

Efficacy of Oral Psyllium in Pediatric Irritable Bowel Syndrome: A Double-Blind Randomized Control Trial

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ABSTRACT

Objective: Pediatric irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder with variable response to various therapeutic agents. Psyllium has been proven to be effective in adults; however, there is no study in children. The objective of this study is to evaluate the efficacy of psyllium husk as compared to placebo in pediatric IBS patients.

Methods: In this double-blind randomized controlled trial, 43 children were assigned to psyllium arm (Group A) and 38 into placebo arm (Group B). Severity is assessed at baseline and after 4 weeks of treatment using IBS severity scoring scale (IBS-SSS) and classified into mild, moderate, and severe categories. Categorical data was compared with chi-square test and paired categorical variable was compared with McNemer test.

Results: Mean ages (\pm SD; in years) of Groups A and B were 9.87 (2.7) and 9.82 (3.17), respectively, with median duration of illness of 12 months. At baseline, type, severity, and parameters (IBS-SSS) of IBS were equally distributed in 2 groups. There was a significant reduction in median interquartile range (IQR) of total IBS-SSS in psyllium versus placebo [75 (42.5–140) vs 225 (185–270); $P < 0.001$] at 4 weeks. Similarly 43.9% in Group A versus 9.7% in Group B attained remission [IBS-SSS < 75 ($P < 0.0001$)]. The mean difference in IBS-SSS between Group A and Group B was -122.85 with risk ratio of 0.64 (95% CI; 0.42–0.83; $P = 0.001$) and absolute risk reduction of 32% (NNT = 3).

Conclusions: Psyllium husk is effective for the therapy of pediatric IBS when compared with placebo in short term.

Key Words: IBS severity scoring scale, irritable bowel syndrome, placebo, psyllium husk, therapeutic trial

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Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder (FGD) common in adults, and is increasingly being recognized in children. It is a chronic relapsing bowel problem associated with abdominal pain, either with or without bloating, along with changes in the bowel habits. It has a significant negative impact on quality of life and social functioning in children (1,2).

IBS prevalence in children across the United States based on parental report ranges from 1.2% to 2.9% (3,4). Prevalence of

What Is Known

- Irritable bowel syndrome (IBS) is a well-recognized functional gastrointestinal disorder in children.
- Therapeutic properties and its mechanism of action of psyllium are known in adults.
- There is a paucity of therapeutic trials in pediatric IBS.

What Is New

- Psyllium husk is effective for therapy of pediatric IBS short duration when compared to placebo.

IBS among Indian school children was reported as 1.3% in a study conducted in New Delhi (5). A recent meta-analysis of 16 cross-sectional studies looking into the epidemiology of pediatric IBS from Asian countries showed a prevalence of 2.8%–25.7% with a pooled prevalence of 12% (6).

Therapy of IBS has been traditionally a multidisciplinary affair (7,8). The ACG 2021 guidelines have addressed multiple modalities for the therapy of IBS in adults including lifestyle modifications, diet therapy (eg, low fermentable oligosaccharides, disaccharides, monosaccharides and polyols diet), psychotherapy, and various medications including rifaximin, tricyclic antidepressants, 5 hydroxytryptophan 3 antagonists (Alosetron), and chloride channel activators (Lubiprostone) (9).

Psyllium is one of the agents approved for treating FGDs especially IBS and functional constipation (10). The efficacy of psyllium may be a result of its water-retaining capacity; the presence of arabinoxylan, which is a prebiotic or due to its immunomodulatory effects (11,12).

There is a paucity of therapeutic trials in children suffering from IBS. In this double-blinded randomized control trial (RCT), we explored the efficacy of psyllium husk on IBS in children.

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PATIENTS AND METHODS

Children in the age group of 4–18 years, attending out Pediatric Gut Clinic outpatient department with symptoms of IBS as per the ROME IV criteria were considered for this study (Appendix 1, Supplemental Digital Content, <http://links.lww.com/MPG/C944> (13)). The study subjects were subsequently classified into the following 3 subtypes of IBS: C-IBS (constipation-predominant IBS): >25% stools are lumpy and hard and <25% of loose (mushy) or watery stools; D-IBS (diarrhea-predominant IBS): >25% stools are loose (mushy) or watery and <25% of stools are hard or lumpy; M-IBS: mixed variety: >25% stools are loose (mushy) or watery and >25% of stools are hard or lumpy (14). Exclusion criteria included: children who were on medications to manage their gastrointestinal (GI) symptoms (such as laxatives, antidiarrheal medications, antibiotics, or probiotics), patients having red flags (blood in stools, nocturnal diarrhea, failure to thrive, perianal fissures or fistula, or prior GI surgeries), and patients with other co-morbidities including cardiac, renal, hepatic, endocrine, or neuro-muscular diseases.

No medications other than the study drug/placebo were allowed during the study. Written informed consent from the parents and assent from the children were obtained before enrollment. The study was approved by the clinical trials registry-India (CTRI/2019/10/021706) and was conducted at the Department of Pediatric Gastroenterology and Hepatology at Post Graduate Institute of Medical Education and Research, Chandigarh, India from June 2016 to December 2017 (18 months).

Study Design

The study was a double-blind placebo RCT (superiority trial).

Drug Administration and Randomization

Of 90 eligible patients, 9 refused to participate and the remaining 81 patients were randomized into 2 groups in a double-blinded manner, using a variable size block randomization technique (accessed on June 20, 2016 with seed number 17095 at randomisation.org). Patients were randomized into 2 groups: Group A, those who would receive psyllium husk and Group B (placebo arm) who would receive an inert sugar, maltodextrin. Both *psyllium* and *maltodextrin* were administered in powder form and subjects were asked to ingest it after mixing with plain water, twice a day. Both powders were administered in the form of radio-opaque sachets, with each sachet containing 3 g of either of the material, to ensure double blinding. A trained pharmacist dispensed the sachets, as per an electronically generated randomization. Patients between 6 and 12 years of age were given 6 g per day and those in the 13–18 year age group were given 12 g per day in two daily divided doses.

Follow-Up

Compliance to the drug therapy was checked periodically by either direct interviewing at follow-up or through telephone. The patients were followed up for therapeutic response at the end of 4 weeks. Patients who defaulted on their dispensed medications or those requiring antibiotic therapy during the study period were excluded from follow-up.

Symptom Analysis

After enrolling, the parents and/or the children were provided with the Bristol stool chart (Appendix 2, Supplemental Digital Content, <http://links.lww.com/MPG/C944>) to evaluate the consistency of the stools and classify into various subtypes of IBS as per the aforementioned criteria. Bristols type 1 and 2 indicate

constipation, with 3 and 4 being normal, and 5–7 indicate diarrhea. The baseline severity was calculated as per the IBS-severity scoring scale (IBS-SSS) at enrolment (15). To the best of our knowledge, this is the first time IBS-SSS is being used in children. It is not validated for subjects less than 18 years of age but is well studied and has been used in many adult interventional trials. We decided to use IBS-SSS score due to the lack of an alternative score for children. Patients were classified as having mild (75–174), moderate (175–299), or severe (300–500) IBS as per IBS-SSS. The symptom response of either the drug arm (Group A) or the placebo arm (Group B) was assessed using the IBS-SSS after 4 weeks of the trial (Appendix 3, Supplemental Digital Content, <http://links.lww.com/MPG/C944>) (15). Direct questioning of children aged more than or equal to 10 years was done and for children below 10 years age, the responses to the questionnaire was elicited from the parents.

Outcome Parameters

The primary outcome parameter was to analyze the fraction of patients in either of the trial arm, who had achieved complete remission defined as IBS-SSS < 75, after 4 weeks of therapeutic trial.

Statistical Analysis

Sample size calculation was done by 1:1 allocation of study subjects into the treatment arm and control arm, with an alpha error of 5%, beta error of 20%, and power of 80%, taking effect size of 60% and standard deviation of primary outcome variable of 1; a sample of 45 in each group was considered appropriate. For comparison of continuous variables with normal distribution, independent sample Student *t* test was used. Noncontinuous variables were compared using Mann Whitney *U* test. Categorical data was compared using chi-square test. Comparison of paired categorical variables was done using McNemer test. Analysis of drug efficacy was done as per intention-to-treat. IBM SPSS version 21 (Chicago, IL) was used for data analysis. *P* value < 0.05 was considered as statistically significant.

RESULTS

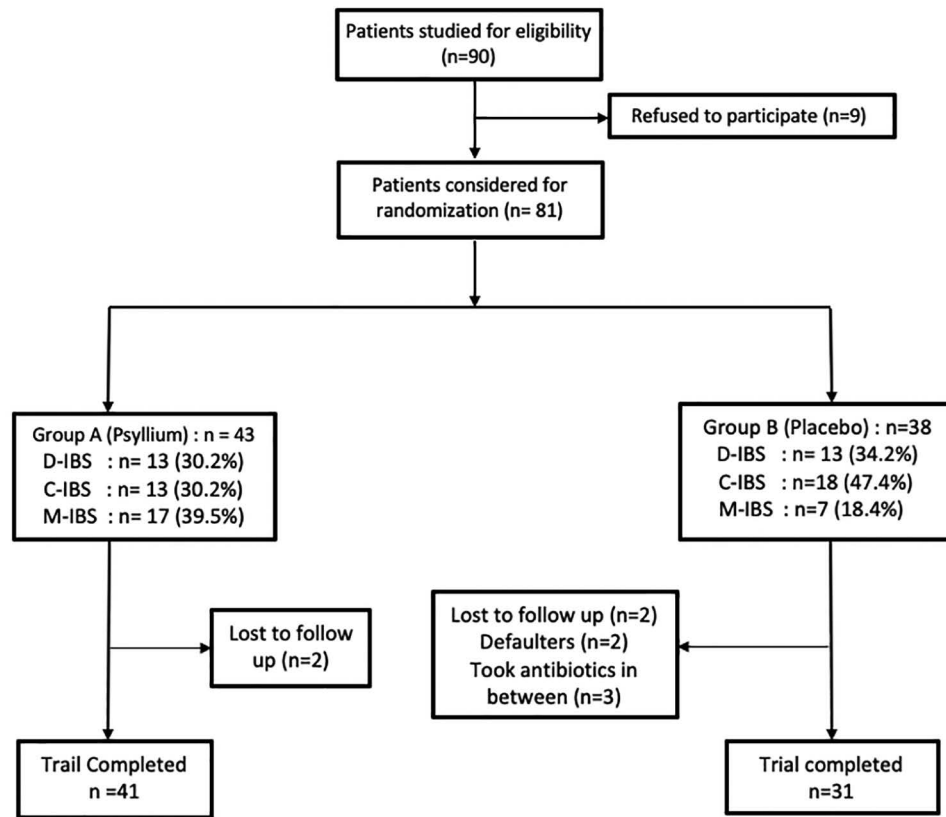
Demography and Baseline Characteristics of IBS (Fig. 1)

Ninety children were eligible for enrollment of which 9 did not give consent to participate. Eighty-one patients post-randomization were distributed into 2 groups: 43 in Group A (Psyllium) and 38 patients in Group B (Placebo). Overall 42 (52%; 42/81) patients had both [12 (15%; 12/81)] or one of their parents [30 (37%; 30/81)] affected with IBS. Forty-one patients in Group A and 31 patients in Group B completed the study (Fig. 1). The baseline characteristics of patients are shown in Table 1.

Of the total spectrum of IBS, 26 (32.1%) were D-IBS, 31 (38.27%) were C-IBS, and 24 (29.63%) were of M-IBS and they were evenly distributed among Psyllium and Placebo groups (*P* = 0.096). There was no significant difference at enrolment across the various parameters constituting the IBS-SSS between Groups A and B (Table 1). Based on the severity, 9 (11.11%) were mild, 44 (54.32%) were moderate, and 28 (34.56%) were in severe IBS category.

Treatment Response Assessment

Forty-one patients from the psyllium limb and 31 patients from the placebo limb completed the trial and were available for outcome assessment. The reasons for attrition are depicted in Figure 1. There was a significant decrease in scoring of each parameter in Group A as compared to Group B (Table 2). There was a



Abbreviations : C-IBS : Constipation pre dominant irritable bowel syndrome, D-IBS : Diarrhea predominant irritable bowel syndrome, M-IBS : Mixed type irritable bowel syndrome

FIGURE 1. Flow of patients in the study.

statistically significant reduction in median (IQR) of total IBS-SSS in Psyllium versus the Placebo [75 (42.5–140) vs 225 (185–270); $P < 0.001$] when assessed at 4 weeks (Fig. 2). After 4 weeks of therapy, 43.9% in Group A versus 9.7% in Group B attained remission defined as IBS-SSS < 75 [$P < 0.0001$]. Similarly 36.6%, 9.8%, and 9.8% were in mild, moderate, and severe categories in Group A whereas 19.4%, 51.6%, and 9.7% in Group B, respectively [$P < 0.0001$] (Table 2, Fig. 3).

Drug Efficacy

In the psyllium limb, the mean IBS-SSS pretreatment was 265.976 ± 84.60 and post therapy, the score decreased to 102.31 ± 94.77 ($P = 0.048$). In the placebo limb, the mean IBS-SSS pretreatment was 289.35 ± 68.41 and post therapy, the score was 225.161 ± 106.54 ($P = 0.00$). From the above data, risk-based estimates and 95% confidence intervals were calculated (Table 1a, Supplemental Digital Content, <http://links.lww.com/MPG/C944>). The relative risk (RR) was 0.64 (95% CI; 0.47, 0.84; $P = 0.0017$). With this the relative risk reduction ($1 - RR$) was 0.36 (36%) and the absolute risk reduction was 0.32 (32%) with number needed to treat (NTT) of 3 (Table 1b, Supplemental Digital Content, <http://links.lww.com/MPG/C944>). The mean difference in IBS-SSS in Group A and Group B was $102.3 - 225.6 = -122.85$. There were no drug-related adverse effects reported in either of the study groups.

DISCUSSION

This RCT was performed to study the efficacy of psyllium in pediatric IBS patients when compared with placebo (maltodextrin). It was noted that patients treated with psyllium had a significant reduction of IBS-SSS after 4 weeks of therapy and 43.9% entered remission when compared to 9.7% in the placebo group. We used a standardized scale, that is, the IBS-SSS for grading the severity of symptoms at the time of enrolment and at the end of the study (after 4 weeks). It was also seen that psyllium was equally effective for improving symptoms in patients with different subtypes of IBS.

Psyllium is a gel forming soluble fiber with high water-holding capacity, which makes the stools bulky and soft (16). It also has an additional prebiotic and immunomodulatory effects. In adults psyllium has also been noted to have a cholesterol lowering effect by absorbing and expelling in stools (16). However there is no study on negative effects on nutrient absorption in children.

The etiology of IBS is multifactorial and jury is still out on the exact trigger initiating this chronic painful condition. This is highlighted by the fact that various modalities including lifestyle changes, yoga, gut sterilizers and agents altering gut secretion or motility, being practiced for controlling symptoms in these patients (17,18).

Dietary fibers have been used for the treatment of IBS and studies in adult population have shown its effectiveness irrespective

TABLE 1. Patient demography, distribution of subtypes of IBS, and severity of IBS

	Psyllium (Group A) n= 43	Placebo (Group B) n= 38	P value
Demographic parameters			
Age, y (mean/ SD)	9.87±2.7	9.82 ± 3.17	0.66
Gender (M:F)	26: 17	22: 16	0.81
Duration of illness, months	11 (6–24)	12 (3–190)	0.26
Family history of IBS total, N (%)	27 (62.7%)	27 (71.0%)	0.59
One parent affected, %	22 (51.2 %)	20 (52.6%)	
Two parents affected, %	5 (11.6%)	7 (18.4%)	
Type of IBS			
D-IBS	13 (30.2%)	13 (34.2%)	0.096
C-IBS	13 (30.2%)	18 (47.4%)	
M-IBS	17 (39.5%)	7 (18.4%)	
Severity of IBS			
Mild	7 (16.3%)	2 (5.3%)	0.25
Moderate	21 (48.8%)	23 (60.5%)	0.25
Severe	15 (34.9%)	13 (34.2%)	0.25
Parameter of IBS-SSS: median interquartile range (IQR)			
Pain score	50 (50–50)	50 (50–75)	0.59
Days score	50 (40–80)	60 (50–72)	0.28
Distension score	50 (25–75)	50 (25–75)	0.86
Satisfaction score	50 (25–75)	50 (25–56)	0.58
Life interference score	50 (25–75)	50 (50–75)	0.91
Total IBS-SSS	275 (200–320)	225–323	0.684

IBS = irritable bowel syndrome; C-IBS = constipation predominant IBS; D-IBS = diarrhea-predominant IBS; IBS-SSS = irritable bowel syndrome severity scoring scale; M-IBS = mixed variety.

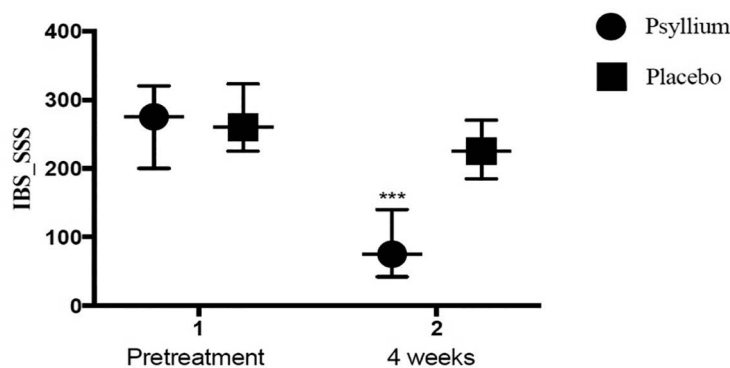
TABLE 2: Median IQR values of individual parameters and severity proportion in Groups A and B, post 4 weeks of therapy based on IBS-SSS

	Psyllium, n = 41 (Group A)	Placebo, n = 31 (Group B)	P value
IBS-SSS			
Pain	Median (IQR) 25 (0–25)	Median (IQR) 50 (25–50)	<0.001
Day score	10 (0–27.5)	50 (30–50)	<0.001
Distension score	25 (0–25)	50 (25–75)	0.002
Satisfaction score	25 (0–25)	50 (25–50)	0.000
Lifestyle score	25 (0–25)	50 (25–50)	<0.001
Total	75 (42.5–140)	225 (185–270)	<0.001
Grades of severity (IBS-SSS)			
Remission (<75)	N (%) 18 (43.9%)	N (%) 3 (9.7%)	
Mild (75–174)	15 (36.6%)	6 (19.4 %)	
Moderate (175–299)	4 (9.8%)	16 (51.6%)	
Severe (300–500)	4 (9.8%)	6 (9.7%)	

IBS-SSS = irritable bowel syndrome severity scoring scale.

of the subtypes (19). An observation similar to ours was noted in a large clinical trial in adults comprising of 275 IBS patients, who reported an improvement in the global satisfaction of bowel habits in 57% patients treated with psyllium versus 35% in the placebo group (20). However, the only difference as compared to ours was the follow up duration, where they have continued trial medications

for 3 months and the symptoms were assessed at the end of each month. Interestingly, only during the first 2 months the pain relief between psyllium and placebo was significantly different and this disappeared during the final month. Similar to our cohort, there was an overall reduction in the severity of the symptoms during all 3 months.



Median (IQR) of IBS severity scoring scale in Psyllium and Placebo

FIGURE 2. Comparison of median interquartile range (IQR) of IBS-SSS in psyllium and placebo limb. IBS-SSS = irritable bowel syndrome severity scoring scale.

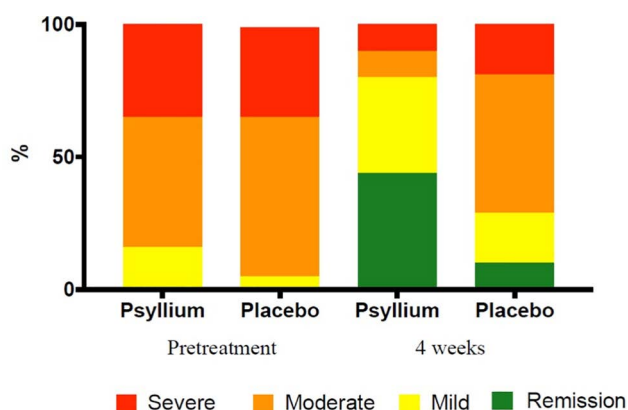


FIGURE 3. Comparison of therapeutic response in psyllium and placebo limb as per the grading of severity in accordance with IBS-SSS. IBS-SSS = irritable bowel syndrome severity scoring scale.

Jalihal et al from India documented improvement in the bowel satisfaction score in the psyllium arm (38% vs 20%) as compared to placebo arm among adults IBS patients. However, as against our observation, there was no relief in abdominal pain or distension (21). Similarly, Prior and Whorwell (22) also showed an improvement in the bowel satisfaction score in psyllium group (82% vs the placebo limb 53%) but without effect on pain or distension. Since psyllium is a bulk-forming laxative, the bowel satisfaction is very well targeted, but the pain relief is very modest. However, we observed an equally efficacious pain relief. Conversely, in our cohort, the psyllium limb had a significant reduction in mean IBS-SSS when compared with the placebo, and the effect of psyllium was maintained across individual constituents of the IBS-SSS, that is, pain, days with symptoms, distension, bowel satisfaction, and life interference. Such differential response in our cohort as compared to adult studies needs to be explored further. The remission rate was also comparable in all IBS subtypes, though it was not the primary objective of the study. Similar observations were also documented in a meta-analysis studying the effect of dietary fiber such as psyllium when compared to placebo or insoluble fiber like bran in adult IBS patients (23).

The most common subtype of IBS found in our cohort was C-IBS followed by D-IBS, as previously reported in Italian children, but a few studies also describe an even distribution of subtypes across the study cohorts (5,24). We also observed that roughly half of the parents were affected with IBS which could be attributed to genetic or shared environmental factors (13,23).

The remission rate in each subgroup was also comparable, that is, D-IBS 41.7%, C-IBS 50.0%, and M-IBS 41.2%. The risk ratio analysis shows that children in psyllium limb has 62% more chance of remission from IBS when compared with the placebo group. The only other trial available in pediatric IBS had shown psyllium would improve abdominal pain in these patients (25). Ours is the first study in pediatric age group looking into the effect of psyllium on various subtypes of IBS in which we found that it was equally effective in alleviating the symptoms irrespective of the subtypes. In our study we had meticulously assessed the symptoms so as not to label a C-IBS as functional constipation. A study conducted in Sri Lanka also emphasizes this fact of differentiating both of the FGIDs (26).

The strength of this study is the application of a proven objective assessment tool in adults—that is, IBS-SSS questionnaire—which was used for the first time in the pediatric age group. This is a score which covers all aspects of the IBS [physical (pain), psychological (satisfaction), and quality of life]. We found this score to be reliable, easy to administer, and parent friendly (especially for children less than 10 years of age). The score is highly reproducible and extremely sensitive to changes (13). Earlier to this, no pediatric trial has used a systematic score to analyze the symptom complex of IBS and classified it based on severity. In our cohort, majority were of moderate severity (54.32%) followed by severe (34.56%), and then mild (11.11%). There was no drug-related adverse effects in either of the trial limbs.

There are a few limitations of present study. First, it is single center study; attrition of subjects was more in placebo limb, probably due to lack of effect of placebo. Second, the outcome was assessed in a shorter duration and there is no data on maintenance of remission after stopping the psyllium. Finally, we did not include the nutritional profile as the outcome variable and therefore not able to comment on the changes in the micronutrients profile due to adsorbing properties of the psyllium.

As per the units policy, patients were followed-up after completion of the study (4 weeks), but the variables such as IBS-SSS are not documented as this was not part of the study (as planned earlier) and therefore not reported here. Psyllium was started in all subjects who were in placebo arm and it was continued in children who responded in psyllium arm. Totally continued for 3–6 months and tapered and stopped over next 1 month. In those who did not respond, psyllium is stopped and assessed for other options (analgesics, antispasmodics, nonpharmacological options such as behavioral therapy and yoga).

These limitations warrant a larger RCT with longer duration of follow-up to determine the efficacy of psyllium, duration of the therapy, and relapse rate in long-term.

CONCLUSIONS

Psyllium husk is effective for the therapy of IBS in children when compared with placebo in short term.

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