negative FBHT, 158 had abdominal pain, 65 had diarrhea, 50 had constipation, 36 had emesis, 103 had nausea, 1 had foul breath, 23 had bloating, and 7 had flatulence.

However, statistical significance between these 2 groups was only reached for constipation, emesis, and nausea, with $P < .001$, .015, and .002, respectively. Children with fructose intolerance and positive FBHT were less likely to have constipation, emesis, and nausea.

Limitations

Limitations of our study included it being retrospective in nature versus a randomized controlled trial. We were also unable to use a standardized tool to collect the data on patients' symptoms. We had to rely entirely on the patients' report of symptoms and what was documented in the charts.

Future Considerations

Now that we have some clinical data to compare the symptoms of FBHT-positive versus FBHT-negative patients, we need to explore the role of dietary modifications. It would also be beneficial to explore this relationship in a dose-dependent manner. For example, FBHT-positive and FBHT-negative patients should be randomized into a low-fructose diet group, high-fructose diet group, or a group null of any dietary modifications. Other factors that should be considered include the type of fructose, the glucose-fructose ratio, and the frequency of intake. Data should be collected to observe any changes in symptoms for all groups of patients. In addition, as Loening-Baucke stated, the degree of constipation should also be taken into account as well as any behavioral or lifestyle changes for the patient. Thus, the role of fructose intolerance and its clinical benefits need to be further explored and clarified.

Conclusions

As we continue to see constipation in our pediatric patients, we must explore ways to help relieve their symptoms. In this article, we investigated the role of fructose intolerance in patients who presented to our clinic with abdominal pain, diarrhea, constipation, emesis, bloating, and flatulence -many of the gastrointestinal symptoms seen in patients with functional bowel syndrome. In our study, we found that the presence of fructose intolerance and positive FBHT was associated with fewer patients with constipation, nausea, and emesis. This connects us back to our discussion earlier looking at the relationship of fructose malabsorption to abdominal pain, bloating, and diarrhea. As we increase fructose ingestion, we see increased fructose malabsorption, partially due to an imbalance of the glucose-fructose ratio. The clinical manifestations of this malabsorption induces a state of fructose intolerance where we see an increase in intestinal motility. This increase in intestinal and colonic molity results in looser stools, which, thus, may help relieve symptoms suffered by patients with CFC. It will be important to better understand the intricacies of this association between fructose intolerance and CFC. Further studies will aid clinical judgement and treatment plans, particularly dietary interventions, for patients with CFC.

Author Contributions

MM: Contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; agrees to be accountable for all aspects of work ensuring integrity and accuracy.
MB: Contributed to conception and design; contributed to acquisition, analysis, and interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

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