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Research Article

Fructose Restricted Diet Improves Quality of Life in Children with Dietary Fructose Intolerance

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Abstract

Objectives: Incomplete fructose absorption can result in gastrointestinal distress symptoms in children, which may impact their quality of life; however, this has not been formally studied. This study evaluates whether dietary fructose restriction improves quality of life and gastrointestinal symptoms in children with breath test confirmed fructose intolerance, as measured by the Pediatric Quality of Life Inventory (PedsQL) and PedsQL Gastrointestinal Symptom Scale (GSS).

Methods: Thirty eight subjects, ages ranging from 8 to 18 years old with a positive hydrogen breath test consistent with fructose intolerance were included. Subjects drank 2 grams of fructose sugar per every kilogram of body weight, with a maximum of 50 grams fructose sugar. Hydrogen was collected every 30 minutes over two hours. Hydrogen production of >20 ppm indicated a positive test. Participants with a positive breath test completed a PedsQL and a GSS assessment worksheet prior to leaving the office on the day of diagnosis. A dietitian then instructed subjects to follow a two-week fructose restricted diet. Subjects were then called exactly 2 weeks after diagnosis, and a post-intervention PedsQL/GSS was administered.

Results: The median age of subjects studied was 12.2 (10.4, 15.1) years. GSS and PedsQL scores showed statistically significant improvement from a mean of 47.2 (± 14) to 72.8 (± 15.5) and 75.0 (13.3) to 88.3 (± 8.9) respectively after the two-week dietary intervention (p value < 0.001 for both). Subjects showed significantly improvement on their total PedsQL score and in 4 out of the 5 PedsQL subscales, namely physical, emotional, school, and psychosocial function (p value < 0.001 for all).

Conclusion: Fructose restricted diet can significantly improve quality of life in fructose intolerant children.

INTRODUCTION

Fructose is a monosaccharide ubiquitous in Western diets of children today. It exists both naturally in many fruits and some vegetables, as well as artificially as a sweetening additive in the form of high fructose corn syrup (HFCS), honey, and sucrose [1]. Comparison of data collected in national surveys over the last three decades identified a marked increase of fructose consumption in Americans two years and older, with

HFCS accounting for 8.3% of total energy intake in 2003-2004 compared to 4.3% in 1989-1991 [1,2]. In the past, fructose malabsorption may have been less of a concern, given the limited quantity of fructose in the diet. However with HFCS representing at least 15.7% of total carbohydrate intake among Americans, effective recognition and management of fructose intolerance is of increasing importance [2].

Fructose malabsorption seems to be an under-recognized problem accounting for non-specific, chronic abdominal complaints in children and adults [3,4] and has been linked to conditions including irritable bowel syndrome [5], small intestine bacterial overgrowth [6], and depression [7,8]. Clinically, fructose malabsorption presents with a variety of symptoms including chronic diarrhea, periumbilical crampy abdominal pain, bloating, nausea, and vomiting [3,4]. Mechanistically, fructose is absorbed passively by facilitated diffusion via GLUT5 transporters located in the brush border membrane of small intestine enterocytes [9,10]. Net movement across the membrane is driven by the energy generated by the solute concentration gradient and is dose dependent with limited absorption capacity even in healthy individuals [1,11]. The presence of unabsorbed fructose in the colon acts as an osmotic laxative that draws fluid into the distal small bowel and colon, resulting in diarrhea [4]. Fermentation of excess fructose also releases organic acids and hydrogen gas which causes bloating, rumbling, and flatulence [12,13]. Hydrogen produced in this process is absorbed into the blood stream and expired through the lungs, which allows analysis of fructose malabsorption via fructose hydrogen breath tests (FHBT) [14].

Many studies have identified the efficacy of fructose restricted diets to improve abdominal symptoms in adults [3,4,15,16], however there is limited research on how dietary fructose restriction affects symptoms in children [4]. Additionally, there is no research evaluating how fructose intolerance impacts quality of life pre- and post-fructose restricted diet within the pediatric population. With the increase in consumption of fructose containing food and beverages, it is important to evaluate whether implementation of a stringent fructose-free diet is beneficial to a child's quality of life. This study will evaluate if a fructose-restricted diet does or does not improve quality of life in children after diagnosis of fructose intolerance by FHBT.

MATERIALS AND METHODS

Subjects

This study was approved by the Cleveland Clinic Institutional Review Board (IRB). It included 38 subjects seen at the pediatric gastroenterology clinic at Cleveland Clinic Children's. Subjects were 8 to 18 years old with a positive hydrogen breath test indicating fructose intolerance. Patients were enrolled as they were diagnosed with fructose intolerance. Patients with underlying gastrointestinal issues including inflammatory bowel disease (IBD), celiac disease, and anorexia were excluded from the study. Exclusion criteria were assessed via history and lab work collected on visits prior to the day subjects tested positive for fructose intolerance via breath testing.

Diagnostic Measurements with Fructose Hydrogen Breath Tests

Each subject drank 2 grams of fructose sugar per every kilogram of body weight, with a maximum amount of 50 grams fructose sugar. Hydrogen was collected every 30 minutes over two hours. A hydrogen production of ≥20 ppm indicated a positive test.

Quality of Life Assessments

The Quality of Life Assessments were carried out using the PedsQL questionnaires, developed by Dr. James W. Varni. All participants completed a Pediatric Quality of Life Inventory Version 4.0 (PedsQL) and a PedsQL Gastrointestinal Symptom Parent Report (GSS). The PedsQL Version 4.0(child report for age 8-12 years; teen report for 13-18 years) is a 23 item questionnaire completed by the child to evaluate health related quality of life (HRQOL) subjects who are either healthy or suffering from an acute or chronic illness (Appendix 1). Four distinct domains of life including physical functioning (8 items), emotional function (5 items), social functioning (5 items), and school functioning (5 items) are evaluated on a scale of 0 to 4, and subsequently scored. This tool is well validated and distinguishes healthy children from acutely or chronically ill children, as well as delineates severity of disease in those affected by a chronic illness [17-21].

The PedsQL GSS scale is a nine item, disease specific questionnaire, which has shown acceptable to excellent measurement properties, allowing it to be used as a common metric to compare common GI specific symptoms in children with both functional and organic GI complaints (Appendix 2) [22,23].

Informed consent was obtained from all study participants on the day fructose intolerance was diagnosed. This was followed by administration of the PedsQL and GSS symptom scales. After the symptom scales were completed, a gastroenterology specific dietician gave instructions for the patient to follow a two-week fructose-restricted diet which included face to face counseling, handouts listing fructose-free foods, and sample meal plans. After two weeks, the dietitian called the patient and administered a second set of Peds QL and GSS symptoms scales. Scores were only collected from those who verbally confirmed adherence to the diet. Both researchers used standard procedures outlined on the questionnaire instructions for scoring symptoms scales.

The PedsQL and GSS are both scaled from 0 to 100, with higher scores indicating higher quality of life. Changes in these measures were computed as the difference of the post-dietary intervention from time of diagnosis (pre). Therefore, improvements in quality of life are indicated by change scores greater than 0.

Statistical Analysis

Changes in PedsQL and GSS were assessed with the one-sample t-test. All analyses were performed on a complete-case basis. All tests were two-tailed and performed at a significance level of 0.05. SAS 9.2 software (SAS Institute, Cary, NC) was used for all analyses.

RESULTS

Patient Characteristics and Clinical Data

The median age of subjects was 12.2 (10.4 to 15.1) years

and 58% were female. The indications for FHBT are indicated in (Table 1). The most common presenting symptom noted was abdominal pain, occurring in 94.7 % of patients, with bloating, flatulence, eructation and diarrhea occurring in over one quarter of patients. Laboratory values of WBC, hemoglobin, platelets, ESR, and TSH were also evaluated at the time of diagnosis and mean values were found to be within a normal range for all subjects (Table 1). Celiac panel testing performed in 28 out of 38 subjects was found to be negative in all cases, with the remaining 10 subjects having no testing documented. Normal laboratory values collected prior to diagnosis of fructose intolerance, suggests that symptoms were due to fructose intolerance and not an alternative underlying pathology.

Changes in Quality of Life with Fructose-Restricted Diet

Children with fructose intolerance had a mean GGS and PedsQL score of 47.2 out of 100 (± 14) and 75 out of 100 (± 13.3) respectively, before dietary intervention. After implementation of a 2-week fructose-free diet, there was improvement in the GSS and PedsQL scores to 72.8 (± 15.5) and 88.3 (± 8.9), respectively (p value < 0.001) (Figure 1). Furthermore, subjects showed significant improvement in 4 out of the 5 PedsQL subscales, namely physical, emotional, school, and psychosocial function (p value < 0.001) (Table 2).

DISCUSSION

It is undeniable that with the increased prevalence and accessibility of fructose in the American diet, identification and effective management of fructose intolerance has become very important. Increased rates of fructose consumption by children has not only contributed to childhood obesity [24] and insulin resistance [25] but has also identified fructose malabsorption as

Table 1: Baseline Demographics and Clinical Characteristics.

	N = 38
Sex	**N (%)**
Female	22 (57.9)
Male	16 (42.1)
Age	**Years**
Median	12.2
Q1, Q3	10.4, 15.1
Presenting Symptoms	**N (%)**
Abdominal Pain	36 (94.7)
Bloating	12 (31.5)
Flatulence	10 (26.3)
Eructation	10 (26.3)
Diarrhea	7 (18.4)
Vomiting	2 (5.3)
Reflux	2 (5.3)
Nausea	2 (5.3)
Fatigue	1 (2.6)
Laboratory Measurements	**Mean (SD)**
WBC (k/uL)	6.7 (2.3)
Hemoglobin (g/dL)	13.7 (1.16)
Platelets (k/uL)	278.6 (51.8)
ESR (mm/hr)	5.7 (3.8)
TSH (mU/L)	2.5 (1.2)

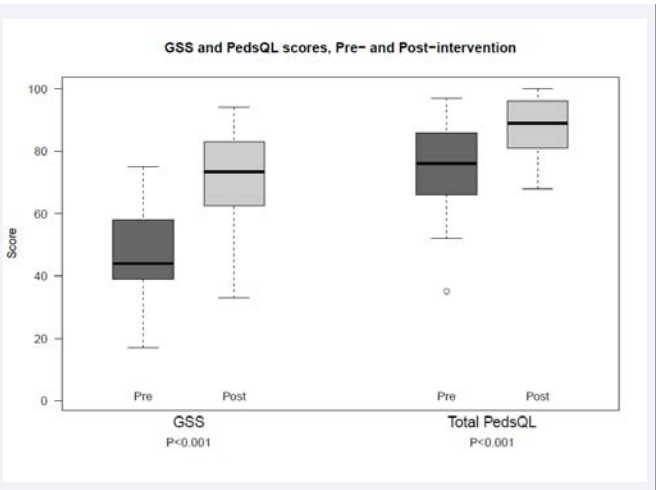

Figure 1 GSS and PedsQL scores, pre- and post- fructose restricted dietary intervention. The horizontal axis indicates the quality of life scoring tool used (GSS vs. PedsQL) and the vertical axis indicates the scores obtained pre- and post- implementation of a fructose-free diet. The box represents the interquartile range (25th and 75th percentile) from the median (horizontal line) and the vertical bars represent the 95% confidence interval. After dietary modification, the pre- and post-GSS and PedsQL scores improved.

an illness with the potential to negatively affect children's quality of life. Health related quality of life research is a rapidly evolving concept within healthcare, as it can not only elucidate the burdens associated with a chronic illness, but also provides information on how therapeutic intervention may alter a patient's quality of life. There is a paucity of data in both the adult and pediatric population as to whether quality of life can be improved with implementation of a fructose-free diet in those with breath test confirmed fructose intolerance.

As in adults, children with fructose intolerance most commonly complain of symptoms including abdominal pain, nausea, vomiting, flatulence, diarrhea, or altered bowel habits. In adults, such symptoms associated with fructose intolerance are under-recognized in those diagnosed with irritable bowel syndrome (IBS) [3]. Although fructose intolerance was previously thought to be more prevalent in adults with IBS, recent studies have identified an equal prevalence of disease in those with functional bowel disorders and healthy individuals [26,27]. Thus, fructose intolerance is best diagnosed when both gastrointestinal symptoms and a positive fructose hydrogen breath test is obtained. The capacity of fructose absorption in normal adults ranges from 15 g to 50g, thus indicating use of a standard maximum of 50g fructose load when conducting fructose breath testing for diagnosis. Interestingly in children fructose malabsorption has been noted to change with age, possibly due to the up regulation of GLUT 5 expression over time [11]. The optimal dose of fructose ingestion to diagnose malabsorption may be more difficult to determine within pediatric population [28]. Nonetheless, FHBT remains the most practical means of diagnosing fructose intolerance in children.

Many studies have noted the benefit of adhering to a low fructose diet in those previously diagnosed with IBS, but later found to have fructose intolerance via breath testing. A study by

Table 2: Comparison of results from the GSS and PedsQL scores pre- and post- dietary intervention. Subjects improved significantly in the GSS and in 4 out of the 5 PedsQL subscale. Mean score improvements ranged from 3 points (Social function score, PedsQL) to 25 points (GSS).

	Pre	Post	Change	T-test p value
GI symptom scale (GSS)				<0.001
Mean (SD)	47.2 (14.0)	72.8 (15.5)	25.3 (16.7)	
95% CI for change			(19.7, 30.9)	
PedsQL total score				<0.001
Mean (SD)	75.0 (13.3)	88.3 (8.9)	13.0 (15.4)	
95% CI for change			(7.7, 18. 3)	
Physical function score (PedsQL)				<0.001
Mean (SD)	73.6 (17.5)	90.0 (9.4)	16.9 (18.5)	
95% CI for change			(10.5, 23.2)	
Emotional function score (PedsQL)				<0.001
Mean (SD)	71.7 (20.2)	87.2 (14.1)	15.7 (21.9)	
95% CI for change			(8.3, 23.1)	
Social function score (PedsQL)				0.099
Mean (SD)	90.4 (12.0)	94.4 (8.7)	3.5 (12.3)	
95% CI for change			(-0. 7, 7.6)	
School function score (PedsQL)				<0.001
Mean (SD)	64.1 (19.9)	81.4 (17.5)	17.7 (22.1)	
95% CI for change			(10.1, 25.3)	
Psychosocial function score (PedsQL)				<0.001
Mean (SD)	75.4 (13.2)	87.8 (10.0)	12.5 (16.2)	
95% CI for change			(7.0, 18.0)	

Johlin et al. indicated that in a population of adults with fructose malabsorption, adherence to a low fructose diet decreased gastrointestinal symptoms (bloating, gas, abdominal pain) and improved quality of life [29]. Improved quality of life manifested itself as the ability to return to normal work patterns, travel without prior bothersome symptoms, and improved social function. In children, a study by Tsampalieros et al. revealed that a in a sample with FHBT confirmed fructose intolerance, 97% who adhered to a low or reduced fructose diet remained symptom free 18-24 months later with continuation of the diet [4]. Although symptom improvement was identified in this study, the effect on quality of life was not evaluated.

The assessment of health care quality of life was performed using the PedsQL and GSS to gather data regarding burden of disease and efficacy of dietary intervention.

The PedsQL allows a child to self-report how symptoms of a chronic illness affect his/her physical, social, emotional, and school functioning. The GSS scale is a newer scale that has been effective when used in conjunction with the PedsQL, to capture data with regards to gastrointestinal symptoms. In our study, we have used both these scales to indicate that a fructose restricted diet is an intervention with the potential to improve a child's quality of life, in as quickly as two weeks. Our findings are particularly significant, as this is the first prospective study that indicates an improvement in emotional, physical, psychosocial and school related functionality after dietary fructose restriction. We also evaluated parents perception alongside self-report by children, which is equally important. Studies indicate that parents perceptions of their child's illness often guide the utilization of healthcare resources, which not only enables prediction of future healthcare costs, but may also affect treatment outcome [30,31].

Some potential limitations of this study include the lack of a control group of healthy subjects to which our pre- and post-intervention data could be compared. Conducting a future study to evaluate the health related quality of life (HRQOL) of children with fructose intolerance as compared to healthy controls may also be beneficial to further elucidate the burden of this chronic illness. Additionally, completing a follow up evaluation using the GSS and PedsQL questionnaire one year after diagnosis may also elucidate whether prolonged adherence to a fructose-free diet has the potential to provide a sustained improved quality of life for these children. In conclusion, this prospective study elucidates the benefits children with fructose intolerance can experience, in as quickly as two weeks, with implementation of a fructose-free diet. Since a child's quality of life can be negatively impacted by symptoms associated with fructose intolerance, it is extremely important that awareness regarding the diagnosis and efficacy of dietary intervention are understood and further studied.

REFERENCES

1. Kyaw MH, Mayberry JF. Fructose malabsorption: true condition or a variance from normality. J Clin Gastroenterol. 2011; 45: 16-21.
2. Duffey KJ, Popkin BM. High-fructose corn syrup: is this what's for dinner? Am J Clin Nutr. 2008; 88: 1722S-1732S.
3. Choi YK, Johlin FC Jr, Summers RW, Jackson M, Rao SS. Fructose intolerance: an under-recognized problem. Am J Gastroenterol. 2003; 98: 1348-1353.
4. Tsampalieros A, Beauchamp J, Boland M, Mack DR. Dietary fructose intolerance in children and adolescents. Arch Dis Child. 2008; 93: 1078.
5. Heizer WD, Southern S, McGovern S. The role of diet in symptoms of irritable bowel syndrome in adults: a narrative review. J Am Diet Assoc. 2009; 109: 1204-1214.

6. Gibson PR, Newnham E, Barrett JS, Shepherd SJ, Muir JG. Review article: fructose malabsorption and the bigger picture. Aliment Pharmacol Ther. 2007; 25: 349-363.

7. Ledochowski M, Widner B, Murr C, Sperner-Unterweger B, Fuchs D. Fructose malabsorption is associated with decreased plasma tryptophan. Scand J Gastroenterol. 2001; 36: 367-371.

8. Varea V, de Carpi JM, Puig C, Alda JA, Camacho E, Ormazabal A. Malabsorption of carbohydrates and depression in children and adolescents. J Pediatr Gastroenterol Nutr. 2005; 40: 561-565.

9. Davidson NO, Hausman AM, Ifkovits CA, Buse JB, Gould GW, Burant CF. Human intestinal glucose transporter expression and localization of GLUT5. Am J Physiol. 1992; 262: C795-800.

10. Burant CF, Takeda J, Brot-Laroche E, Bell GI, Davidson NO. Fructose transporter in human spermatozoa and small intestine is GLUT5. J Biol Chem. 1992; 267: 14523-14526.

11. Jones HF, Butler RN, Brooks DA. Intestinal fructose transport and malabsorption in humans. Am J Physiol Gastrointest Liver Physiol. 2011; 300: G202-206.

12. Riby JE, Fujisawa T, Kretchmer N. Fructose absorption. Am J Clin Nutr. 1993; 58: 748S-753S.

13. Southgate DA. Digestion and metabolism of sugars. Am J Clin Nutr. 1995; 62: 203S-210S.

14. Beyer PL, Caviar EM, McCallum RW. Fructose intake at current levels in the United States may cause gastrointestinal distress in normal adults. J Am Diet Assoc. 2005; 105: 1559-1566.

15. Shepherd SJ, Gibson PR. Fructose malabsorption and symptoms of irritable bowel syndrome: guidelines for effective dietary management. J Am Diet Assoc. 2006; 106: 1631-1639.

16. Fernández-Bañares F, Rosinach M, Esteve M, Forné M, Espinós JC, Maria Viver J. Sugar malabsorption in functional abdominal bloating: a pilot study on the long-term effect of dietary treatment. Clin Nutr. 2006; 25: 824-831.

17. Varni JW, Seid M, Rode CA. The PedsQL: measurement model for the pediatric quality of life inventory. Med Care. 1999; 37: 126-139.

18. Varni JW, Seid M, Kurtin PS. PedsQL 4.0: reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. Med Care. 2001; 39: 800-812.

19. Varni JW, Seid M, Knight TS, Uzark K, Szer IS. The PedsQL 4.0 Generic Core Scales: sensitivity, responsiveness, and impact on clinical decision-making. J Behav Med. 2002; 25: 175-193.

20. Varni JW, Burwinkle TM, Seid M, Skarr D. The PedsQL 4.0 as a pediatric population health measure: feasibility, reliability, and validity. Ambul Pediatr. 2003; 3: 329-341.

21. Chan KS, Mangione-Smith R, Burwinkle TM, Rosen M, Varni JW. The PedsQL: reliability and validity of the short-form generic core scales and Asthma Module. Med Care. 2005; 43: 256-265.

22. Varni JW, Bendo CB, Denham J, Shulman RJ, Self MM, Neigut DA, et al. PedsQL gastrointestinal symptoms module: feasibility, reliability, and validity. J Pediatr Gastroenterol Nutr. 2014; 59: 347-355.

23. Varni JW, Lane MM, Burwinkle TM, Fontaine EN, Youssef NN, Schwimmer JB. Health-related quality of life in pediatric patients with irritable bowel syndrome: a comparative analysis. J Dev Behav Pediatr. 2006; 27: 451-458.

24. Bray GA, Nielsen SJ, Popkin BM. Consumption of high-fructose corn syrup in beverages may play a role in the epidemic of obesity. Am J Clin Nutr. 2004; 79: 537-543.

25. Elliott SS, Keim NL, Stern JS, Teff K, Havel PJ. Fructose, weight gain, and the insulin resistance syndrome. Am J Clin Nutr. 2002; 76: 911-922.

26. Nelis G, Vermeeren MA, Jansen W. Role of fructose-sorbitol malabsorption in the irritable bowel syndrome. Gastroenterology. 1990; 99: 1016-1020.

27. Symons P, Jones MP, Kellow JE. Symptom provocation in irritable bowel syndrome. Effects of differing doses of fructose-sorbitol. Scand J Gastroenterol. 1992; 27: 940-944.

28. Jones HF, Burt E, Dowling K, Davidson G, Brooks DA, Butler RN. Effect of age on fructose malabsorption in children presenting with gastrointestinal symptoms. J Pediatr Gastroenterol Nutr. 2011; 52: 581-584.

29. Johlin FC Jr, Panther M, Kraft N. Dietary fructose intolerance: diet modification can impact self-rated health and symptom control. Nutr Clin Care. 2004; 7: 92-97.

30. Janicke DM, Finney JW, Riley AW. Children's health care use: a prospective investigation of factors related to care-seeking. Med Care. 2001; 39: 990-1001.

31. Seid M, Varni JW, Segall D, Kurtin PS. Health-related quality of life as a predictor of pediatric healthcare costs: a two-year prospective cohort analysis. Health Qual Life Outcomes. 2004; 2: 48.

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