Gender Differences in Associated Gastrointestinal Symptoms and the Diagnostic Work-up for Chronic Constipation

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**Purpose:** To evaluate female and male patients with constipation and compare the associated gastrointestinal (GI) symptoms as well as the diagnostic tests used to evaluate the etiology of constipation in the outpatient setting.

**Methods:** Our study population consisted of adult patients presenting to any Emory Clinic with a diagnosis of constipation based on ICD-9 code 564.0 between June 2004 and June 2008. A retrospective chart review was performed to evaluate patient characteristics, associated GI symptoms, and diagnostic tests and procedures performed for evaluation. We compared the differences between females and males in symptoms associated with constipation as well as the diagnostic tests (labs and colonoscopy) performed to evaluate the etiology of constipation. The odds ratios and confidence intervals were calculated using the Mantel-Haenszel Common Odds Ratio Estimate and p-values were obtained using Chi Square statistics.

**Results:** To date, we have identified 61 patients with the diagnosis of constipation, mean age = 50 (SD of 16 years). Forty-four patients were females and 17 patients were males. Forty-eight percent of females were overweight or obese (BMI >25) compared to 82% males that were overweight or obese (P = 0.015, OR= 0.196, CI: 0.049-0.778). Heartburn was present at the same rate between females and males (30% vs. 29%, respectively, P= 0.625, OR= 1, CI: 0.291-3.392). Females tended to be less likely than males to have abdominal pain and/or bloating associated with constipation (59% vs 43%, P = 0.209, OR= 0.532, CI=0.17-1.65). In the evaluation of constipation, females were less likely than males to have laboratory work up (82% vs. 94%, P= 0.215, OR= 0.3, CI=0.032-2.44). Also, there was a trend towards fewer colonoscopies being performed in females to evaluate constipation compared to males (55% vs 65%, P = 0.336, OR 0.655, CI: 0.206-2.084). However, the symptoms and procedures differences highlighted above did not reach statistical significance.

**Conclusion:** From this sample of patients with constipation in our clinics, we found that there might be some differences between males and females with regard to associated GI symptoms and the diagnostic work-up. Also, in our population, males with constipation were more likely to be obese than females. However, additional patients need to be studied to confirm and better understand these differences as well as their impacts on clinical outcomes.

Proton Pump Inhibitors Do Not Affect the Lactulose Hydrogen Breath Test in IBS Subjects

Mark Pimentel, MD, FRCPC, David Law, MD. GI Motility, Cedars Sinai Medical Center, Los Angeles, CA.

**Purpose:** Evidence is mounting for a role for small intestinal bacterial overgrowth (SIBO) in IBS. Recently, some have questioned the validity of breath testing in the context of the common overlap between IBS and GERD and thus the use of proton pump inhibitors (PPI). The aim of this study was to compare the prevalence of an abnormal lactulose breath test (LBT) in IBS patients among subjects currently taking and not taking PPI medication.

**Methods:** Consecutive Rome I positive IBS subjects, referred for LBT, were enrolled in a prospectively collected database study. After inclusion criteria, subjects completed a questionnaire. This questionnaire inquired about their current symptoms and medication usage. All subjects then underwent a lactulose breath test. The prevalence of abnormal breath test results was compared between IBS subjects currently using and not using PPI medication. A multi-component analysis of the breath tests hydrogen profile was also compared between groups. Finally, the presence or absence of methane on breath test was compared between groups.

Results: A total of 555 (429 female) subjects completed the study. Among these, 106 subjects (19.1%) were current PPI users. Among IBS subjects on PPI, 46.2% met criteria for a positive LBT based on an increase of hydrogen of 20 ppm or greater, before 90 min over baseline as the determinant of a positive test. However, this was not different from the non-PPI using IBS subjects of whom, 56.3% were positive on LBT among 449 subjects (OR=0.67, CI=0.436-1.017). Additionally, the average amplitude of rise in the first peak in PPI users was 28.0±33.3 ppm from baseline. This was not different from 27.5±29.1 ppm seen in non-PPI users (p = 0.89). Likewise, the average rise in the second peak in PPI users was 48.5±43.8 ppm from baseline; in non-PPI users, it was 49.3±37.6 ppm (p = 0.87). The arrival of first peak in PPI users was 56.4±23.0 min compared to 58.2±26.1 min in non-PPI users (p = 0.58). However, one difference was noted. Among subjects receiving PPI medication, 7.5% had methane detection on LBT. This was significantly lower than 15.4% in subjects not taking PPI (OR=0.39, CI=0.18-0.82).

**Conclusion:** Proton-pump inhibitors do not appear to affect hydrogen production on lactulose breath test in IBS patients. However, there may be an association between PPI use and the prevalence of methane production.

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Validation of a Simple Tool (Constipation Minus Diarrhea) for Evaluating Constipation Symptom Outcomes in IBS

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**Purpose:** Patients with Irritable Bowel Syndrome (IBS) may have constipation or diarrhea predominance. Most often patients experience both. A problem with IBS outcome measurement is the subjective nature. In previous studies, we employed a visual analogue scoring scale (VAS) where patients rate their own symptom severity of constipation and diarrhea using a VAS score. In this study we attempt to validate an approach that combines these in a “constipation minus diarrhea” severity score to account for the balance of both symptoms and patient subjective over reporting.

**Methods:** Subjects with IBS by Rome I criteria were asked to complete a daily stool diary for one week, where they recorded each bowel movement and rated their stool consistency using the Bristol stool score. After submitting their diaries, they were asked to rate both their constipation (C) and diarrhea (D) symptoms on a VAS scale from 0-100 mm, with 100 mm representing severe symptoms. The VAS scores for C and D and a score of C minus D (C-D) was compared to the true stool events of the previous week including frequency and consistency (Bristol stool score). This comparison was used to validate the usefulness of the simple C-D method.

**Results:** Among the 84 IBS subjects enrolled, C-D scores predicted constipation based on stool frequency and Bristol stool score. By correcting for the purity of constipation compared to diarrhea using this C-D score, a better correlation was seen with the preceding week of stool diary form and frequency (see Table). In addition, a second method was used to validate the C-D technique by comparing the mean C-D score in constipation subjects (>3 days with bowel movement in previous week). In this case the mean C-D score was 74.1±34.5 compared to 3.0±5.42 for patients >3 days with bowel movement in that week (P<0.001). While the C severity alone also discriminated these two groups, the difference was less impressive (P<0.01). In subjects with mean Bristol stool score in preceding week ≤2, the C-D mean score was 25.4±56.0 compared to subjects with mean Bristol score of >2 where the C-D was -11.1±53.6 (P<0.01). Using constipation severity by VAS alone, there was no significant difference between these same two Bristol stool categories (P=0.29).

**Conclusion:** IBS patients’ self-assessment of constipation and diarrhea severity with a VAS is effective in predicting constipation based on stool frequency and Bristol score. Based on VAS, calculating a C-D score which controls for a patient’s tendency to exaggerate or minimize their symptoms was an even better predictor of stool diary based measures of constipation compared to constipation VAS severity alone.
Probiotic Benefits Demonstrated in a Clinical Setting Translate to Meaningful Benefits in the Real World: Post Marketing Experience with the Probiotic Strain Bifidobacterium Infantis 35624
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Purpose: Clinical benefits of the probiotic strain Bifidobacterium infantis 35624 for IBS relief have previously been reported; however, clinical data does not necessarily translate to noticeable benefits within a practice setting. To understand the real world benefits, data was collected from a sampling of over 20,000 unique subjects purchasing this probiotic as a dietary supplement from an online retail setting.

Methods: Consumers were queried at the first purchase (n=25,833) and again on a subsequent repeat purchase (n=8,484). The vast majority of the first time purchasers (18,833; 74%) received a recommendation to purchase the probiotic from their physician.

Results: Among first time purchasers, 56% received a sample; 40% received a recommendation only. Reported compliance rate with sample usage was 97.2%. The main influence for purchase of the product was the physician recommendation (60.3%), outweighing the sample (15%) or any other sources of recommendation. Among the repeat purchasers asked about their experience with the product, the speed and magnitude of the benefits reported were consistent with clinical trial experience. Of the 7,782 responses to time of product use before onset of noticeable benefit, 14.8% responded “less than one week”, 28.9% 1 to 2 weeks, 24.3% 2 to <3 weeks and 10.3% 3 to <4 weeks for a total of 78.3% in the first month; 92% stated the magnitude of the benefit met or exceeded their expectations, which were largely shaped by the recommending physician.

Conclusion: This survey, while uncontrolled, provides a snapshot of what happens after patients leave the physician’s office with a recommendation for a dietary supplement. The time to onset of benefits, and the magnitude of these benefits, are consistent with data from clinical trials with the novel probiotic product, the speed and magnitude of the benefits reported were consistent with data from clinical trials with the novel probiotic product, and the time to onset of benefits, and the magnitude of these benefits, are consistent with data from clinical trials with the novel probiotic strain in this product, adding to the evidence of the utility of supplementation benefit.


Research was conducted as part of post-marketing efforts to understand patient experience with the product.

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Investigation of Dried Plums in Constipation – A Randomized Controlled Trial
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Purpose: Treatment of chronic constipation (CC) remains challenging with 50% of patients reporting dissatisfaction with current therapy. There is an unmet need for natural, safe, convenient and tasty alternatives. Dried plums/plums have been traditionally used for CC but its efficacy is not known. Aim: To investigate and compare the effects of dried plums and psyllium on constipation symptoms, taste and tolerability.

Methods: Subjects with CC (Rome III) were enrolled in an 8 week, single-blinded, randomized cross-over study. After a one week assessment of baseline stool and bowel symptoms on a prospective diary, subjects received either dried plums (50 grams BID, fiber = 6 gm/day) or psyllium (11 grams BID, fiber = 6 gm/day) for 3 weeks each. Next, after a one week washout period, they were crossed over to the other therapy for 3 weeks. Subjects maintained a daily symptom and stool diary. Individual and overall constipation related symptoms (rated=3 (markedly worse) to +3 (markedly better)) and taste were assessed. The primary outcome measure was number of complete spontaneous bowel movements per week (CSBM).

Results: (*p=0.01): 40 constipated subjects (n=5 = 3/7, mean age = 38 years) participated. The number of CSBMs per week increased significantly (p=0.01) with both plums and psyllium when compared to baseline but there was no difference between treatments. The stool consistency and straining effort did not change with both treatments (p=n.s). Global constipation symptoms improved with plums (+1.67) and with psyllium (+1.35), but there was no difference. There were no differences in palatability and tolerability between plums and psyllium, and both were safe.

Conclusion: Constipation symptoms improved with both dried plums and with psyllium and to a similar extent. Dried plums are safe and an effective option in the management of (mild to moderate) chronic constipation and should be considered as first line therapy. Supported by grant from California Dried Plum Board and NIH R01 DK057100.

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Co-existence of Lactose and Fructose Malabsorption in a Community Population
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Purpose: Combined lactose and fructose malabsorption can co-exist in the same patient. We have encountered patients who present with function bowel complaints despite avoidance of milk products. The most frequent complaints are intermittent diarrhea, postprandial diarrhea and bloating, flatulence, abdominal pain. These patients have symptom improvement after avoidance of high fructose containing foods.

Methods: We have conducted a chart review of 179 patients who underwent hydrogen breath tests using glucose, fructose, and lactose between January 2007 and December 2008. These patients were excluded from thyroid disease, celiac sprue, microscopic colitis, inflammatory bowel disease, and bacterial overgrowth. A sudden rise in breath hydrogen of 15 ppm above baseline was considered a “positive” test. Patients with “positive” glucose test were considered to have small bowel bacterial overgrowth and they were excluded from data analysis. Patients with “positive” lactose test were included in data analysis.

Results: Nineteen patients from a pool of 179 (11%) are found to have lactose malabsorption. Mean age of this group is 50 years (range 26-89). There are 15 females and 4 males. Within this group of 19 patients, 10 patients (53%) have both “positive” lactose and “positive” fructose tests. Most common symptom is abdominal pain (70%). Most common previous diagnosis is irritable bowel syndrome (40%). Combined lactose and fructose malabsorption is 6% (10 out of 179) in our community population.

Conclusion: Co-existence of lactose and fructose malabsorption is uncommon (6%). However, up to half of those who have lactose malabsorption also have fructose malabsorption. Although it is rare, patients with persistent symptom despite dietary modification should be offered fructose breath test. Furthermore, the sequence of glucose-fructose-lactose breath tests should not be interrupted if patient is found to have “positive” fructose test.