Published in final edited form as:

J Pediatr Gastroenterol Nutr. 2018 June ; 66(Suppl 3): S52–S55. doi:10.1097/MPG.0000000000001859.

Demographic and Clinical Correlates of Mucosal Disaccharidase Deficiencies in Children with Functional Dyspepsia

Bruno P. Chumpitazi^{1,2}, Claudia C. Robayo-Torres^{1,2,3,6}, Cynthia M. Tsai^{1,2}, Antone R. Opekun^{1,2}, Susan S. Baker⁴, Buford L. Nichols^{1,2,3}, and Mark A. Gilger^{1,2,5}

¹Baylor College of Medicine, Department of Pediatrics, Section of Gastroenterology, Hepatology, and Nutrition, Houston, TX

²Texas Children's Hospital, Houston, TX

³USDA/ARS Children's Nutrition Research Center, Houston, TX

⁴University of Buffalo, Department of Pediatrics, Buffalo, NY

⁵Children's Hospital of San Antonio, San Antonio, TX

⁶Pediatric Specialist Network P.A

Abstract

Background—A subset of children with functional gastrointestinal disorders (FGIDs), which includes functional dyspepsia, may have duodenal disaccharidase deficiencies.

Objectives—To determine the frequency, demographics and clinical characteristics associated with duodenal disaccharidase deficiencies in children with functional dyspepsia.

Methods—Children ages 4–18 years undergoing esophagogastroduodenoscopy (EGD) evaluation for dyspepsia were enrolled in either a retrospective (Study 1) or prospective (Study 2) evaluation. Those with histologic abnormalities were excluded. Duodenal biopsies were obtained for disaccharidase enzyme analysis. In the retrospective study both demographic and clinical characteristics were obtained via chart review. In the prospective study, parents completed the Rome II Questionnaire on Gastrointestinal Symptoms prior to the EGD.

Results—129 children (n=101 study 1; n=28 study 2) were included. Mean age was 11.2 ± 3.8 (SD) years in study 1 and 10.6 ± 3.2 years in study 2. Forty-eight (47.5%) of subjects in study 1 and 13 (46.4%) of subjects in study 2 had at least one disaccharidase deficiency identified. All those with a disaccharidase deficiency in both studies had lactase deficiency with 8 (7.9%) and 5 (17.9%) of those in studies 1 and 2, respectively, having an additional disaccharidase deficiency. The second most common disaccharidase deficiency pattern was that of pan-disaccharidase deficiency in both studies. In study 1 (where both race and ethnicity were captured), self-identified Hispanic (vs. non-Hispanic, $P < 0.05$) and Non-White (vs. White, $P < 0.01$) children were more

Name and address for correspondence: Bruno P. Chumpitazi, MD, MPH; 6701 Fannin Street; CCC 1010.03; Houston, TX 77030, Fax: 832-825-3633, Phone: 832-822-3131, chumpita@bcm.edu.

Declaration of Authorship

Design of the study (all authors); data collection (CRT, CMT, SSB); initial drafting of the manuscript (BLN, BPC); critical revision and approval of the manuscript (all authors).

likely to have lactase deficiency. Age, gender, and type of gastrointestinal symptom were not associated with presence or absence of a disaccharidase deficiency.

Conclusion—Approximately half of children with functional dyspepsia undergoing EGD were identified as having a disaccharidase deficiency (predominantly lactase deficiency). Race/Ethnicity may be associated with the likelihood of identifying a disaccharidase deficiency. Other clinical characteristics were not able to distinguish those with vs. without a disaccharidase deficiency.

Keywords

Lactose; Ethnicity; Pediatric; Lactase; Sucrase; Isomaltase; Palatinase; Glucoamylase

INTRODUCTION

Childhood abdominal pain related functional gastrointestinal disorders (FGIDs) are highly prevalent; they affect approximately 13% of children worldwide.(1) Childhood FGID etiology is multifactorial with factors potentially including: inflammation, dysmotility, psychosocial distress, visceral hyperalgesia, and carbohydrate intolerance.(2) Carbohydrate intolerance as a potential factor is supported by studies identifying that a subset of children with FGIDs are deficient in at least one of several duodenal disaccharidase enzymes.(3, 4) These enzymes (such as lactase) are needed to hydrolyze carbohydrate bonds and facilitate carbohydrate absorption across the epithelial membrane. As seen in congenital sucrase isomaltase deficiency, disaccharidase deficiency may result in failure to thrive, bloating, abdominal pain, and changes in bowel habits (e.g., diarrhea).(5)

The largest study to date in children with FGIDs evaluating duodenal disaccharidase activity was conducted in a primarily (88%) non-Hispanic White population within a quaternary center in the Midwest of the United States; the investigators found that approximately 49% of those evaluated had at least one disaccharidase deficiency.(3) Whether this finding is more generalizable to other populations of children of a different racial/ethnic composition has not been determined. In addition it is currently unknown to what extent duodenal disaccharide deficiencies may be present in children of different FGID subtypes such as functional dyspepsia (FD). Our objectives therefore were to: 1) Determine the prevalence of disaccharidase abnormalities in children with FD from a population with a significant Hispanic composition; and 2) Determine whether clinical characteristics may predict disaccharidase deficiency in this population.

METHODS

Two studies of similar construct are combined in this report, and each study received separate Baylor College of Medicine Institutional Review Board approval. The first study is a single center retrospective chart review study conducted between December 2011 to May 2013. The charts included were those of children from four to eighteen years of age with chronic dyspepsia (either abdominal pain, nausea, bloating, or vomiting) who completed esophagogastroduodenoscopy (EGD) evaluation with biopsies sent for disaccharidase enzyme activity analysis by their primary gastroenterologist. Dyspeptic symptom duration was three months. Children found to have potential organic etiologies (e.g., peptic ulcer

disease) or histologic abnormalities (e.g., villous blunting) were excluded. No child with abnormal celiac serologies, Marsh histologic findings, or with a clinical diagnosis of celiac disease was included. The presence or absence of the following symptoms were searched for during the chart review: abdominal pain, nausea, vomiting, bloating, flatulence, reflux/heartburn, constipation, diarrhea, and eructation. Demographic information for the retrospective chart review included: self-identified race (White, African American, Asian, Mixed, Other, Undefined), self-identified ethnicity (Hispanic or non-Hispanic), age, and gender. Ethnicity categorization of Hispanic vs. Non-Hispanic followed the most recent United States Census Bureau guidelines and allowed subjects to self-identify both a race and ethnicity status (6). Some subjects did not provide their self-identified race and/or ethnicity. Recommendations for either dietary restriction or enzyme supplementation were captured.

The second study was similar to the first study; however, rather than relying solely on retrospective chart review the parents of children with chronic dyspepsia were prospectively approached at the time of the EGD to complete the pediatric Rome II Questionnaire on Gastrointestinal Symptoms (7). Participants provided permission for two additional duodenal biopsies for disaccharidase enzyme analysis. The same exclusion criteria (organic etiologies and/or histologic abnormalities) were used. Unfortunately, in the prospective study Hispanics were captured as a separate race rather than ethnicity. This precluded combining of race/ethnicity analyses between the two cohorts as the race/ethnicity data was captured differently. In addition, subsequent interventions following the EGD were not captured.

Combining the above studies for this manuscript was done for several reasons. First, both studies focused on the same population (children with functional dyspepsia completing duodenal disaccharidase evaluations). Second, both studies were similarly designed. For example, they both captured demographic and clinical symptom information. Finally, it was felt that the combination of both retrospective and prospectively collected data increased the overall plausibility of the findings.

Disaccharidase Enzyme Analysis

Two biopsies were obtained from the second portion of the duodenum. All duodenal biopsies obtained for disaccharidase enzyme analysis were frozen in liquid nitrogen immediately after being obtained. These biopsy specimens were sent to the laboratory of Susan Baker at the University of Buffalo where enzyme activity was determined based on the Dahlqvist method (8). In the retrospective study lactase, sucrase, maltase, and palatinase were determined. In the prospective study glucoamylase rather than palatinase was determined. The normal disaccharidase enzyme activity cut-off values were laboratory-specific: lactase ($>5 \mu\text{mol/g/min}$); sucrase ($>25 \mu\text{mol/g/min}$); maltase ($>100 \mu\text{mol/g/min}$); glucoamylase ($>25.5 \mu\text{mol/g/min}$); and palatinase ($>4.3 \mu\text{mol/g/min}$) (9). Quality control measures were in place in the Baker laboratory and included: the tissue arrived within 24 hours, on dry ice, the tissue remained frozen and intact, the tissue did not have discoloration, and adequate tissue amount was provided. In addition quality control and agreement were ensured by comparing results with other national disaccharidase evaluation laboratories.

Statistical Analyses

Statistical analyses were done using IBM SPSS software (version 23, Armonk, NY). Data are described using frequencies, means and standard deviation (SD). Pearson chi square test was used when assessing categorical variables. Independent t-tests were used to compare non-categorical variables. A p value of < 0.05 was considered as statistically significant.

RESULTS

Retrospective Study

One hundred one children with a mean age of 11.2 ± 3.8 years were included. Sixty-five (64.4%) of the children were female, and 35 (35.6%) were male. Self-identified race was as follows: White 84 (83.2%), African-American 5 (5.0%), Asian 4 (4.0%), and undefined 8 (8.0%). Twenty-five (from 93 who provided their ethnicity status) were Hispanic. Gastrointestinal symptoms included: abdominal pain in 90 (89.1%), vomiting in 40 (39.6%), diarrhea in 38 (37.6%), nausea in 36 (35.6%), constipation in 36 (35.6%), flatulence in 20 (19.8%), and bloating in 14 (13.9%).

Forty-eight (47.5%) subjects had a disaccharidase deficiency (Table 1). Though different patterns of disaccharidase deficiency were encountered, all subjects with a deficiency had lactase deficiency as one of the abnormalities (Table 1). Additional disaccharidase deficiencies among the children were broken down as shown in Table 1. Non-White subjects (compared to Whites) were more likely to have a disaccharidase deficiency: 8/9 (88.9%) vs. 35/84 (41.6%), respectively, $p = 0.01$. Hispanics (compared to non-Hispanics) were more likely to have a disaccharidase deficiency: 16/25 (64.0%) vs. 27/68 (39.7%), respectively, $p < 0.05$. Hispanic children with a deficiency only had lactase deficiency. We found no relationship of any disaccharidase activity with either age or gender or clinical symptoms (data not shown).

Five subjects had pandisaccharidase deficiency (PDD) which accounted for all those with sucrase and maltase deficiencies. Of those with PDD, 4 were males, 4 were White, and 1 was Asian. The mean age of these subjects was 10.8 ± 3.5 y (range: 6.3 to 15.2 y). The symptoms among these subjects were abdominal pain in 5 (100%), vomiting in 2 (40%), flatulence in 1 (20%), eructation 1 (20%), constipation 2 (40%), diarrhea 1 (20%), and heartburn in 2 (40%). None had either nausea or bloating.

Over a mean follow-up period of 3.7 ± 4.7 (SD) months, dietary restriction (n=37) and/or enzyme (in all cases lactase) therapy (n=4) were recommended. Subjects with an identified disaccharidase deficiency vs. without an identified deficiency were more likely to be started on a CHO restriction diet [(29/48) vs. (8/53), $p < 0.001$] or an enzyme supplement [(4/48) vs. (0/53), $p < 0.05$].

Prospective Study

Thirty-two children were enrolled of whom four were subsequently excluded because of celiac disease (n=3) or *H. pylori* (n=1). Of the remaining 28 subjects, 16 (57.1%) were female. The overall mean age was 10.6 ± 3.2 (range: 4.1-16.1) years. Race/ethnicity was

classified as 18 (64.3%) White, 7 (25.0%) Hispanic, 2 (7.1%) Asian, and 1 African-American (3.6%).

Thirteen (46.4%) had normal disaccharidase activity. All fifteen with abnormal disaccharidase activity (53.6%) had low lactase; additionally, 5 (17.9%) had low maltase, 4 (14.3%) had low sucrase, and 4 (14.3%) had low glucoamylase. A total of 3 (10.7%) had pan-disaccharidase deficiency. Clinical symptoms did not differentiate those with vs. without a disaccharidase deficiency (Table 2). Though not statistically significant, non-White vs. White subjects were more likely to have a disaccharidase deficiency [7/10 (70.0%) vs. 8/18 (44.4%), $P=0.25$].

DISCUSSION

This is the largest study to evaluate both the frequency and clinical characteristics of disaccharidase deficiency in a population of children with functional dyspepsia with a significant Hispanic contribution. Similar to previous studies in a more non-Hispanic White predominant population, we found that approximately 50% of children with functional dyspepsia had a disaccharidase deficiency (3). New is our finding that Hispanic and non-White children with functional dyspepsia are more likely to have an identified duodenal disaccharidase deficiency. In addition, we found symptoms (whether captured retrospectively or prospectively) were not associated with the presence/absence of a disaccharidase deficiency. These findings, combined with that of others, suggest that disaccharidase deficiency in children with functional dyspepsia is relatively prevalent.

Given the relatively high prevalence of disaccharidase deficiencies identified in our overall functional dyspepsia subject population, there may be consideration, particularly in non-Whites and Hispanics, to assess for duodenal disaccharidase activity at the time of an EGD. It should be noted however that pursuing an EGD and subsequent disaccharidase testing may be costly and/or unavailable, particularly in low-resource settings. In addition, only certain specialized laboratories are able to perform the disaccharidase evaluation; therefore, availability may be more limited. Potential alternatives for disaccharidase evaluation in children with functional dyspepsia would include hydrogen breath testing, C^{13} carbohydrate labeled breath testing, or carbohydrate tolerance tests with assessment of blood glucose following ingestion of a test carbohydrate (2, 5). While these have the advantage of being non-invasive, only a single test carbohydrate is evaluated at a time. With respect to potential therapies for an identified disaccharidase deficiency, these may include dietary therapies and/or enzyme replacement. There is a relative paucity of rigorous dietary data in those with functional dyspepsia, though avoidance of fats, wheat, and carbohydrates (including fermentable carbohydrates such as lactose) have been suggested as a treatment strategy (2, 10). Enzyme replacement for children with congenital sucrase isomaltase deficiency is well established; however, enzyme replacement in children with functional dyspepsia remains to be established (11).

Our findings related to racial/ethnic differences in lactase deficiency in our functional dyspepsia subjects parallel findings of racial/ethnic differences in both healthy subjects and in children with gastrointestinal disorders. In healthy subjects, adult-onset hypolactasia is

more common in African Americans and Hispanics as compared to Whites (12). Furthermore, lactase deficiency becomes more prevalent in most of the world population (other than in populations such as northern Europeans) beginning after the age of six years (13). With respect to lactase deficiency in children with FGIDs, Barr et al. used lactose hydrogen breath testing to identify a higher proportion of lactose malabsorption in both Hispanic and African-American children as compared to White children (14). Similarly, Pfefferkorn et al. identified a higher prevalence of lactase deficiency in African-American vs. White children with inflammatory bowel disease (15). Whether the prevalence of lactase deficiency identified in our subjects with functional dyspepsia parallels normal biology or represents a variation (e.g., earlier presentation than would otherwise be expected or transient deficiency) remains to be determined (16). Therefore though we found that those with duodenal enzyme deficiencies were more likely to have been recommended a dietary restriction or enzyme supplementation, future multi-center studies are needed in children with FGIDs to determine the clinical relevance of these deficiencies.

Despite evaluating both retrospectively and prospectively captured clinical data we did not find an association between duodenal disaccharidase deficiency and the presence/absence of a particular gastrointestinal symptom. Though carbohydrate malabsorption has classically been associated with diarrhea and flatulence, symptoms in relation to carbohydrate malabsorption may depend on several factors including: the amount of carbohydrate ingested, whether the carbohydrate is ingested with other fermentable carbohydrates, the gastric emptying rate of the carbohydrate meal, colonic microbiome composition, and colonic microbiome adaptation to the diet (2, 17, 18). The potential role of these factors in children with functional dyspepsia in relation to carbohydrate intolerance remains to be determined.

Though lactase deficiency was by far the most common abnormality identified in our study, the second most common was that of PDD. PDD was also the second most common abnormality identified in a review of over 27,000 duodenal mucosal biopsies (9). Given that the evaluated duodenal disaccharidase enzymes are found on different genes, it is highly unlikely that genetic mutations in each evaluated enzyme would account for PDD. Rather, it has been suggested that identifying PDD may be attributed to sample processing error (9). In part, the lack of symptom correlation with the identification of a disaccharidase deficiency may support this premise. However we note that the specimens were rigorously obtained and placed in liquid nitrogen soon after being obtained and processed rapidly – particularly in the prospective trial. Other possibilities for PDD include unidentified underlying inflammation, slow (transient) enzyme recovery following a gastrointestinal infection, small bowel bacterial overgrowth, or shared inhibitory regulatory factors (16, 19–21). The role of shared activities is demonstrated by sucrase activity driving maltase enzyme activity and regulating normal in vivo starch digestion to glucose (22).

Study limitations include lack of standardization, particularly in the retrospective data, with respect to uniform evaluations for other organic disorders (e.g., obtaining celiac serologic testing in all subjects) or with Rome classification using a validated questionnaire in all subjects. Another limitation is further characterization of the different races (e.g., northern European vs. southern European in those who were White) as this may impact the incidence

of disaccharidase deficiencies. A larger prospective study addressing these limitations in children with functional dyspepsia with evaluation of duodenal disaccharidases would be helpful.

There are several strengths to this study. First, with regard to the retrospective portion, data were obtained from subjects undergoing standard medical care. Therefore these data are likely to be more generalizable to other pediatric gastroenterology settings. In addition, a prospective study is presented which largely supports the findings of the retrospective study – thereby increasing the plausibility of the results.

In summary, we found approximately half of the children with functional dyspepsia have a disaccharidase deficiency. Mucosal lactase deficiency was detected more frequently in non-Whites and Hispanic patients. PDD, a combined deficiency of all 4 assayed enzymes, with normal histology, was detected in 6.2% of all FGID biopsies. Clinical characteristics were not able to distinguish those FGID patients with or without a disaccharidase deficiency.

Acknowledgments

Sources of support: Research support from QOL Medical; Supported, in part by, NIH Digestive Disease Center Grant P30 DK56338 which funds the Texas Medical Center Digestive Disease Center and by a generous contribution from D.R. and G.P. Laws to the BCM G.I. Research Laboratory Fund.

Abbreviations

EGD	Esophagogastroduodenoscopy
FGIDs	Functional Gastrointestinal Disorders
PDD	Pandisaccharidase deficiency

References

1. Korterink JJ, Diederik K, Benninga MA, et al. Epidemiology of pediatric functional abdominal pain disorders: a meta-analysis. *PLoS One*. 2015; 10(5):e0126982. [PubMed: 25992621]
2. Chumpitazi BP, Shulman RJ. Dietary Carbohydrates and Childhood Functional Abdominal Pain. *Ann Nutr Metab*. 2016; 68(Suppl 1):8–17. [PubMed: 27355647]
3. El-Chammas K, Williams SE, Miranda A. Disaccharidase Deficiencies in Children With Chronic Abdominal Pain. *JPEN J Parenter Enteral Nutr*. 2015
4. Karnsakul W, Luginbuehl U, Hahn D, et al. Disaccharidase activities in dyspeptic children: biochemical and molecular investigations of maltase-glucoamylase activity. *J Pediatr Gastroenterol Nutr*. 2002; 35(4):551–6. [PubMed: 12394383]
5. Chumpitazi BP, Robayo-Torres CC, Opekun AR, et al. Congenital sucrase-isomaltase deficiency: summary of an evaluation in one family. *J Pediatr Gastroenterol Nutr*. 2012; 55(Suppl 2):S36. [PubMed: 23103651]
6. Mays VM, Ponce NA, Washington DL, et al. Classification of race and ethnicity: implications for public health. *Annu Rev Public Health*. 2003; 24:83–110. [PubMed: 12668755]
7. Caplan A, Walker L, Rasquin A. Validation of the pediatric Rome II criteria for functional gastrointestinal disorders using the questionnaire on pediatric gastrointestinal symptoms. *J Pediatr Gastroenterol Nutr*. 2005; 41(3):305–16. [PubMed: 16131985]
8. Dahlqvist A. Method for Assay of Intestinal Disaccharidases. *Anal Biochem*. 1964; 7:18–25. [PubMed: 14106916]

9. Nichols BL Jr, Adams B, Roach CM, et al. Frequency of sucrase deficiency in mucosal biopsies. *J Pediatr Gastroenterol Nutr.* 2012; 55(Suppl 2):S28–30. [PubMed: 23103647]
10. Duncanson KR, Talley NJ, Walker MM, et al. Food and functional dyspepsia: a systematic review. *J Hum Nutr Diet.* 2017
11. Treem WR, McAdams L, Stanford L, et al. Sacrosidase therapy for congenital sucrase-isomaltase deficiency. *J Pediatr Gastroenterol Nutr.* 1999; 28(2):137–42. [PubMed: 9932843]
12. Bailey RK, Fileti CP, Keith J, et al. Lactose intolerance and health disparities among African Americans and Hispanic Americans: an updated consensus statement. *J Natl Med Assoc.* 2013; 105(2):112–27. [PubMed: 24079212]
13. Curry A. Archaeology: The milk revolution. *Nature.* 2013; 500(7460):20–2. [PubMed: 23903732]
14. Barr RG, Levine MD, Watkins JB. Recurrent abdominal pain of childhood due to lactose intolerance. *N Engl J Med.* 1979; 300(26):1449–52. [PubMed: 449886]
15. Pfefferkorn MD, Fitzgerald JF, Croffie JM, et al. Lactase deficiency: not more common in pediatric patients with inflammatory bowel disease than in patients with chronic abdominal pain. *J Pediatr Gastroenterol Nutr.* 2002; 35(3):339–43. [PubMed: 12352524]
16. Zimmer KP, Scholz D, Naim HY. Transient sucrose and starch intolerance. *J Pediatr Gastroenterol Nutr.* 2012; 55(Suppl 2):S39–40. [PubMed: 23103653]
17. Chumpitazi BP, Cope JL, Hollister EB, et al. Randomised clinical trial: gut microbiome biomarkers are associated with clinical response to a low FODMAP diet in children with the irritable bowel syndrome. *Aliment Pharmacol Ther.* 2015; 42(4):418–27. [PubMed: 26104013]
18. Hertzler SR, Savaiano DA. Colonic adaptation to daily lactose feeding in lactose maldigesters reduces lactose intolerance. *Am J Clin Nutr.* 1996; 64:232–36. [PubMed: 8694025]
19. Sherman P, Wesley A, Forstner G. Sequential disaccharidase loss in rat intestinal blind loops: impact of malnutrition. *Am J Physiol.* 1985; 248(6 Pt 1):G626–32. [PubMed: 3159266]
20. Nichols BL, Avery SE, Karnsakul W, et al. Congenital maltase-glucoamylase deficiency associated with lactase and sucrase deficiencies. *J Pediatr Gastroenterol Nutr.* 2002; 35(4):573–9. [PubMed: 12394387]
21. Daileida T, Baek P, Sutter ME, et al. Disaccharidase activity in children undergoing esophagogastroduodenoscopy: A systematic review. *World J Gastrointest Pharmacol Ther.* 2016; 7(2):283–93. [PubMed: 27158545]
22. Nichols BL. Metabolic impacts of maltase deficiencies. *J Pediatr Gastroenterol Nutr.* this supplement.

What is known

- A subset of children with FGIDs (which includes functional dyspepsia) undergoing EGD were reported to have low mucosal disaccharidase activities.
- Of these, lactase deficiency has been reported to be most frequent.
- Whether these findings are applicable to other childhood populations of varying race/ethnicity composition is unknown.

What is new

- Within a population with a large Hispanic component, approximately 50% of children with functional dyspepsia were found to have a disaccharidase deficiency.
- Lactase deficiency was more prevalent in Hispanic and Non-White children.
- Pan-disaccharidase deficiency was found in approximately six percent.
- Other clinical characteristics, including gastrointestinal symptoms, did not distinguish between those with vs. without a disaccharidase deficiency.

Table 1

Disaccharidase deficiencies determined in 101 Children with Functional Dyspepsia

Enzyme	$\mu\text{M}/\text{min}/\text{g protein}$	No. of children (%)
Lactase	< 5	48 (47.5)
Sucrase	< 25	5 (5.0)
Maltase	< 100	5 (5.0)
Palatinase	< 5	7 (6.9)

Table 2

Symptoms in Children with Functional Dyspepsia Classified by Normal or Abnormal Duodenal Disaccharidase Activity Levels

Symptoms	Abnormal (N = 15)	Normal (N = 13)	P-Value
Abdominal Pain	15 (100%)	13 (100%)	1.00
Nausea	13 (87%)	11 (85%)	1.00
Bloating	10 (67%)	8 (62%)	0.78
Feeling of Fullness	13 (87%)	9 (69%)	0.37
Poor Appetite/Early Satiety	14 (93%)	8 (62%)	0.07
Pain Association with BMs	14 (93%)	10 (77%)	0.31
Vomiting	8 (53%)	7 (54%)	0.98
Diarrhea	5 (33%)	5 (39%)	0.78
Constipation	9 (60%)	9 (69%)	0.71
Fecal Incontinence	8 (53%)	5 (40%)	0.43
Flatus	9 (60%)	8 (62%)	0.93
Reflux	9 (60%)	10 (77%)	0.43
Limitation on Activities	12 (80%)	12 (100%)	0.23