Exploratory Comparative Effectiveness Trial of Green Kiwifruit, Psyllium, or Prunes in US Patients With Chronic Constipation

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INTRODUCTION: Psyllium and prunes are proven treatments for chronic constipation (CC). Asian studies suggest that kiwifruit may also benefit CC symptoms. We report a partially randomized, comparative effectiveness trial evaluating kiwifruit, psyllium, and prunes in US patients with CC.

METHODS: Adults with CC at a US medical center were randomized to 3 natural treatments. Eligible patients had ≤3 complete spontaneous bowel movements (CSBM) per week and were partially randomized to green kiwifruit (2/d), prunes (100 g/d), or psyllium (12 g/d) for 4 weeks. The primary endpoint was the proportion of patients in each group reporting an increase of ≥1 CSBM per week compared with baseline for at least 2 of 4 treatment weeks. Key secondary outcomes included stool frequency, stool consistency, and straining assessed daily. Treatment satisfaction and adverse events (AEs) were also measured. Standard statistical methods were used, and a P < 0.05 was considered significant.

RESULTS: Seventy-nine patients with CC (mean age = 42.7 years, 87% female, and 77% white) were partially randomized. Complete data were available for 75 patients (kiwifruit 29, prunes 24, and psyllium 22). For the primary endpoint, proportions of CSBM responders were similar for the treatments. For secondary outcomes comparing treatment weeks 3 and 4 to baseline, there was a significant increase in weekly CSBM rate with all 3 treatments (P < 0.003); stool consistency significantly improved with kiwifruit (P = 0.01) and prunes (P = 0.049); and straining significantly improved with kiwifruit (P = 0.003), prunes (P < 0.001), and psyllium (P = 0.04). Patients randomized to the kiwifruit group reported significant improvement in bloating scores (P = 0.02). AEs were most common with psyllium and least common with kiwifruit. At the end of treatment, a smaller proportion of patients were dissatisfied with kiwifruit compared with prunes or psyllium (P = 0.02).

DISCUSSION: Kiwifruit, prunes, and psyllium improve constipation symptoms in patients with CC. Kiwifruit was associated with the lowest rate of AEs and dissatisfaction with therapy.

INTRODUCTION

Chronic constipation (CC) is a common gastrointestinal (GI) disorder with a global population prevalence of 7%–14% (1,2) and accounts for almost 4 million outpatient visits per year (3). According to the Rome IV criteria, the spectrum of CC disorders includes both functional constipation (FC) and irritable bowel syndrome with constipation (IBS-C). Patients with CC report various bowel symptoms such as reduced stool frequency, hard stool consistency, straining, or a sensation of incomplete evacuation, with or without significant abdominal symptoms such as pain and bloating. Reductions in disease-related quality of life and work productivity along with significant direct and indirect costs are also associated with CC (4).

There are a number of over-the-counter and prescription medications available for FC and IBS-C. Over-the-counter products such as fiber supplements, osmotic laxatives, and stimulants can improve bowel-related complaints but offer little benefit for and in some cases can exacerbate abdominal symptoms. Prescription treatments such as prosecretory or prokinetic agents can offer benefits for bowel and abdominal complaints but at substantial cost and with a measurable risk of adverse effects. In many countries, including the United States, market forces have led to barriers which can limit access to expensive prescription medications for nonlethal quality of life conditions such as CC. In general, available medical treatments for CC offer a therapeutic gain over placebo of 7%–15%, making clear the unmet need for...
other effective treatments (4–6). Coupled with increasing societal concerns regarding the long-term safety of chronically dosed medications, there has been a gradual shift in public opinion toward more “natural” nonpharmacologic solutions for a wide range of medical conditions, including CC.

In the United States, 2 commonly used natural treatments for CC are psyllium and dried plums (prunes). Psyllium is a poorly fermentable fiber with water-holding, gel-forming capabilities (7). Prunes contain both fiber as well as sorbitol, resulting in a laxative effect by increasing stool water and volume through several mechanisms (8). Both psyllium and prunes have been shown in randomized controlled trials (RCTs) to be of benefit for bowel symptoms such as stool frequency and consistency in patients with CC (8–10).

Green kiwifruit has long been used as a natural remedy to improve GI complaints. In traditional Chinese medicine, it has been used to aid digestion, prevent kidney stones, and even as a treatment for cancer (11). Kiwifruit is often promoted for its antioxidant capacity derived from high levels of vitamin C, folate, and beneficial phytochemicals such as β-carotene (11). A growing body of literature supports the benefits of kiwifruit for gut health and in particular, abdominal discomfort and bowel regularity. Potential laxative effects of kiwifruit have been ascribed not only to fiber but also to oligosaccharides and the proteolytic enzyme, actinidin (12). In recent studies from Asia and Europe, daily consumption of 2 green kiwifruit improved constipation symptoms in constipated individuals, without adversely affecting bowel habits (13–16). There are no RCT data on the effectiveness and tolerability of kiwifruit from North American patients with CC. Thus, we conducted a comparative effectiveness study of 3 natural treatment options, green kiwifruit, prunes, and psyllium in US patients with CC.

METHODS

This was an exploratory, partially randomized comparative effectiveness trial with a parallel group design whereby patients were assigned in a 1:1:1 fashion to kiwifruit, prunes, or psyllium. The protocol was approved by the Michigan Medicine Institutional Review Board and registered with ClinicalTrials.gov (NCT 03569527).

Patient population

Adult patients meeting the Rome IV criteria for either FC or IBS-C were consecutively recruited from the gastroenterology and primary care clinics at the University of Michigan and through print and online advertising. Inclusion criteria were having CC for the past 3 months, with symptoms onset at least 6 months earlier, the absence of loose stools without the use of laxatives, as well as the presence of other CC symptoms listed below. Laxative usage (including herbal and other supplements) outside of that specified by the study protocol was not allowed during study participation. Patients were eligible for treatment allocation if they reported an average daily abdominal pain score that was ≤7 on an 11-point numerical rating scale (NRS, 0-no pain, 10-worst pain), had ≥3 complete spontaneous bowel movements (CSBMs) per week, and had at least 2 of the following: straining, hard/lumpy stools, incomplete emptying of bowels, utilization of manual maneuvers for relief, and a sensation of obstruction/blockage on ≥25% of BMs. Exclusion criteria included having any of the following: severe abdominal pain (>7 on NRS), presence of alarm signs (e.g., GI bleeding, unexplained iron deficiency anemia, and unexplained weight loss), active anal fissure, significant comorbid chronic disease (e.g., active treatment for malignancy, severe renal or cardiac disease, inflammatory bowel disease, known diffuse motility disorder, connective tissue disease, etc.), history of GI surgery (other than appendectomy and cholecystectomy if performed >6 months preceding enrollment), and neurological diseases (e.g., multiple sclerosis, Parkinson’s disease, spinal cord injury, or cerebrovascular accident). Patients reporting pregnancy, currently taking probiotics, antibiotics, opioids, or reporting allergies to kiwifruit, prunes, or psyllium were also excluded. The ingestion of kiwifruit, prunes, and/or psyllium products outside the study protocol was not allowed.

Study protocol

Eligible patients were asked to participate in a study evaluating the effectiveness of 3 natural treatment options (kiwifruit, prunes, and psyllium) to improve CC and related symptoms. Researchers and participants were not blinded to the allocated intervention. After collection of informed consent and baseline information on relevant comorbidities and underlying medical conditions, participants were entered into a 2-week baseline screening period to assess their symptoms through daily questionnaires. Patients who satisfied eligibility criteria were partially randomized and were supplied 2 green kiwifruit (Actinidia delicosa var. Hayward, fiber = 6 g/d), 100 g of prunes (Kirkland, fiber = 6 g/d), or 12 g of psyllium (Metamucil, Procter & Gamble, fiber = 6 g/d) daily for the 4-week treatment period. After the 4-week treatment period, patients entered into a 2-week observation period (Figure 1).

Green kiwifruit has a limited growing season and availability from May through November. To accommodate the growing season and fruit availability, the first 30 consented participants were assigned to the kiwifruit group. The remainder of eligible patients were randomized through computer generation to the prune or psyllium arms of the study.

Eligible patients met with a clinical research coordinator and research diettian at the University of Michigan Medical Center to discuss their treatment regimen. Patients in the kiwifruit group were instructed to consume 2 whole, peeled kiwifruits per day for 4 consecutive weeks. Patients in the prune group were instructed to consume 50 g (about 6 prunes) twice per day for 4 consecutive weeks. Patients in the psyllium group were instructed to consume 6 g dissolved in water twice per day for 4 consecutive weeks. All participants were instructed to avoid the consumption of other foods and food products containing kiwifruit, prunes, or psyllium outside that provided as part of the study protocol. Participants were also instructed to refrain from adding any new high-fiber fruits and/or vegetables into their diets during the study. Dietary assessments were conducted by collection of 3-day food diaries after the screening period and after the treatment intervention (Figure 1) (17). If a patient did not pass a BM for 3 or more days, the use of rescue medication (Polyethylene Glycol 3350 and Bisacodyl) was allowed.

Symptom assessment

Throughout the 8-week study period, participants recorded daily symptoms as detailed below through an online symptom assessment tool. After the treatment intervention, participants were asked standardized questions by study staff evaluating perceptions on symptom improvement, rescue medication use, and tolerability of the intervention. Overall treatment satisfaction (yes or no) was assessed at the end of the treatment period.
Clinical endpoints
The primary endpoint was the CSBM responder rate defined as the proportion of participants in each group reporting an increase of ≥1 CSBMs per week compared with the baseline screening period for at least 2 of the 4 treatment weeks.

Secondary endpoints evaluated the effects of the interventions on other important constipation symptoms including stool frequency, stool consistency, straining, and a sensation of incomplete evacuation. The mean weekly CSBM rate from treatment weeks 3 and 4 was compared with baseline screening. Stool consistency was assessed in 2 ways. A stool consistency responder was defined as a participant who reported an increase in mean BSFS score of ≥1 compared with baseline scoring for at least 2 of 4 treatment weeks. Mean weekly BSFS score over weeks 3 and 4 of the treatment period was also compared with baseline screening. Straining (11-point NRS) and a sensation of complete evacuation after a BM (yes/no) were assessed once daily. Mean weekly straining score during treatment weeks 3 and 4 as well as the proportion of patients reporting a sensation of incomplete evacuation during treatment weeks 3 and 4 were compared with corresponding data from the baseline period.

Abdominal and sensory symptoms were also assessed. Daily individual symptom scores for abdominal pain, abdominal discomfort, bloating, and urgency were assessed through 11-point NRS. Mean weekly symptom scores for abdominal and sensory symptoms collected during weeks 3 and 4 of the treatment period were compared with corresponding data collected during the baseline screening period.

Statistical analysis plan
To compare baseline demographics and characteristics across all 3 groups, a balanced analysis of variance was used to examine differences in continuous independent variables (age, body mass index, weekly CSBM rate, abdominal pain, abdominal discomfort, bloating, stool consistency, and straining). Categorical baseline variables (age, sex, diagnosis, and race) were compared using chi-squared tests for statistical significance. Differences in the primary endpoint (proportion reporting an increase of ≥1 CSBMs per week for at least 2 of the 4 treatment weeks) were assessed using chi-squared tests for statistical significance, and 1-sample test of binomial proportions was used to generate the upper and lower limits of the 95% confidence interval (CI). Differences in the average weekly CSBM rate for treatment weeks 3 and 4 across all 3 groups were compared using balanced analysis of variance. Within-group CSBM rates were compared using paired t tests. Differences in stool consistency response (proportion reporting an increase of ≥1 BSFS score per week for at least 2 of the 4 treatment weeks) were assessed using chi-squared tests for statistical significance, and 1-sample test of binomial proportions was used to generate the upper and lower limits of the 95% CI. Paired t tests were used to compare the within-group mean scores (as averaged over each treatment week) for daily stool consistency, straining, abdominal pain, abdominal discomfort, bloating, and urgency. Differences in adverse event (AE), satisfaction, and dissatisfaction reports were assessed using chi-squared tests for statistical significance. P values of ≤0.05 were considered statistically significant. Statistical analyses were performed using SAS (version 9.4, SAS Institute, Cary, NC). This was an exploratory study and thus not powered to detect effectiveness as measured by a change in clinical endpoints. A target of 26 subjects in each treatment group (total 80 subjects) was proposed to represent sufficient patient numbers to make preliminary conclusions based on study results.

RESULTS
Demographics and eligibility
Of the 247 patients approached for study recruitment between May 2018 and July 2019, 109 were enrolled for baseline screening. After baseline screening, 79 patients (69 female [87%], median age of 42.7 years [range 18–76 years], 61 [77%] white) satisfied inclusion criteria and were randomized (Figure 2). Slightly more than 60% of the study population was treatment naive, with the most common forms of previous or current treatment including the usage of laxatives and dietary modifications (e.g., FODMAP diet). Other reasons for exclusion before treatment allocation included loss to follow-up, failure to schedule, and concurrent constipation-based research participation. Eighty-one percent of patients were recruited through digital clinical trial recruiting platforms (internal institutional site and My Total Health, Wilmington, DE), 10% through the University of Michigan gastroenterology clinics, and 9% from referrals and other methods.

Dropouts were similar between the treatment groups. A very small group of the study population (9% total; 4 prunes, 3 psyllium) was instructed by study staff to reduce their daily treatment intake by 50% after experiencing significant increases in abdominal symptom distress during the intervention. Demographic and baseline screening symptom severity scores were similar between groups except that the prunes group reported higher abdominal discomfort scores at baseline (Table 1). Results from dietary assessments before and after the study period demonstrated no significant change in macronutrient consumption outside of the treatment intervention.

Primary outcome
For the primary outcome, the CSBM responder rate was 45% for the kiwifruit group (13/29; 95% CI [0.27–0.63]), 67% for the prunes group (16/24; 95% CI [0.48–0.86]), and 64% for the psyllium group (14/22; 95% CI [0.44–0.84]). There were no statistically significant differences between the treatment interventions for the primary outcome (P = 0.22) (Figure 3). Individual significance tests between kiwifruit and prunes (P = 0.12), kiwifruit and psyllium (P = 0.19), as well as prunes and psyllium (P = 0.22) were tested for statistical significance. Differences in adverse event (AE), satisfaction, and dissatisfaction reports were assessed using chi-squared tests for statistical significance. P values of ≤0.05 were considered statistically significant. Statistical analyses were performed using SAS (version 9.4, SAS Institute, Cary, NC). This was an exploratory study and thus not powered to detect effectiveness as measured by a change in clinical endpoints. A target of 26 subjects in each treatment group (total 80 subjects) was proposed to represent sufficient patient numbers to make preliminary conclusions based on study results.
Secondary outcomes

**Constipation symptoms.** For stool frequency, mean CSBM/week rates significantly increased for all 3 interventions compared with the baseline screening period. Participants in the prunes group demonstrated the greatest increase (+2.7) in mean CSBMs/week during treatment weeks 3 and 4 compared with baseline screening when compared with kiwifruit (+1) and psyllium (+1.7) (Table 2 and Figure 4). When the entire 4-week treatment period was compared with baseline, results were similar, with prunes subjects demonstrating the greatest mean change (+2.1; \( P < 0.001 \)) over both kiwifruit (+1; \( P = 0.049 \)) and psyllium (+1.4; \( P = 0.005 \)) subjects. Conversely, kiwifruit subjects demonstrated the smallest mean change in frequency.

There was no statistically significant difference in responder rates for stool consistency between treatment groups: 28% (8/29; 95% CI [0.11–0.44]) for the kiwifruit group, 17% for prunes (4/24; 95% CI [0.02–0.32]), and 32% for psyllium (7/22; 95% CI [0.12–0.51]). Kiwifruit (+0.4) and prunes (+0.5) produced the greatest mean change for stool consistency from baseline to treatment weeks 3 and 4. Psyllium (+0.2) had a lower mean change for stool consistency. Improvement in stool consistency for weeks 3 and 4 vs baseline within cohort was statistically significant for kiwifruit (\( P = 0.01 \)) and prunes (\( P = 0.049 \)), but not for psyllium (Table 2). Between-group differences were not statistically significant collectively or between individual treatment groups (kiwifruit-to-prunes: \( P = 0.50 \), kiwifruit-to-psyllium: \( P = 0.19 \), and prunes-to-psyllium: \( P = 0.22 \)).

There were significant improvements in mean straining scores for kiwifruit (\(-1.1; P = 0.003\)), prunes (\(-1.9; P < 0.001\)), and psyllium (\(-1.2; P = 0.04\)) subjects from baseline screening to treatment weeks 3 and 4 (Table 2). Improvements in mean straining scores were statistically similar by group (\( P = 0.37 \)) and between individual treatment groups (kiwifruit-to-prunes: \( P = 0.05 \), kiwifruit-to-psyllium: \( P = 0.36 \), and prunes-to-psyllium: \( P = 0.18 \)).

The mean proportion of BMs with a sensation of incomplete evacuation was statistically similar after baseline for kiwifruit (77%), prunes (80%), and psyllium (79%) subjects. There were significant decreases in the mean proportion of reported BMs...
with a sensation of incomplete evacuation for the kiwifruit (−17%; $P = 0.01$), prunes (−26%; $P = 0.001$), and psyllium (−16%; $P = 0.03$) groups at treatment weeks 3 and 4 compared with baseline (Figure 5). Differences in the mean change for the proportion of BMs with incomplete evacuation were statistically similar when compared across groups ($P = 0.49$).

**Abdominal and sensory symptoms.** Abdominal and sensory symptom variables were statistically similar at baseline. Differences in the mean change between all 3 groups from baseline screening to treatment weeks 3 and 4 were not statistically significant for all abdominal and sensory symptom variables. There was no significant improvement of the individual symptoms of abdominal pain and abdominal discomfort compared with baseline for both the kiwifruit group and the prunes group. Patients randomized to the kiwifruit group reported significant improvement in bloating scores ($P = 0.02$). Furthermore, patients randomized to the psyllium group reported significant improvement in abdominal discomfort and urgency scores (Table 2).

**Satisfaction with therapy.** There were differences in treatment satisfaction among the 3 treatment interventions at the completion of the 4-week treatment period. For kiwifruit subjects, 68% (19/28; 95% CI [0.49–0.82]) expressed satisfaction with the intervention, compared with 48% for prunes (11/23; 95% CI [0.27–0.68]) and 48% for psyllium (10/21; 95% CI [0.26–0.69]) (Figure 6). Differences in the proportion of patients expressing satisfaction with each therapy were not statistically significant

### Table 1. Demographics and baseline characteristics of screened subjects

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Kiwifruit (n:30)</th>
<th>Prunes (n:23)</th>
<th>Psyllium (n:23)</th>
<th>$P$ value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average age (yr)</td>
<td>43.1 ± 14.9</td>
<td>41.88 ± 17</td>
<td>43.0 ± 17.2</td>
<td>0.96</td>
</tr>
<tr>
<td>Sex—n (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.60</td>
</tr>
<tr>
<td>Female</td>
<td>25 (83)</td>
<td>24 (92)</td>
<td>20 (87)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5 (17)</td>
<td>2 (8)</td>
<td>3 (13)</td>
<td></td>
</tr>
<tr>
<td>Diagnosis—n (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.73</td>
</tr>
<tr>
<td>FC</td>
<td>19 (63)</td>
<td>19 (73)</td>
<td>16 (70)</td>
<td></td>
</tr>
<tr>
<td>IBS-C</td>
<td>11 (37)</td>
<td>7 (27)</td>
<td>7 (30)</td>
<td></td>
</tr>
<tr>
<td>Race—n (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.45</td>
</tr>
<tr>
<td>White</td>
<td>21 (70)</td>
<td>20 (77)</td>
<td>20 (87)</td>
<td></td>
</tr>
<tr>
<td>Black/African American</td>
<td>4 (13)</td>
<td>3 (11)</td>
<td>1 (5)</td>
<td></td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>0 (0)</td>
<td>1 (4)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>3 (10)</td>
<td>0 (0)</td>
<td>2 (8)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2 (7)</td>
<td>2 (8)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Treatment naive—n (%)</td>
<td>19 (63)</td>
<td>15 (58)</td>
<td>14 (61)</td>
<td>0.91</td>
</tr>
<tr>
<td>Laxative usage—n (%)</td>
<td>8 (27)</td>
<td>4 (16)</td>
<td>5 (22)</td>
<td>0.59</td>
</tr>
<tr>
<td>Average BMI (kg/m²)</td>
<td>27.9 ± 6.5</td>
<td>29.1 ± 6.7</td>
<td>30.0 ± 12</td>
<td>0.67</td>
</tr>
<tr>
<td>CSBMs per week</td>
<td>1.4 ± 1.9</td>
<td>1.0 ± 1.3</td>
<td>1.1 ± 1.1</td>
<td>0.60</td>
</tr>
<tr>
<td>Abd pain score</td>
<td>2.9 ± 2.4</td>
<td>2.2 ± 1.6</td>
<td>2.6 ± 1.6</td>
<td>0.04</td>
</tr>
<tr>
<td>Abd discomfort score</td>
<td>3.8 ± 2.5</td>
<td>3.4 ± 1.8</td>
<td>4.3 ± 1.7</td>
<td>0.32</td>
</tr>
<tr>
<td>Bloating score</td>
<td>4.3 ± 2.3</td>
<td>4.2 ± 2.1</td>
<td>4.3 ± 1.8</td>
<td>0.96</td>
</tr>
<tr>
<td>Stool consistency</td>
<td>3.2 ± 1.1</td>
<td>3.1 ± 0.87</td>
<td>2.9 ± 1.0</td>
<td>0.56</td>
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<tr>
<td>Straining score</td>
<td>5.4 ± 1.9</td>
<td>5.3 ± 1.6</td>
<td>5.4 ± 1.7</td>
<td>0.98</td>
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</table>

Abd, abdominal; BMI, body mass index; CSBM, complete spontaneous bowel movement; FC, functional constipation; IBS-C, irritable bowel syndrome with constipation.

* $P$ values ≤0.05 were considered significant.

Figure 3. Proportion of participants in each group reporting an increase of $≥1$ in the mean number of complete spontaneous bowel movements per week for $≥2$ treatment weeks compared with baseline screening.
Conversely, 17% of prunes (4/23; 95% CI [0.02 – 0.32]) and 38% of psyllium (8/21; 95% CI [0.17 – 0.59]) subjects expressed dissatisfaction with their assigned treatment, compared with 7% of those receiving kiwifruit (2/28; 95% CI [0.01 – 0.24]). This difference in dissatisfaction between kiwifruit and the other groups was statistically significant (P = 0.02) (Figure 6).

**Harms/safety assessment.** For the overall study cohort, the most commonly reported AEs included abdominal pain, bloating, and gas. An inventory of AEs reported by ≥5% of all study subjects by treatment group can be found in Figure 7. Compared with prunes and psyllium subjects, kiwifruit subjects were significantly less likely to report abdominal pain as an AE. Both kiwifruit and psyllium subjects were significantly less likely to report bloating as an AE compared with prunes (Figure 6). There were no serious AEs reported by study subjects. The proportion of subjects who dropped out of the study were similar between treatment groups (Figure 6). The most common reasons for dropout included worsening symptoms during the intervention and inability to schedule/attend study visits.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Kiwifruit (n = 29)</th>
<th>Prunes (n = 24)</th>
<th>Psyllium (n = 22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avg CSBMs per week</td>
<td>1.2</td>
<td>1.0</td>
<td>1.1</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>0.64</td>
</tr>
<tr>
<td>Avg stool consistency per week</td>
<td>3.2</td>
<td>3.1</td>
<td>2.9</td>
</tr>
<tr>
<td>P value</td>
<td>0.01</td>
<td>0.049</td>
<td>0.47</td>
</tr>
<tr>
<td>Avg straining per week</td>
<td>5.4</td>
<td>5.3</td>
<td>5.2</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>0.04</td>
</tr>
<tr>
<td>Avg bloating per week</td>
<td>4.2</td>
<td>4.1</td>
<td>4.3</td>
</tr>
<tr>
<td>P value</td>
<td>0.02</td>
<td>0.30</td>
<td>0.32</td>
</tr>
<tr>
<td>Avg abdominal pain per week</td>
<td>2.8</td>
<td>2.1</td>
<td>2.5</td>
</tr>
<tr>
<td>P value</td>
<td>0.74</td>
<td>0.68</td>
<td>0.64</td>
</tr>
<tr>
<td>Avg abdominal discomfort per week</td>
<td>3.7</td>
<td>3.2</td>
<td>4.2</td>
</tr>
<tr>
<td>P value</td>
<td>0.50</td>
<td>0.30</td>
<td>0.11</td>
</tr>
<tr>
<td>Avg urgency per week</td>
<td>5.1</td>
<td>4.5</td>
<td>4.9</td>
</tr>
<tr>
<td>P value</td>
<td>0.46</td>
<td>0.75</td>
<td>0.03</td>
</tr>
</tbody>
</table>

CSBM, complete spontaneous bowel movement.

*Stool consistency was a self-report measure from 1 to 7 based on the Bristol Stool Form Scale; straining, abdominal pain, abdominal discomfort, bloating, and urgency were self-reported based on an 11-point numerical rating scale (from 0 to 10, with 10 being the most severe). A P value of <0.05 was considered a significant difference for the mean variable weekly rate score at baseline to treatment weeks 3 and 4 within the given arm.

Figure 4. Mean weekly complete spontaneous bowel movements by treatment group.
DISCUSSION

This exploratory comparative effectiveness study assessed 3 natural treatments in patients with CC. This study represents the first data addressing the effectiveness and tolerability of kiwifruit on CC in the United States.

Our results are consistent with previously published studies examining the effects of natural treatments in patients with CC, although the existing literature is dominated by comparisons of different commercially available fiber preparations (18). Several previous studies have measured the impact of dietary interventions on stool weight and transit time. For example, in constipated patients with low baseline fiber intake, prunes have been shown to increase stool water content and stool frequency without affecting whole gut transit time (8). In an RCT comparing prunes to psyllium in patients with CC, CSBMs per week and stool consistency scores improved significantly more with prunes than psyllium (10). Both interventions were similarly tolerated. Although kiwifruit is a popular digestive aid in Asia, there remains a relative paucity of comparative literature describing its impact on bowel habits and effectiveness as a treatment in patients with CC.

One open-label study in constipated Chinese patients demonstrated a 55% response rate after 4 weeks of kiwifruit, similar to the results reported in the current study (15). Similarly, kiwifruit was found to improve stool frequency and decrease colonic transit time compared with baseline (14). In a study of 11 healthy volunteers from Spain, kiwifruit was found to increase stool frequency without affecting intestinal gas transit or causing bloating or abdominal distension (19). A report from a European and Asian crossover study demonstrated that both kiwifruit and psyllium improved CSBMs per week, but data regarding tolerability and comparative effectiveness are not available (16). Finally, a crossover study comparing gold-fleshed kiwifruit to psyllium demonstrated similar improvements in constipation for both groups, but again tolerability was not reported (20).

In the current study, prunes and psyllium led to significant and sustained increases in stool frequency over the 4-week treatment period. Kiwifruit exerted its greatest effects on stool frequency in the first 2 weeks of treatment, but this effect was less robust in weeks 3 and 4 (Figure 4). Such an effect with kiwifruit has not been reported in previous studies (14,15). Nonetheless, kiwifruit produced a statistical similar proportion of CSBM responders and significantly increased mean CSBM rate in weeks 3 and 4 compared with baseline (P = 0.002). Furthermore, improvements in other constipation symptoms including stool consistency and straining were significant and/or durable over 4 weeks of treatment with kiwifruit. As part of this study, we did not measure colonic transit time. Previous studies have found that although stool frequency does not correlate with colonic transit time, stool consistency measured by the Bristol Stool Form Scale does modestly correlate with colonic transit time (21). There were no statistically significant between-group differences in stool consistency observed in this study.

There were some notable differences in the tolerability of kiwifruit, prunes, and psyllium (Figure 7). The 3 interventions were generally safe, with no serious AEs reported. Overall, kiwifruit patients reported fewer adverse effects than those reported by patients treated with prunes and psyllium. Significantly fewer kiwifruit than prunes and psyllium subjects reported abdominal pain as an AE. Fewer kiwifruit and psyllium subjects reported bloating as an AE compared with prunes. This may be related to the fact that kiwifruit and psyllium are categorized as low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols while prunes contain the fermentable carbohydrate, sorbitol.
The absolute proportion of patients with CC reporting treatment satisfaction was highest in the kiwifruit group (68% kiwifruit, 48% for prunes and psyllium), although between-group differences were not statistically significant ($P > 0.05$ for all comparisons). However, the proportion of patients with CC reporting treatment dissatisfaction was lowest in the kiwifruit group. There was a statistically significantly lower proportion reporting treatment dissatisfaction between kiwifruit and the other groups (7% kiwifruit vs 17% prunes and 38% psyllium, $P = 0.02$). It is interesting when one considers the totality of the data reported in this study. Our data suggest that treatment satisfaction and dissatisfaction are driven by more than increasing stool frequency. It is likely that other parameters including stool consistency, straining, tolerability, and subjective parameters such as taste and texture of the intervention also influence treatment satisfaction and dissatisfaction. The differences in patient acceptance and tolerability among these natural treatments have not been previously reported. Whether such issues might

**Figure 6.** Post-treatment product satisfaction and dissatisfaction report. Satisfaction and dissatisfaction were assessed through standardized, yes or no questions after treatment. **P** value statistical significance less than 0.05.

**Figure 7.** Adverse event reports by treatment group. Adverse events featured were reported by ≥5% of all study subjects and assessed through standardized, yes or no questions after treatment. **P** value statistical significance less than 0.05.
Study Highlights

WHAT IS KNOWN
- Patients with chronic constipation are increasingly seeking natural treatments.
- Psyllium and prunes are proven treatments for chronic constipation.
- Asian studies suggest that kiwifruit may also benefit constipation symptoms, but the data supporting the use of kiwifruit in US populations are lacking.

WHAT IS NEW HERE
- Kiwifruit, psyllium, and prunes all improved bowel movements in constipated patients.
- Bloating was only improved in patients randomized to the kiwifruit group.
- Kiwifruit was associated with the lowest rate of adverse events and dissatisfaction with therapy.

influence the choice of and/or adherence to kiwifruit, prunes or psyllium among patients with CC requires further study.

Strengths of this study include the modified randomized design, blinded analysis, and robust clinical endpoints. Shortcomings of our study design include the small sample size, which may have led to a type II error for some study results. Other potentially important weaknesses include the relative homogeneity of our study population, the inability to blind the study, and the inability to properly randomize the kiwifruit group due to the fruit’s limited growing season. In addition, although we attempted to exclude secondary causes of constipation with our enrollment criteria, it is possible that our study cohort included subjects with pelvic floor dysfunction which would not be expected to improve with any of the study interventions. One would expect such an issue to affect all 3 arms of the study equally and our results are likely to reflect what would be expected in real world clinical practice where most patients with CC do not undergo testing to identify pelvic floor dysfunction.

Patients are increasingly seeking evidence-based natural treatments for many medical conditions, including CC. Many patients believe that natural products are safer and less costly than treatments for many medical conditions, including CC. Many practice where most patients with CC do not undergo testing to

CONFLICTS OF INTEREST

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