



Clinical Research

Clinical evaluation of *Bilvadileha* in the management of irritable bowel syndrome

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Abstract

Irritable bowel syndrome (IBS) is one of the most common conditions encountered in clinical practice but one of the least well understood. Symptoms of this disorder are chronic, sometimes severe and often respond poorly to treatment, resulting in reduced quality of life. There is no specific test for IBS, although diagnostic tests may be performed to rule out other problems. In present clinical trial 51 patients of IBS were registered out of which 46 patients completed the treatment. *Bilvadileha* was administered for the duration of 12 weeks. The therapy showed statistically significant improvement in all the clinical features of IBS as well as in the IBS severity score.

Key words: Ayurvedic management, *Bilvadileha*, irritable bowel syndrome

Introduction

Irritable bowel syndrome (IBS) is a vague term for a variety of diseases causing discomfort in the gastro-intestinal tract which causes great morbidity in the population. IBS is also called by many names, among them colitis, mucous colitis, spastic colon, or spastic bowel are few. It is a functional bowel disorder characterized by chronic abdominal pain, discomfort, bloating and alteration of bowel habits in the absence of any organic cause.^[1] Certain psychological conditions are also more common in those with IBS. Diarrhea or constipation may predominate, or they may alternate (classified as IBS-D, IBS-C or IBS-A, respectively). IBS may begin after an infection (post-infectious, IBS-PI), a stressful life event, or onset of maturity without any other medical indicators.^[2] IBS affects 15-20% of Indian population.^[3] It occurs more often in women than in men and it begins before the age of 35 in about 50% of people.^[4] Psychological factors like stress, anxiety etc., plays an important role in the manifestation of IBS.^[5]

IBS is relatively a recent concept and as such is a new entry into the realm of clinical medicine itself. As there is no single disorder in Ayurveda which can be exactly co-relate with IBS because Ayurveda is based entirely on different basic principles. Some conditions in particular, quite practically similar with IBS in their clinical picture. These are *Atisara*,^[6]

Pravahika, *Grahani*^[7] and *Pakvashayagata Vat*.^[8] In Ayurvedic system of medicine, the concept of psychosomatic disorders has been widely discussed.^[9] According to *Charaka*, *Sharira* and *Manasika Doshas* are interdependent on each other.^[10] One follows other, so the diseases, which are derived from them, also cannot exist without one another. Hence while understanding the “*Samprapti*” (pathogenesis) of IBS, one has to give importance to *Annavaha*, *Purishava*, *Rasavaha* and *Manovaha Srotodushti*.

In the management of IBS many formulations have been mentioned in modern medicine. Modern therapeutic molecules may provide instant relief in these cases, but are tend to develop a number of adverse drug reactions and no permanent cure is visible. Knowing this, the current suffering population is looking toward new remedies from other systems of medicines, which can provide relief without manifesting any inconvenience. *Bilvadileha*,^[11] a promising herbal drug compound that is being successfully prescribed by Ayurvedic physicians without any side effect since centuries is evaluated for its clinical efficacy in the condition of IBS in the present study.

Aims and objective

The objective is to evaluate the efficacy of *Bilvadileha* in IBS.

Materials and Methods

Patients attending OPD of Department of *Kayachikitsa* and *Rog Nidana* and *Vikruti Vijnana*, fulfilling the criteria for inclusion were selected irrespective of sex, race, caste and religion, between the age group of 18-65 years.

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Bilvadileha

Bilvadileha was prepared by Arya Vaidya Sala, Kottakkal - 676 503, Kerala, India. The ingredients and the parts used are given in Table 1.

Pattern of study

The study was an open label, single group and non-controlled clinical trial.

Timelines

1. Washout/preparatory period (if required): 4 weeks
2. Treatment period: 12 weeks

CTRI registration

This clinical trial has been registered under CTRI (Ref-CTRI/2012/01/002348).

Ethical clearance

The study was approved by Institutional Ethics Committee (Ref PGT/7-A/Ethics/210-11/1858).

Eligibility criteria

1. Patients of either sex with age between 18 and 65 years
2. Known case of IBS as per Rome III criteria:^[12]
(Symptoms of recurrent abdominal pain or discomfort and a marked change in bowel habit for at least 6 months, with symptoms experienced on at least 3 days/month in the last 3 months associated with two or more of the following:
 - Pain is relieved by defecation
 - Onset associated with change of frequency of stools
 - Onset associated with a change in form (appearance) of stools.
3. Willing and able to participate in the study.

Exclusion criteria

1. Patients with bleeding per rectum.
2. Mixed infection with parasites such as round worms, hook worms etc.
3. Patients with evidence of malignancy.
4. Patients with diabetes mellitus (B.S. [F] >126 mg% and/or B.S. [2 h. PP] >200 mg% or hemoglobin A1c (HbA1c > 6.5%).
5. Patient with poorly controlled hypertension (>160/100 mm Hg).

Table 1: Each 10 g of *Bilvadileha* contains

Drug	Botanical name	Part used	Quantity (g)
<i>Bilva moola</i>	<i>Aegle marmelos</i>	Root	16
<i>Jeerna guda</i>	Old Jaggery	-	8
<i>Ghana</i>	<i>Cyperus rotundus</i>	Rhizome	0.125
<i>Dhanyaka</i>	<i>Coriander sativum</i>	Fruit	0.125
<i>Jeeraka</i>	<i>Cuminum cyminum</i>	Fruit	0.125
<i>Truti</i>	<i>Elettaria cardamomum</i>	Seed	0.125
<i>Twak</i>	<i>Cinnamomum zeylanicum</i>	Stem bark	0.125
<i>Naga Kesara</i>	<i>Mesua ferrea</i>	Stamen	0.125
<i>Shunthi</i>	<i>Zingiber officinale</i>	Rhizome	0.125
<i>Maricha</i>	<i>Piper nigrum</i>	Fruit	0.125
<i>Pippali</i>	<i>Piper longum</i>	Fruit	0.125

6. Patients on prolonged (>6 weeks) medication with corticosteroids, anti-depressants, anti-cholinergics, etc., or any other drugs that may have an influence on the outcome of the study.
7. Patients suffering from major systemic illness necessitating long term drug treatment Rheumatoid arthritis, tuberculosis, psycho-neuro-endocrinal disorders, etc.
8. Patients who have a past history of atrial fibrillation, acute coronary syndrome, myocardial infarction, stroke or severe arrhythmia in the last 6 months.
9. Symptomatic patient with clinical evidence of heart failure.
10. Patients with concurrent serious hepatic disorder (defined as aspartate amino transferase (AST) and/or alanine amino transferase (ALT), total bilirubin, alkaline phosphatase (ALP) >2 times upper normal limit) or renal disorders (defined as serum creatinine >1.2 mg/dL), severe pulmonary dysfunction (uncontrolled bronchial asthma and/or chronic obstructive pulmonary disease), or any other condition that may jeopardize the study.
11. Alcoholics and/or drug abusers.
12. History of hypersensitivity to the trial drug or any of its ingredients.
13. Pregnant/lactating woman.
14. Patients who have completed participation in any other clinical trial during the past 6 months.
15. Any other condition which the principal investigator thinks may jeopardize the study.

Investigation

Routine investigations were done, before (to rule out any other pathology) and after treatment (to assess any untoward effect of trial drug during the regimen).

Hematology

Hemoglobin, total leucocyte count, differential leucocyte count (neutrophil, eosinophil, basophil, lymphocytes, monocytes), erythrocyte sedimentation rate.

Bio-chemistry

Blood sugar (fasting, PP), HbA1c, blood urea, serum uric acid, mg/dl, serum creatinine, serum glutamic oxaloacetic transaminase (AST), serum glutamic-pyruvic transaminase. (ALT), total protein, serum albumin, serum globulin, A/G ratio, serum bilirubin, conjugated bilirubin, unconjugated bilirubin, serum ALP.

Stool examination (Microscopic)

Parasites (ova/cyst), mucous, vegetative cells, occult blood.

This disease being a functional disorder, rest of the biochemical and stool examination were conducted to rule out the exclusion criteria and after treatment the safety profile of the drug.

Interventions

Bilvadileha has been administered to the patients at the dose of 10 g twice a day orally after food with luke warm water for the duration of 12 weeks.

Methods of assessment

The assessment of IBS was done at the interval of 14 days on the basis of relief in chief complaints of IBS, disease specific Ayurvedic parameters and IBS severity score.^[13]

Response at 12 weeks

- Positive response to treatment-decrease in IBS severity score by >50%.
- Partial response to treatment-decrease in IBS severity score by 30-50%.
- No response to treatment-decrease in IBS severity score by <30%.

Observations and Results

A total of 51 patients were registered. Out of which 5 were drop out (Out of 5 patients drop out, 4 got transferred at another station. Cause of drop out for one patient was unknown and 46 completed the treatment [Table 2]. All the patients were complaining about chronic and recurrent abdominal pain (100%). Abdominal bloating was found in 96.08%; IBS-C in 1.96%; IBS-D in 98.04%; Passage of mucus in 94.12%; Urgency of bowel movements in 88.24% patients [Table 3].

In the present study, *Udara Shula* (Pain in abdomen), *Anaha* (Distention of the abdomen) and *Udara Atopa* (Tympanitis) was found in 100% patients whereas *Pravahana* (Tenesmus) in 96.08% patients, *Mala Tyaga Asantushti* (dissatisfaction after defecation) in 98.04% patients, *Mala Durgandha* (Foul odor of stool) in 74.51% patients, *Bhojanopranta Mala Tyaga* (Defecation after taking meals) in 80.39% patients and *Guda Shula* (Pain in the perianal region) was found in 41.18% patients [Table 4].

After completion of therapy, chronic and recurrent abdominal pain improved by 67.09%, Abdominal bloating by 100%; IBS-D by 86.96%, passage of mucus by 100%; Urgency of bowel movements by 97.50%; Feeling of incomplete evacuation by 89.13% [Table 5]. All these improvements were statistically highly significant ($P < 0.001$). *Bivadi leha* has shown 95.65% improvement in *Pravahana*. *Udara Shula* was improved by 67.39%; *Anaha* (Distention of the abdomen) by 93.48%; *Mala tyaga Santushti* (Satisfaction after defecation) by 89.13%; *Kapha Nihssarana* (Mucus in stool) by 100%; *Udara Atopa* by 97.83%; *Mala Durgandha* (Foul odour of stool) by 100%; *Bhojanopranta Mala Tyaga* by 100%; *Guda Shula* by 67.39% [Table 6]. All these improvements were also statistically highly significant ($P < 0.001$). Effect of therapy on IBS severity score showed a relief of 64.59% that was statistically highly significant ($P < 0.001$) [Table 7]. In stool, no any significant pathological changes were seen in before and after treatment stool examination.

Out of 46 patients, after the completion of treatment with *Bilvadileha*, positive response to treatment was found in 37 (80.43%) patients, 7 (15.21%) patients showed Partial response

Table 2: Total number of subjects registered for therapy

Status	No. of patients
Registered	51
Completed treatment	46
Drop out	5

Table 3: Chief complaint's wise distribution of 51 patients

Chief complaints	No. of patients	Percentage
Chronic or recurrent abdominal discomfort or pain	51	100
Abdominal bloating	49	96.08
Constipation (IBS-C)	1	1.96
Diarrhoea (IBS-D)	50	98.04
Urgency of bowel movements	45	88.24
Feeling of incomplete evacuation	51	100
Passage of mucus	48	94.12

IBS: Irritable bowel syndrome

Table 4: Disease specific symptoms wise distribution of 51 patients

Disease specific symptoms	No. of patients	Percentage
<i>Pravahana</i> (tenesmus)	49	96.08
<i>Udara Shula</i> (pain in abdomen)	51	100
<i>Anaha</i> (distention of abdomen)	51	100
<i>Mala Tyaga Asantushti</i> (dissatisfaction after defecation)	50	98.04
<i>Kapha Nihssarana</i> (mucus in stool)	48	94.12
<i>Mala Durgandha</i> (foul odour of stool)	38	74.51
<i>Udara Atopa</i> (tympanitis)	51	100
<i>Bhojanopranta Mala Tyaga</i> (defecation after taking meals)	41	80.39
<i>Gud Shula</i> (pain in perianal region)	21	41.18

Table 5: Effect of therapy on chief complaints

Chief complaints	Mean score	Percentage	SD	SE	t	P
Chronic or recurrent abdominal discomfort or pain	0.84	67.39	0.36	0.05	15.83	<0.001
Abdominal bloating	0.89	100	0.31	0.04	19.20	<0.001
Constipation (IBS-C)	0	-	-	-	-	-
Diarrhea (IBS-D)	0.87	86.96	0.34	0.05	17.32	<0.001
Urgency of bowel movements	0.84	97.50	0.36	0.05	15.83	<0.001
Feeling of incomplete evacuation	0.89	89.13	0.31	0.04	19.20	<0.001
Passage of mucus	0.95	100	0.20	0.03	31.46	<0.001

IBS: Irritable bowel syndrome, SD: Standard deviation, SE: Standard error

to treatment and 2 (4.34%) patients reported no response to the treatment [Table 8].

Discussion

All the cardinal symptoms and associated symptoms along with IBS severity score improved in a statistically highly significant manner ($P < 0.001$). *Bilva* roots are the main ingredient of the formulation *Bilvadileha*. The roots are sweet, astringent, bitter and febrifuge; useful in diarrhea, dysentery, dyspepsia, gastralgia, palpitation, seminal weakness, uropathy, vomiting, intermittent fever, swellings and gastric irritability in infants.^[14]

Table 6: Effect of therapy on disease specific symptoms

Disease specific symptoms	Mean score	Percentage	SD	SE	t	P
<i>Pravahana</i> (tenesmus)	0.95	95.65	0.20	0.03	31.46	<0.001
<i>Udara Shula</i> (pain in abdomen)	0.84	67.39	0.36	0.05	15.83	<0.001
<i>Anaha</i> (distention of abdomen)	0.93	93.48	0.25	0.03	25.39	<0.001
<i>Mala Tyaga Santushti</i> (satisfaction after defecation)	0.87	89.13	0.34	0.05	17.32	<0.001
<i>Kapha Nihsarana</i> (mucus in stool)	0.95	100	0.20	0.03	31.46	<0.001
<i>Mala Durgandha</i> (foul odor of stool)	0.73	100	0.44	0.06	11.29	<0.001
<i>Udara Atopa</i> (tympanitis)	0.97	97.83	0.14	0.02	45	<0.001
<i>Bhojanopranta Mala Tyaga</i> (defecation after taking meals)	0.82	100	0.38	0.05	14.62	<0.001
<i>Gud Shula</i> (pain in perianal region)	0.39	100	0.49	0.07	5.37	<0.001

SD: Standard deviation, SE: Standard error

Table 7: Effect of therapy on IBS severity score

IBS severity score	Mean score	Percentage	SD	SE	t	P
	198.04	64.59	52.20	7.69	25.73	<0.001

SD: Standard deviation, SE: Standard error, IBS: Irritable bowel syndrome

Table 8: Overall effect of therapy

Effect of therapy	No. of patients	Percentage
Positive response to treatment	37	80.43
Partial response to treatment	7	15.22
No response to treatment	2	4.34

Vitiation of *Agni* (*Mandagni*) is the main reason for IBS. This ultimately results in *Ama* formation and may lead to diarrhea or constipation. *Bilva*, due to its *Kashaya*, *Tikta Rasa*, *Katu Vipaka* and *Laghu Guna* acts as *Agni Deepana* and also *Amapachaka*. *Kashaya Rasa* and *Ushna Virya* help in reducing the colonic motility. *Sangrahi* property of *Bilva* is very useful to treat the increased frequency of defecation and the consistency of stool. In *Bilvadileha* in addition to *Bilva*, *Prakshepa Dravyas* like *Dhanyak*, *Jirak*, *Ela*, *Keshar*, *Twak*, *Trikatu*, *Musta*, have properties like: *Deepana*, *Pachak*, *Kaphahara*, *Vedanasthapak*, *Rasayana*.

Thus, due to different properties of its ingredients, *Bilvadileha* has properties like: *Tridosahara*, *Deepana*, *Pachana*, *Amanashaka*, *Grahi*, *Vibandhahara* and *Vatanulomana* which checks the *Samprapti* (pathogenesis) and pacify the symptoms of IBS. Pharmacological activities such as antidiarrheal,^[15] antidysentery, antibacterial, antiprotozoal, antispasmodic, antidepressant, antifungal, anti-giardiasis, anthelmintic, antispasmodic, anti-inflammatory,^[16] carminatives etc., check the IBS-PI. Having *Rasayana* effect, relieve the psychological factors such as anxiety fear etc., it may enhance the *Bala* of *Deha* and *Indriya*.

Conclusion

On the basis of this study, it can be concluded that the trial drug *Bilvadileha* is found to be effective in relieving symptoms of IBS. There was no adverse drug reaction seen during the period of trial. Further studies can be should be carried out with larger sample size in different places with a standard control drug in order to obtain more data the effect of this novel drug compound in management IBS.

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हिन्दी सारांश

इरिटेबल बावेल सिंड्रोम में बिल्वादि लेह का चिकित्सीय अध्ययन

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इरिटेबल बावेल सिंड्रोम (आई.बी.एस.) दैनिक चिकित्सीय व्यवहार में पायी जाने वाली सामान्य व्याधि है। इस व्याधि के लक्षण चिरकारी एवं कभी-कभी तीव्र होते हैं। जिसके कारण रूग्णों की जीवन गुणवत्ता कम हो जाती है। आई.बी.एस. की कोई विशेष निदानात्मक परीक्षा नहीं है। लेकिन सामान्य प्रयोगशालीय परीक्षण दूसरी व्याधि व्यच्छेदन के लिए किये जाते हैं। इस व्याधि की सम्प्राप्ति में मानसिक भावों का बहुत महत्वपूर्ण योगदान है। इस चिकित्सा अध्ययन में ४६ रूग्णों को बिल्वादि लेह १० ग्राम भोजनोत्तर उष्ण जल से दिन में २ बार १२ सप्ताह तक दिया गया। चिकित्सा कालावधि पूरी होने के बाद व्याधि के सभी लक्षणों यथा द्रवमल प्रवृत्ति, उदरशूल, आनाह, आटोप, सकफमल प्रवृत्ति आदि में तथा आई. बी. एस. सिविएरिटी स्कोर पर सांख्यिक दृष्टि से महत्वपूर्ण लाभ पाया गया।