

## Partially hydrolyzed guar gum in pediatric functional abdominal pain

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### Abstract

**AIM:** To assess the effects of partially hydrolyzed guar gum (PHGG) diet supplement in pediatric chronic abdominal pain (CAP) and irritable bowel syndrome (IBS).

**METHODS:** A randomized, double-blind pilot study was performed in sixty children (8-16 years) with functional bowel disorders, such as CAP or IBS, diagnosed according to Rome III criteria. All patients underwent ultrasound, blood and stool examinations to rule out any organic disease. Patients were allocated to receive PHGG at dosage of 5 g/d ( $n = 30$ ) or placebo (fruit-juice  $n = 30$ ) for 4 wk. The evaluation of the efficacy of fiber supplement included IBS symptom severity score (Birmingham IBS Questionnaire), severity of abdominal pain (Wong-Baker Face Pain Rating Score) and bowel habit (Bristol Stool Scale). Symptom scores were completed at 2, 4, and 8 wk. The change from baseline in the symptom severity scale at the end of treatment and at 4 wk follow-up after treatment was the primary endpoint. The secondary endpoint was to evaluate compliance to supplementation with the PHGG in the

pediatric population. Differences within groups during the treatment period and follow-up were evaluated by the Wilcoxon signed-rank test.

**RESULTS:** The results of the study were assessed considering some variables, such as frequency and intensity of symptoms with modifications of the bowel habit. Both groups were balanced for baseline characteristics and all patients completed the study. Group A (PHGG group) presented a higher level of efficacy compared to group B (control group), (43% vs 5%,  $P = 0.025$ ) in reducing clinical symptoms with modification of Birmingham IBS score (median  $0 \pm 1$  vs  $4 \pm 1$ ,  $P = 0.025$ ), in intensity of CAP assessed with the Wong-Baker Face Pain Rating Score and in normalization of bowel habit evaluated with the Bristol Stool Scale (40% vs 13.3%,  $P = 0.025$ ). In IBS subgroups, statistical analysis shown a tendency toward normalization of bowel movements, but there was no difference in the prevalence of improvement in two bowel habit subsets. PHGG was therefore better tolerated without any adverse effects.

**CONCLUSION:** Although the cause of pediatric functional gastrointestinal disorders is not known, the results show that complementary therapy with PHGG may have beneficial effects on symptom control.

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**Key words:** Functional bowel disorders; Partially hydrolyzed guar gum; Pediatric chronic abdominal pain; Fiber diet

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## INTRODUCTION

Functional gastrointestinal disorders (FGIDs) are defined as a variable combination of chronic or recurrent gastrointestinal (GI) symptoms; they are age dependent and not explained by structural or biochemical abnormalities<sup>[1]</sup>. Chronic abdominal pain (CAP) is the most common condition in FGIDs. It is usually functional without objective evidence of an underlying organic disorder. Apley *et al*<sup>[2]</sup> introduced the term recurrent abdominal pain (RAP) for the first time in pediatric literature, using it to describe a condition whereby children have experienced at least 3 bouts of pain, severe enough to affect activities, over a period of at least 3 mo. In 1999, the Pediatric Rome Working Group introduced standardized symptom-based criteria for pediatric FGIDs with the publication of the Rome II criteria<sup>[3]</sup>. In 2006, the "Rome Committee"<sup>[4]</sup> defined new diagnostic criteria (Roma III) for pediatric FGIDs, differentiating functional abdominal pain (FAP) from dyspepsia and irritable bowel syndrome (IBS) in that the pain is at a different site with normal bowel habits. The exact prevalence of CAP in children is not known. It seems to account for 2%-4% of all pediatric office visits<sup>[5]</sup>. Several studies suggested that 13% of middle-school students and 17% of high school students have weekly experience of abdominal pain<sup>[6,7]</sup>. According to these criteria, IBS is an FGID characterized by abdominal pain or discomfort, accompanied by altered bowel habits (constipation, IBS-c or diarrhea, IBS-d or alternating)<sup>[8]</sup>. It has been shown that some factors, especially psychological factors, dietary habits, and frequency of exercise, are associated with onset and course of IBS<sup>[9-11]</sup>. The term "functional" is not real but conceptual and the pathogenesis can be correlated with alterations of visceral sensitivity, increased intestinal permeability, chronic inflammation and presence of a genetic predisposition<sup>[12]</sup>. Pharmacotherapy generally cannot be recommended for children with FAP, except in the context of clinical trials. Drugs should only be given in exceptional cases<sup>[13,14]</sup>. Up to 40% of children undergo alternative or complementary therapy such as reassurance, phytotherapy, dietary restrictions or homeopathy<sup>[15]</sup>. The putative benefit of such methods has not been documented by controlled clinical trials.

The beneficial effects of water-soluble dietary fibers have received attention as complementary therapy in FGIDs, especially in FAP and IBS, for their ability to modify bowel pattern, accelerate oral-to-anal transit and decrease intracolonic pressure and alleviate pain<sup>[16,17]</sup>. Partially hydrolyzed guar gum (PHGG) is a vegetal, water-soluble, non-viscous, non-gelling dietary fiber that is derived from guar gum, a water-soluble, viscous, gelling polysaccharide found in the seeds of the guar plant. The saccharide component of guar gum is galactomanan<sup>[18]</sup>. Parisi *et al*<sup>[19]</sup> showed, in an adult open trial, that PHGG supplementation is followed by a decrease of IBS symptoms, such as abdominal pain and bowel habit. Feldman *et al*<sup>[20]</sup>, in a small, prospective, randomized,

double-blind, controlled trial, have revealed that fiber supplementation can improve symptoms in children with FAP. Despite this, there have been no recently available published randomized controlled trials (RCTs) to support the use of fiber in the treatment of CAP in a pediatric population.

The aim of this study was to assess the effect of PHGG diet supplement on CAP and IBS symptoms in paediatric population.

## MATERIALS AND METHODS

Sixty patients were prospectively enrolled in the study and randomly assigned to one of 2 study arms (PHGG group or group A: 30 patients; placebo group or group B: 30 patients). Median age was 12.8 years (range 8-16 years) with a greater predominance of females (62% girls and 38% boys). CAP and IBS patients were defined according to the Rome III criteria.

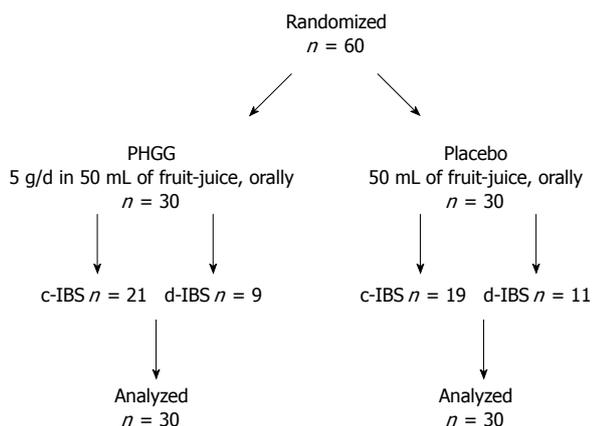
All patients were identified into two subgroups: 21/30 (70%) and 19/30 (63%) with constipation-predominant IBS in group A and B respectively; 9/30 (30%) and 11/30 (37%) with diarrhoea-predominant IBS in group A and B respectively. At baseline, the two groups were not statistically different, with respect to age, sex, alterations in bowel movements, incidence and intensity of self-reported symptoms. Subjects' overall baseline demographic and clinical characteristics are summarized in Table 1. All patients underwent ultrasound, blood and stool examinations to exclude organic disease. Seven days before joining the study, patients were asked to not use any medication. The study was performed in accordance with the Declaration of Helsinki and was approved by the local ethics committee. Informed consent was obtained for each patient. All patients completed the trial without any dropouts. Figure 1 is a flow diagram showing the subjects' progression through the study. Patients were consecutively recruited from November 2010 to May 2011, in the Pediatric Gastroenterology Unit of the University of Messina, and randomly assigned to two groups (1:1, PHGG group or group A: 30 patients; placebo group or group B: 30 patients) to receive either a beverage of PHGG (Benefibra, Novartis Consumer Health) at a dosage of 5 g/d in 50 mL of fruit-juice ( $n = 30$ ) or matching placebo (fruit-juice,  $n = 30$ ) for 4 wk. For technical reasons of non-laboratory reproducibility of an inert and odorless powder, the placebo consisted of a fruit juice. As in other studies, PHGG was mixed with fruit juice during meals or between meals.

The manufacturer had no role in the conception, design or conduct of the study or in the analysis or interpretation of the data. Randomization was based on a computer-generated list. Supplementation was stopped after 4 wk and patients were followed up for a further 4 wk. GI symptoms were assessed with the "Birmingham IBS Symptom Questionnaire", "Wong Baker Faces Pain Rating Score" and "Bristol Stool Scale". The Birmingham IBS symptoms score consists of 11 questions based

**Table 1** Baseline demographic and clinical data

	PHGG group A	Placebo group B	P value
n	30	30	
Age (yr)	12.3 ± 2.0	13.1 ± 1.5	0.16
Sex (male/female)	12/18	11/19	0.88
Self-reported pain	3.7 ± 1.2	3.5 ± 1.5	0.15
c-IBS	21/30 (70%)	19/30 (63%)	0.75
d-IBS	9/30 (30%)	11/30 (37%)	0.64

Values are mean ± SD or n (%). PHGG: Partially hydrolyzed guar gum; IBS: Irritable bowel syndrome.



**Figure 1** Flow diagram of the progress through the study. PHGG: Partially hydrolyzed guar gum; IBS: Irritable bowel syndrome.

on the frequency of IBS related symptoms. Each question had a standard response scale with symptoms all being measured on a 6-point Likert scale ranging from 0 = none of the time, to 5 = all of the time (Table 2). Wong-Baker Faces Pain Rating Score was used to evaluate CAP severity with a variable score from 0 = no hurt, to 5 = hurts worst. The Bristol Stool Scale classifies the form and consistency of stools into 7 categories (from separate hard lump to entirely liquid stools).

All patients were assessed clinically at 2, 4, and 8 wk (T1, T2, T3) by means of a physical examination and the scoring systems from baseline (Table 3). At T2, compliance with treatment (worse, unchanged, better) was also assessed. Adverse events or any use of other drugs were recorded. Primary outcome was reduction in the frequency and intensity of clinical symptoms and correlation with the improvement of character of stool. Secondary outcome was the evaluation of compliance and safety of PHGG in children.

### Statistical analysis

Data are given as mean ± SD. Differences between groups were evaluated by the Kruskal-Wallis one-way analysis of variance (ANOVA). Nominal variables were analyzed with Pearson's chi-square test and Fisher's exact test when, in a 2 × 2 table, one cell had an expected frequency ≤ 5. Differences within groups during the treatment period and follow-up were evaluated by the Wilcoxon signed-rank test. The statistical level of sig-

**Table 2** Modified by Birmingham Score Questionnaire<sup>[36]</sup>

Constipation	Diarrhoea	Pain
Hard bowel motions	Loose, mushy or watery bowel motions	Discomfort or pain
Straining	Diarrhoea	Discomfort or pain after eating
Constipation	Leaked or soiled Urgency	Sleep problem
	Mucus or slime	

Each question had a standard response scale with symptoms all being measured on a 6-point Likert Scale ranging from 0 = none of the time to 5 = all of the time.

nificance was set at the 5% level ( $P < 0.05$ ). The system utilized was IBM SPSS Statistics Processor.

## RESULTS

The results of the study were assessed considering some main variables, such as improving frequency and intensity of the symptoms and modifications of the bowel habit.

### Overall rating of frequency symptoms

At the enrolment visit (T0), mean score evaluation of principal IBS related symptoms (Birmingham Score) confirmed that symptoms were present almost every day, together with a strong functional disability in both groups. Overall, 15 of the 60 (24%) participants with IBS reported treatment success. Those in the PHGG group were more likely to have treatment success than those in the control group (43% *vs* 5%,  $P = 0.025$ ). Responders with significant reduction of Birmingham IBS score (median 0 ± 1 *vs* 4 ± 1,  $P = 0.025$ ) was shown in the PHGG group *vs* placebo at both 4 wk and 8 wk (Table 3). The total score and the three subscale scores for constipation, diarrhoea and pain symptoms of the Birmingham score were significantly improved at the 4 and 8 wk evaluations compared to the baseline in the PHGG group. The supplementation response was comparable both in IBS-d and IBS-c subgroups. In group B, no significant difference was found in comparisons at any evaluation time point for any subscale score.

### Bowel habits

At baseline all patients were shown a wide range of alterations in bowel movements, evaluated with Bristol Stool Scale, without any difference in the two treatment groups. Effects of PHGG supplementation (5 g/d) for 4 wk on fecal output in IBS-d and IBS-c subsets *vs* placebo were also evaluated. In group A, there was a tendency toward normalization of bowel movements, which is highlighted by the progressive normalization of Bristol Stool Scale at type 3 or 4 (Table 3). In particular, 16 (26.6%) of 60 patients had normalized bowel habits: in the PHGG group the prevalence of improvement was 40% (12 patients), while it was 13.3% (4 patients) in the placebo group ( $P = 0.025$ ). This result remained constant during the follow-up 4 wk. There was no difference in the prevalence of

**Table 3** Outcome measures at baseline (T0), at 4 wk of supplementation (T2) and after 8 wk (mean  $\pm$  SD)

	Group A PHGG 5g/d (n = 30)			Group B Placebo (n = 30)		
	Baseline	4 wk (T2)	8 wk (T3)	Baseline	4 wk (T2)	8 wk (T3)
Birmingham Score <sup>a</sup>	28.5 $\pm$ 7.16	24.3 $\pm$ 6.02	23.0 $\pm$ 6.15	29.5 $\pm$ 6.94	28.4 $\pm$ 8.39	28.7 $\pm$ 7.54
Bristol Stool Score <sup>a</sup>						
IBS-c	1.00 $\pm$ 1.02	2.02 $\pm$ 1.50	2.32 $\pm$ 1.50	1.16 $\pm$ 0.89	1.76 $\pm$ 1.04	1.65 $\pm$ 1.08
IBS-d	5.02 $\pm$ 0.63	4.01 $\pm$ 0.16	4.07 $\pm$ 0.12	5.54 $\pm$ 0.32	4.86 $\pm$ 0.96	4.89 $\pm$ 0.73
Wong-Baker Score <sup>a</sup>						
	2.15 $\pm$ 0.14	1.86 $\pm$ 0.14	1.63 $\pm$ 0.16	2.16 $\pm$ 0.17	2.04 $\pm$ 0.17	2.05 $\pm$ 0.19

<sup>a</sup> $P < 0.05$  vs placebo (Wilcoxon 2-sample test). PHGG: Partially hydrolyzed guar gum; IBS: Irritable bowel syndrome.

improvement in two bowel habit subsets ( $P > 0.05$ ).

### Intensity of the abdominal pain

There was no difference in pain intensity reported at baseline between the groups as Wong-Baker Face Pain Rating Score. During the course of study, there was a decrease in the intensity of pain in the group of children given PHGG, which was not seen in the placebo-supplemented group (Table 3). However, this result was not statistically significant ( $P > 0.05$ ), compared with baseline at wk 4 and 8. Improvement of clinical symptoms in group A was correlated with a change of bowel habit and persisted 4 wk (T8) after cessation of PHGG supplementation. The clinical response was comparable both in IBS-d and IBS-c subgroups (Table 3). Analysis of the data confirmed optimal compliance and safety of PHGG dietary supplementation.

## DISCUSSION

CAP is common in children and adolescents. In most children, CAP is functional without objective evidence of an underlying organic disorder. Children with CAP are more likely than children without CAP to have headache, joint pain, anorexia, vomiting, nausea and altered bowel habit assignable to IBS<sup>[21]</sup>. Physicians must decide whether to order diagnostic tests or use conservative management. The presence of alarm symptoms or signs suggests higher pretest probability and prevalence of organic disease and may justify the performance of diagnostic tests. CAP can cause long absences from school and markedly worsens quality of life of the children and parents<sup>[22,23]</sup>.

In a recent American study, the diagnostic evaluation of CAP in a tertiary center in United States was found to cost approximately \$6000 per patient<sup>[24]</sup>. The first treatment step is an age-appropriate assessment through the reassurance of the child and family on the absence of organic causes, but this does not mean that abdominal pain is not a real problem. Cognitive behavioral therapy, however, is an effective form of alternative treatment<sup>[25,26]</sup>.

A thorough review of literature, with a focus on RCTs, revealed a paucity of studies examining effectiveness of pharmacologic and dietary interventions. Definitive statements concerning therapeutic efficacy are quite

limited. Huertas-Ceballos *et al.*<sup>[15]</sup>, in a meta-analysis, failed to reveal any therapeutic benefit from a low-lactose or high-fiber diet for children with CAP. Therapeutic trials in adults with CAP associated with IBS symptoms have revealed a high rate of the placebo-response, confirming that non-pharmacological therapies alone are often adequate for many patients. PHGG is a soluble fiber with important properties, such as non-viscous texture, normal fermentation, non gelling, high hydrophilic potential and no interference with micronutrient absorption<sup>[27]</sup>. There is clear evidence that fiber decreases whole gut transit time, accelerates oral-to-anal transit, and decreases intracolonic pressure reducing abdominal pain. Fiber may represent a mainstay in the FAP and IBS therapeutic algorithm. Results of fiber supplementation in the adult population in patients with FAP and IBS has produced contrasting results, and the main reason for the variation is correlated with different types of fiber used<sup>[28,29]</sup>. The main distinction between soluble and insoluble fiber is essential as only soluble fiber such as PHGG dissolves in water and is widely metabolized in the large bowel, thus producing short-chain fatty acids, leading to selective stimulation of microbial growth<sup>[30,31]</sup>. PHGG may also act as prebiotic, thus modulating intestinal microbiota. Weaver *et al.*<sup>[32]</sup>, in experimental studies in rats, demonstrated that PHGG administration was accompanied by a rise in butyrate concentrations of colonocytes. Tuohy *et al.*<sup>[33]</sup> showed that PHGG supplementation in healthy volunteers caused selective increase in the percentage of *Bifidobacteria* and *Lactobacilli* with beneficial modulation of microbiota that has been reported to ameliorate IBS symptoms, with a decrease in pain and flatulence<sup>[34]</sup>.

Bijkerk *et al.*<sup>[35]</sup> observed in an adult population that, although general fiber supplementation globally alleviates IBS symptoms, the beneficial effect is mainly associated with the use of soluble fiber rather than insoluble fiber. This study demonstrated that soluble fiber is effective in decreasing global IBS symptoms<sup>[36]</sup> but was no better than a placebo. Some of these above mentioned studies on the use of fiber in adult populations were biased as they confirmed that the placebo response in IBS patients ranged from 20%-50%. In our study, the placebo response was much lower than expected.

In 2012, a systematic review identified 3 RCTs evalu-

ating fiber supplementation in children with FGIDs. Patients were supplemented with different dietary fiber types for 4-6 wk<sup>[37]</sup>. Among these, the Feldman<sup>[20]</sup> study, a randomized, double-blind, placebo-controlled trial, is the only study in children with CAP (26 for group) recruited from primary care practices and supplemented with soluble fibers. Improvement of symptoms in treated patients with fiber not was significant *vs* the placebo-group. In patients with IBS symptoms with modification of the bowel habit, water-soluble fibers, such as PHGG, decrease symptoms also with a prebiotic effect, beneficial modification of the intestinal microflora and selective increase of *Lactobacilli* and *Bifidobacteria*<sup>[38]</sup>. PHGG was therefore tolerated and preferred by patients, indicating higher success of soluble fiber than bran or insoluble fiber. The present findings confirm the beneficial effects of PHGG at 5 g/d and in the short term (4 wk). Our study can be considered the first prospective, randomized, controlled, single-blind, clinical trial conducted with this particular fiber supplementation (PHGG) in pediatric CAP and IBS. Some limitations should caution against generalizing from the results of this study, such as the classification at baseline of CAP according to severity of symptoms (mild, moderate and severe) and lack of knowledge of dietary habits in patients enrolled. Given the good results obtained for the first time, it is important to confirm these preliminary data on a greater number of patients and also to consider the active role of liquid fiber in improvement of symptoms. The efficacy of this approach has proven how dietary management is more effective than pharmacological therapy in children with CAP and IBS.

In summary, fiber supplementation can be considered an important option in pediatric CAP and IBS. Water-soluble fiber, such as PHGG, is preferable to insoluble fiber. Moreover, initial studies have shown that fiber may act as a prebiotic, thus increasing the therapeutic benefits. Further placebo-controlled studies are needed to evaluate whether PHGG can also be seen as a maintenance therapy of CAP.

## COMMENTS

### Background

Functional bowel disorders, such as chronic abdominal pain (CAP), are frequent in children and similar to adult irritable bowel syndrome (IBS). Some children with CAP develop substantial disability and limitations in physical and psychosocial functions. There is little evidence of the efficacy of conventional medical treatment while there is a moderate evidence for the efficacy of complementary therapy (diet, fibers, low-lactose intake) in the adult population. Water-soluble fibers, such as oats, barley and gums in psyllium, can be safe in IBS symptoms.

### Research frontiers

Water-soluble fibers are known for their ability to modify bowel patterns, accelerate oral-to-anal transit, decrease intracolonic pressure and alleviate pain. Functional abdominal disorders, such as abdominal pain and IBS, are frequent also in pediatric populations and should stimulate the trend to conservative therapy.

### Innovations and breakthroughs

To date, there has been a limited number of studies regarding specific optional treatment in CAP and IBS. This is the first study in a pediatric population that showed a clinically significant improvement of the symptoms in pediatric functional gastrointestinal disease with dietary manipulation. The small sample

size and a low placebo effect may indicate a requirement for request powered and well designed randomized controlled trials on the clinical effectiveness and safety of dietary treatment.

### Applications

The findings in this study indicate that fiber supplementation can be considered an important therapeutic option in pediatric IBS.

### Peer review

It is very well written and the topic is very interesting for the readers. This is an important topic for gastroenterologists, clinicians, surgeons, Critical Care doctors and nutritionists.

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