Original Article

Partially Hydrolyzed Guar Gum in the Treatment of Irritable Bowel Syndrome with Constipation: Effects of Gender, Age, and Body Mass Index

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ABSTRACT

Background/Aims: Partially hydrolyzed guar gum (PHGG) relieves symptoms in constipation-predominant irritable bowel syndrome (IBS) and may have prebiotic properties. However, the correlation between the effectiveness of PHGG and patient characteristics has not been examined. We aimed to investigate the effect of PHGG in symptom relief on constipation-predominant IBS according to gender, age, and body mass index (BMI). **Patients and Methods:** Sixty-eight patients with IBS entered a 2-week run-in period, followed by a 4-week study period with PHGG. Patients completed a daily questionnaire to assess the presence of abdominal pain/discomfort, swelling, and the sensation of incomplete evacuation. The number of evacuations/day, the daily need for laxatives/enemas and stool consistency-form were also evaluated. All patients also underwent a colonic transit time (CTT) evaluation. **Results:** PHGG administration was associated with a significant improvement in symptom scores, use of laxatives/enemas, stool form/consistency and CTT. At the end of the study period and compared with baseline, the number of evacuations improved in women, patients aged ≥ 45 years and those with BMI ≥ 25 ($P < 0.05$ for all comparisons); abdominal bloating improved in males ($P < 0.05$), patients < 45 years ($P < 0.01$) and those with BMI < 25 ($P < 0.05$). A decrease in the number of perceived incomplete evacuations/day was reported in patients with a BMI ≥ 25 ($P < 0.05$). Reductions in laxative/enema use were recorded in females ($P < 0.05$), patients < 45 years ($P < 0.01$), and patients with BMI < 25 ($P < 0.05$). **Conclusions:** Gender, age, and BMI seem to influence the effect of PHGG supplementation in constipated IBS patients. Further studies are needed to clarify the interaction of such parameters with a fiber-enriched diet.

Key Words: Constipation, guar gum, irritable bowel syndrome

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Irritable bowel syndrome (IBS) represents the most frequent disorder of the gastrointestinal tract. This syndrome is characterized by recurrent episodes of abdominal pain and discomfort, as well as functional alterations of the bowel not underlined by structural or biochemical modifications.[1] The etiology of IBS is still poorly understood. Several factors, including impaired gastrointestinal motility, visceral hypersensitivity, dysfunctions of the brain–bowel axis, and/or psychosocial disorders have been associated with this condition.

As many as 20% of the adult population has symptoms of IBS; it is more common in women and under age 35 years.[2,3] The severity of symptoms is associated with increasing body mass index (BMI).[4]

The prevalence of IBS has increased in the last decades, especially in Western countries.[1,5] Up to 65% of patients affected by IBS associate their symptoms with some particular food, which may elicit an "abnormal" response.[5] As a result, many patients modify their dietary habits and increase the

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fiber intake. However, reports on dietary interventions for the management of IBS are generally inconclusive, although a recent meta-analysis showed that the oral supplementation with fiber can be effective.[6,7] In fact, a reduction in the intake of fibers and liquids results in a decreased fecal volume and in an increase of fecal hardness, associated with an insufficient motility of the colon. Recent evidence supports the use of soluble fibers (compared with insoluble ones) in the relief of IBS symptoms.[8]

Guar gum is a gel-forming galactomannan, obtained from *Cyamoposis tetragonolobus*, a leguminous plant grown mainly in India and Pakistan.[9] Since 1953, the seeds of the guar plant have been processed into guar gum; this compound is widely used in food industry as thickener and emulsion stabilizer.[9] However, because of its high viscosity, guar gum cannot be easily incorporated in foods and beverages. Therefore, guar gum may be partially hydrolyzed by using β-endo-mannanase. The resulting partially hydrolyzed guar gum (PHGG) is a water-soluble compound, characterized by low viscosity.[9] When used experimentally, PHGG relieved symptoms in constipation-predominant and diarrhea-predominant forms of IBS and improved the quality of life.[10] Moreover, PHGG appears to exert prebiotic properties, by increasing the concentration of intestinal short-chain fatty acids, *Lactobacilli* and *Bifidobacteria*.[9,10] However, as yet no systematic studies have examined the correlation between efficacy of PHGG and patients' demographics/characteristics.

The aim of this study is to investigate the effects of PHGG in symptom relief in patients with constipation-predominant IBS, to determine if beneficial effects correlate with gender, age, and BMI.

PATIENTS AND METHODS

Study setting

This prospective, open-label observational study was conducted at the Gastroenterology Unit of Clinical and Experimental Medicine Department of University Hospital "Federico II" (Naples, Italy), between January and October 2009. All patients signed an informed consent form before being included in the study. The study was carried out in accordance with the Helsinki Declaration and the protocol was approved by the local Ethics Committee.

Patients

Inclusion criteria were age >18 years; diagnosis of IBS with predominant constipation symptoms according to Rome III criteria,[11] absence of predominant dyspepsia, and/or gastroesophageal reflux disease symptoms; absence of gastrointestinal diseases and good health status. Exclusion criteria were previous major surgery of the abdomen; use of PHGG in the 4 months prior to the study initiation; treatment with drugs altering gastrointestinal functions (anticholinergics, spasmolytics, prokinetics, opioids, laxatives, antidepressants, and serotonin agonist/antagonists); presence of cardiac, renal, neurologic, neoplastic, endocrine/metabolic, liver, or connective tissue diseases; and potential childbearing without the use of proper contraceptive drugs.

Experimental protocol and study evaluations

The study protocol comprised a 2-week run-in period followed by a 4-week study period in which patients received treatment with PHGG. Patients were instructed to take PHGG every day, in a glass of water after breakfast, no later than 9:00 am. A description of the study assessments during each period is provided in Table 1. At baseline, all patients filled a standardized questionnaire to assess the severity of IBS symptoms according to Rome III criteria.[11] Patients were enrolled if they had abdominal pain or discomfort ≥3 times/month in the 3 months before enrolment in the study, associated with variations in the frequency of evacuations and/or alteration in stool consistency and form.

During the run-in and the study periods, all patients were asked to complete a daily questionnaire to assess as follows: The presence of abdominal pain, bloating, and discomfort, all measured with a visual analogue scale (VAS) ranging from 0 to 100 mm; the sensation of incomplete evacuation, measured with a VAS; the number of evacuations during the day; the use of laxatives or enemas (yes/no); stool consistency and form, according to Bristol scale, as suggested by Rome III Committee.[12]

At baseline and at the end of the study period, all patients completed the Short Form-36 (SF-36) questionnaire to evaluate physical and mental health (for a complete

Table 1: Schedule of assessments made during the run-in and study periods

	Baseline	Run-in period		Study period			
		Week 1	Week 2	Week 1	Week 2	Week 3	Week 4
Assessment of IBS symptoms severity	V						
Assessment of daily symptoms		V	V	V	V	V	V
SF-36 questionnaire	V						V
CTT	V						V

IBS: Irritable bowel syndrome, SF-36: Short Form-36, CTT: Colonic transit time

review of this questionnaire, please see http://www.sf-36.org/).[13] Additionally, they underwent a colonic transit time (CTT) examination in which radio-opaque markers were administered on three consecutive days.[14] Subsequent radiography of the abdomen was performed on days 4 and 7; if markers were still detectable on day 7, further radiography was performed on day 10. This CTT technique was employed due to the simplicity of procedure and the reduced level of radiation exposure.[15]

Statistical analysis and calculation of sample size

Assuming that alpha is 0.05 and the effect size (F) is 3.35, we extrapolated the following statistical power (1-β error probability) for each sample size: 0.75 for 20 cases; 0.85 for 24; 0.90 for 28; 0.95 for 36. Data were analyzed by descriptive statistics. The severity of symptoms experienced during the 2 weeks of run-in period was compared with that reported during the last week of the study period by Student's *t* test for paired data, both on the overall sample of patients and after stratification of patients according to gender, age (<45 vs ≥ 45 years), and BMI (<25 vs ≥ 25 kg/m^2). The analysis of data retrieved from the SF-36 questionnaire was analyzed with the ANOVA test. A $P < 0.05$ was considered statistically significant. The study protocol planned the inclusion of almost 30 patients. Sample size was calculated on the basis of a preliminary evaluation of constipation data variability, in particular the CTT. All statistical analyses were performed with SPSS software (version 17.0).

RESULTS

Safety/tolerability

No adverse events potentially attributed to PHGG administrations were reported. No adverse events related to PHGG treatment were reported by patients during the study.

Patient population

In total, 108 consecutive patients were screened and 40 were not included in the study because they did not meet the eligibility criteria. Baseline characteristics of the 68 patients (median age: 37 years; range 19–62) included in the study are summarized in Table 2. More females (73.3%) than males were enrolled. Males and patients with a BMI ≥ 25 were significantly older than females and patients with a BMI < 25, respectively ($P < 0.05$). The mean BMI was 24.4; however, BMI was significantly greater in patients aged ≥ 45 years and in males than in those < 45 years and in females, respectively ($P < 0.05$).

Analysis in the overall population

The results observed in the overall population are summarized in Table 3. A significant reduction in the severity of abdominal swelling was observed during the study period compared with run-in values ($P < 0.05$), whereas the improvement in abdominal pain, although noticeable, did not reach statistical significance. The administration of PHGG was associated with a significant increase in the number of evacuations ($P < 0.05$ compared with run-in period) and a significant improvement in the sensation of incomplete evacuation ($P < 0.05$). The need for laxatives or enemas was significantly reduced during the study period compared with the run-in phase ($P < 0.05$). Significant improvements were also observed both in the stool form/consistency and in the CTT during the study period ($P < 0.05$ compared with run-in period).

When compared with baseline values, a trend toward an improvement in SF-36 scores was reported at the end of the study period, although a significant difference was not reached in any subscale [Figure 1].

Subgroup analysis

The results observed after the stratification of patients according to gender, age, and BMI are summarized in Table 4. No significant differences in abdominal pain were observed after stratification of patients according to gender, age, and BMI, whereas a decrease in the severity of abdominal swelling during the study period (compared with values reported during the run-in phase), was reported in males, patients <45 years and those with BMI < 25 ($P < 0.05$).

On the other hand, the number of evacuations significantly increased in females, patients aged ≥ 45 years and those with BMI ≥ 25 ($P < 0.05$). A trend toward an improvement in the sensation of incomplete evacuation was observed in all subgroups, but a significant reduction from run-in values was reported only in patients with a BMI ≥ 25 ($P < 0.05$).

Table 2: Baseline characteristics of enrolled patients

	Overall	Gender		Age (years)		BMI (kg/m^2)	
		Males	Females	<45	≥45	<25	≥25
Total number of patients	68	18	50	46	22	45	23
Males, number	18	18	0	9	9	11	7
Age, median (range)	37 (19-62)	47 (25-62)	33 (19-57)	28 (19-44)	54 (51-62)	29 (19-62)	51 (21-58)*
BMI, mean±standard deviation (range)	24.4±2.7 (20.5-29.5)	25.0±2.4 (23.1-29.5)	24.0±2.7 (21.1-29.4)	23.5±2.3 (21.1-25.4)	26.1±2.6 (22.5-29.5)[a]	22.8±1.4 (20.5-24.8)	27.1±2 (25.4-29.5)

[a]*P*<0.05. BMI: Body mass index

The need for laxatives or enemas was significantly reduced during the study period in females, patients aged <45 years, and patients with BMI < 25, when compared with run-in phase ($P < 0.05$).

Stool form and consistency improved in all the subgroups of patients during the study period, with respect to run-in phase, regardless of gender, age, and BMI ($P < 0.05$).

CTT significantly decreased in males, females, in patients with BMI < 25, and in those with BMI ≥ 25 ($P < 0.05$), whereas no differences between run-in phase and study period were observed when stratifying patients according to age.

Table 3: Results of the overall analysis

Total number of patients	Run-in period 68	Study period 68
Abdominal swelling, VAS (mm)	26.0±10.0	17.2±10.1*
Abdominal pain, VAS (mm)	10.4±10.6	7.9±5.6
Number of evacuations/day	0.38±0.22	0.51±0.20*
Number of perceived incomplete evacuations/day	1.11±1.07	0.48±0.43*
Days on laxatives/enemas	0.11±0.13	0.03±0.10*
Stool form/consistency (Bristol scale), score	1.97±0.96	2.8±0.6*
CTT, hours	46.2±7.79	39.1±6.9*

*P<0.05. All data are expressed as mean±standard deviation. CTT: Colonic transit time, VAS: visual analog scale

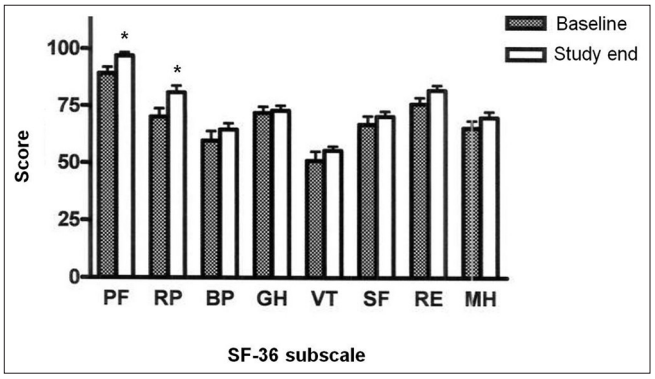

Figure 1: Short Form-36 scores, by subscale, in the total patient population (n=68), at baseline and the end of study period. *P < 0.05 vs baseline. PH, physical functioning; RP, role limitations due to physical problems; BP, bodily pain; GH, general health perceptions; VT, vitality; SF, social functioning; RE, role-limitations due to emotional problems; MH, mental health

Table 4: Results of the subgroup analysis

	Run in		Study period	
Gender	**Male**	**Females**	**Male**	**Females**
Number of patients	18	50	18	50
Abdominal swelling, VAS (mm)	26.3±14.5	25.2±22.0	16.0±6.2*	18.0±11.3*
Abdominal pain, VAS (mm)	15.1±10.6	8.7±5.2	9.6±3.0*	8.0±4.2
Number of evacuations/day	0.40±0.23	0.39±0.18	0.6±0.07	0.6±0.09*
Number of perceived incomplete evacuations/day	1.31±1.12	1.04±1.24	0.5±0.33*	0.42±0.24*
Days on laxatives/enemas	0.096±0.091	0.14±0.12	0.04±0.09	0.07±0.09*
Stool form/consistency (Bristol scale), score	1.5±0.53	2.14±1.03	2.8±0.5*	2.9±0.7*
CTT, hours	46.7±7.7	44.9±8.5	38.9±5.9*	39.2±7.3*
Age	**<45 years**	**≥45 years**	**<45 years**	**≥45 years**
Number of patients	46	22	46	22
Abdominal swelling, VAS (mm)	26.6±10.5	23.3±17.3	17.0±10.9*	18.0±11.0
Abdominal pain, VAS (mm)	11.9±9.5	7.3±5.8	9.0±6.4	8.3±4.1
Number of evacuations/day	0.41±0.23	0.35±0.09	0.59±0.08*	0.60±0.08*
Number of perceived incomplete evacuations/day	1.40±1.28	0.54±0.36	0.50±0.30*	0.40±0.20
Days on laxatives/enemas	0.13±0.12	0.12±0.12	0.06±0.08*	0.07±0.10
Stool form/consistency (Bristol scale), score	1.95±0.99	2.00±0.95	2.90±0.70*	2.80±0.40*
CTT, hours	46.9±7.9	44.9±7.9	40.0±6.6*	37.3±7.5*
BMI	**<25**	**≥25**	**<25**	**≥25**
Number of patients	45	23	45	23
Abdominal swelling, VAS (mm)	29.0±17.2	19.6±15.6	18.0±10.8*	17.0±9.3
Abdominal pain, VAS (mm)	11.2±11.7	9.0±7.0	9.1±7.5	8.0±7.1
Number of evacuations/day	0.42±0.22	0.34±0.12	0.59±0.08*	0.6±0.09*
Number of perceived incomplete evacuations/day	1.41±1.32	0.60±0.35	0.50±0.30*	0.40±0.30*
Days on laxatives/enemas	0.13±0.12	0.12±0.11	0.07±0.09*	0.04±0.08*
Stool form/consistency (Bristol scale), score	1.90±0.90	2.00±1.13	2.80±0.60*	2.90±0.70*
CTT, hours	45.6±8.3	47.4±7	39.2±7.14*	39±6.8*

*P<0.05 vs Run in. All data are expressed as mean±standard deviation. BMI: Body mass index, CTT: Colonic transit time, VAS: Visual analog scale

The analysis of SF-36 results did not disclose any significant difference between baseline values and those reported at the end of the study period; however, a trend toward an improvement was observed in most subscales, in all subgroups of patients [Figure 2].

DISCUSSION

This study, performed in order to assess the effects of PHGG in IBS, confirmed the beneficial effect of this therapeutic strategy, in line with previous experiences.[16–20] In particular, we observed an overall improvement of the abdominal swelling, an increase in the number and quality of evacuations and a reduction in the CTT. On the other hand, abdominal pain did not significantly improve, further confirming previous findings.[16,17]

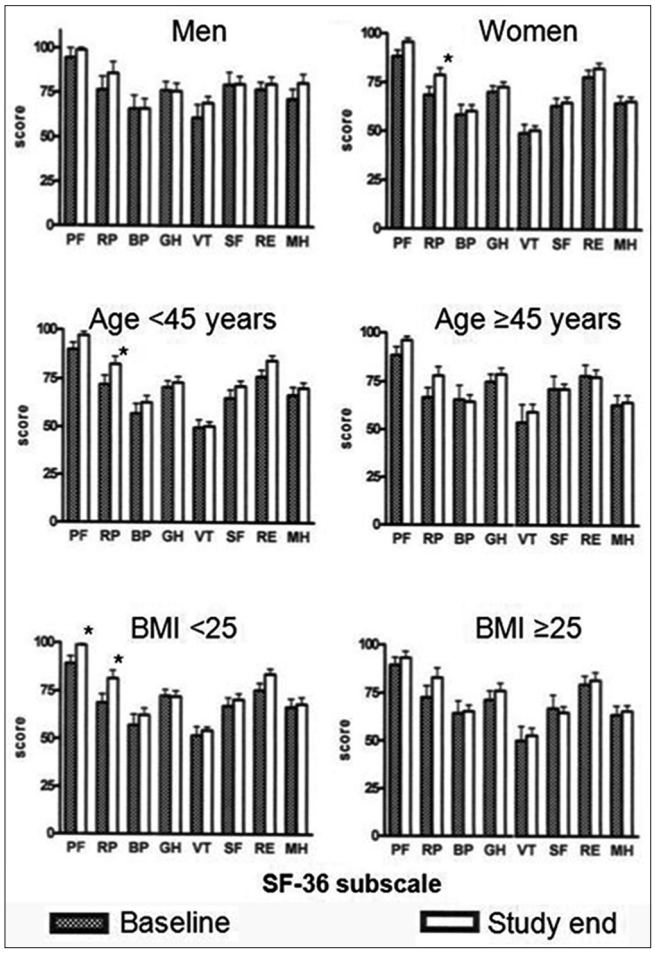

Figure 2: Short Form-36 scores, by subscale, after stratification of patients according to gender, age, and BMI at baseline and at the end of study period. *$P < 0.05$ vs baseline. PH, physical functioning; RP, role limitations due to physical problems; BP, bodily pain; GH, general health perceptions; VT, vitality; SF, social functioning; RE, role-limitations due to emotional problems; MH, mental health

In particular, we showed that the number of evacuations is significantly enhanced following the ingestion of fiber in women, in patients ≥45 years and in those with BMI ≥ 25. Moreover we also found, in women, a decrease of number of days with laxatives and/or enemas use already showed in a previous study.[21] The global improvement in women may be attributed, at least in part, to the better compliance to prescribed dietary regimen enriched with fiber in males; therefore, PHGG increases the total intake of soluble fiber that further enhances the improvement of bowel function.[22] Moreover, middle-aged women have a significantly slower colonic transit than young women,[23] driving older women to a higher intake of fiber. In addition, we must consider that the aging-associated oxidative stress may cause morphologic alterations of intestinal bacterial cells, probably also gender related, and the use of PHGG can improve microbiota environment.[24,25] The increase in the number of evacuations in patients with BMI > 25 could be associated with a larger stool volume, with a consequent improvement in pelvis mechanics in these overweight patients, who may have a poor "abdominal contractility."[26]

Our study has also demonstrated a significant reduction in the severity of abdominal swelling in males, in patients <45 years and in those with BMI < 25. Most males tend to have greater abdominal strength (and a corresponding rise in pelvic angle) compared with females (especially those in menopause, due to the decreased production of estrogens), which may explain the improvement in abdominal swelling observed in males.[26] On the other hand, the decreased swelling reported in patients with BMI < 25 can be dependent on a low carbohydrate intake, which may also increase the prebiotic function exerted by PHGG.[22]

The modifications induced by PHGG on bowel microflora have been reported in animal and human studies. In two studies on rats, the administration of PHGG resulted in an increase of bowel concentrations of butyrate, one of the most important sources of energy for epithelial cells.[25] In a study on healthy volunteers, PHGG supplementation significantly increase the proliferation of *Bifidobacteria* and *Lactobacilla*.[20] Okubo has hypothesized that the *in vivo* effect of PHGG can be attributed to the degradation of fibers by bacteria, thus promoting the growth of *Bifidobacteria* and *Lactobacilla*.[25] The selective increase in the growth of *Bifidobacteria* and *Lactobacilla* modifies the bowel microflora, improves the symptoms of IBS and, in particular, provides a relief from pain and abdominal swelling, as observed in our study and in previous experiences.[27,28] Taken together, these findings might suggest that PHGG supplementation can restore the physiological balance of bowel microflora.[29]

The reduced need for laxatives reported by women and in patients <45 years can be directly correlated with the greater fiber intake in women and/or with an actual increase in fiber content in patients with a low fiber intake.[22] In the present analysis, we reported a marked improvement CTT in all patients, with a consequent normalization of the form and the consistency of stools, probably due to the increase in fecal volume and to the stimulation of peristalsis.

Lastly, we also investigated the importance of psychological factors as determinants of IBS, via the SF-36. To our knowledge, only one study has evaluated the effects of PHGG on quality of life of patients with IBS.[17] We reported an improvement in most subscales, although this did not reach statistical significance. The lack of any statistical difference may be attributed, at least in part, to the short period of observation and relatively to the low number of study participants. In fact, a significant improvement in quality of life after fiber supplementation was observed in another study over a 3–6 months period.[17]

It must be acknowledged that this study has several limitations. First, the low number of patients may limit the robustness of the results. Second, the lack of a control cannot allow distinguishing between spontaneous improvement and the actual effect of PHGG. However, the short period of observation, which is *per se* another limitation, may suggest an active effect of PHGG in IBS patients. Moreover, the benefit of this type of naturalistic, observational study is that the data obtained represents a real-life overview based on actual clinical practice.[30]

In conclusion, our study has confirmed the overall improvement with PHGG supplementation of symptoms correlated with stipsis in IBS with predominant constipation. Moreover, to our knowledge, we are the first to report a differential effect of PHGG with gender, age, and BMI. Further investigation on the pathogenesis of IBS and large-scale randomized trials would contribute to our knowledge and improve the treatment of this disease.

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