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ROLE OF TRIPHALA CAPLETS IN PATIENTS SUFFERING FROM CHRONIC CONSTIPATION: A DOUBLE BLIND PLACEBO CONTROLLED STUDY

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ABSTRACT

Background: Many patients believe that regularity of bowel movements is an important factor for good health. Constipation leads to numerous physical and psychological impairments. Due to limitations of currently available treatment options there is a felt-need for a clinically effective and safe drug for treating constipation. **Aims:** The present study was aimed to evaluate the clinical efficacy and safety of Triphala in constipation. **Methods and Material:** Fifty subjects of either sex, aged more than eighteen years with constipation and associated symptoms and were willing to comply with the study procedures were included in the study. Subjects were randomized into two groups & received either Triphala or Placebo caplets. All the patients were evaluated at intervals of two weeks basis for a period of one month. Assessment was done on the basis of subjective and objective parameters. **Statistical analysis:** Unpaired t test, Fisher's exact test and repeated measures of ANOVA using Friedman test. **Results:** Subjects treated with Triphala showed significant improvement in relief of clinical symptoms. No significant difference was observed in the patients treated with Placebo. No adverse drug reactions were reported in both groups. **Conclusion:** It was observed that treatment with Triphala is safe and effective in patients with chronic constipation. The outcome of the study has a pronounced effect regarding to the direct cost of therapy as treatment with Triphala is economical.

INTRODUCTION

A satisfactory definition of constipation has remained a challenge. Most of the medical community defines constipation as “infrequent stools”; however, in contrast, patients consider constipation to be “passing of hard stools” or “straining to have a bowel movement”. Many patients believe that “regularity of bowel movements” is an important factor for good health and regularity may be defined as “a daily bowel movement or a bowel movement at the same times each day or both”.^[1] Constipation is defined as having a bowel movement fewer than three times per week. Constipation can be a result of a primary motor disorder or other systemic diseases, or an adverse effect of many drugs or chronic illness. The etiology of constipation is multifactorial and the important causes are immobility, inadequate fluid and dietary fiber intake, and drugs. The consumption of a fiber-depleted diet has been implicated in constipation and increased dietary-fiber intake has been shown to accelerate colonic transit and produce more frequent, bulky stools.^[2,3]

Constipation leads to numerous physical and psychological impairments. Constipation may be exacerbated by physical immobility as a bedridden patient is not able to respond to defecatory signals. Other factors such as underlying illness, medications and dietary inadequacies also contribute to constipation in a bedridden patient.^[4] The concurrently associated disorders may include hemorrhoids, anal fissures and endocrine dysfunction. In majority of patients with diabetes mellitus, constipation may be the most common gastrointestinal complaint.^[5] There is paucity of data to suggest that aging significantly affects colonic motor function.^[6] However, elderly women use laxatives more often^[7] and constipation is common in persons above 65 years of age.^[8] Constipation is common during pregnancy^[9] and some women report constipation just prior to menstruation.^[10]

The most commonly associated symptoms of constipation include flatulence, bloating, abdominal pain, feeling of incomplete evacuation, anorexia and feeling of nausea and vomiting. With constipation stools are usually hard, dry, small in size, and difficult to eliminate. Dehydration, changes in diet and activity, and certain drugs are frequently to blame to slow transit of stool. When stool moves slowly, too much water is absorbed from the stool, and it becomes hard and dry. Gradual enlargement of the rectum and poor coordination of the pelvic and anal muscles sometimes contribute to or cause constipation.^[11]

The management of constipation extends well beyond the use of laxatives. Symptomatic control, advice on diet, increase in fluid intake, improvement in mobility and toileting contributes to an effective outcome. The use of laxatives for treating constipation is deeply rooted in medical and social traditions, but the abuse of laxatives have been shown to be associated with various short- and long-term adverse effects.^[12,13] Patients with intractable constipation are likely to benefit from physiological studies. Identification of the underlying abnormality, such as pelvic floor dysfunction allows determination of patients who may benefit from surgical treatment or pelvic floor retraining.^[14]

Currently available treatment options for constipation are associated with various limitations either due to the latency period of action or due to adverse effects. Docusates have a latency of action of five to seven days. Osmotic laxatives have latency up to five days and may lead to bloating, colic and flatulence. Bulk forming agents are stool normalizers rather than true laxatives and saline laxatives can produce an undesirable strong purgative action, while lubricants cause irritation with long-term use.^[15] Due to limitations of currently available treatment options there is a “felt-need” for a clinically effective and safe drug for treating constipation. Triphala is a pure herb formulation which contains three herbs *terminalia chebula*, *terminalia bellerica*, *phyllanthus emblica*.^[16,17] Triphala is used to promote appetite, aid in digestion and treatment of constipation as well.^[18,19,20] Studies are necessary in Indian patients to study the efficacy and safety of Triphala in chronic constipation. Triphala caplets, a single formulation have undergone detailed Toxicological evaluation in experimental animals and phase -1 clinical evaluation in human subjects to establish its safety profile at R & D Center, The Himalaya Drug Company, Bangalore, India.^[21] This study was aimed to evaluate the clinical efficacy and safety of Triphala in chronic constipation.

MATERIALS AND METHODS

Randomized double blind placebo controlled study was carried out in fifty patients suffering from chronic constipation, attending the out patient department of Ayurvedic hospital, between June 2010 to November 2010 after obtaining approval from Institutional Ethical Committee and applicable local regulatory authority and in accordance Helsinki Declaration of 1975, as revised in 2008 (5).

Fifty subjects of either sex, aged more than eighteen years with constipation and associated symptoms like flatulence, belching, abdominal pain and also patients with normal hematological and biochemical parameters were included in the study provided they will be able to attend the clinic on all the assessment visits, willing to give the informed consent, and willing to comply with the study procedures. Individuals with intestinal complications like ulcerative colitis, severe systemic illness like gastro-intestinal, respiratory and cardiac problems were excluded from the study. Those who were not ready to provide informed consent or comply with the study procedures were excluded from the study.

The patients with complaints of constipation were explained the nature of the study and their written consent was obtained. The patients were clinically examined after a detailed history regarding their disease. A total of 50 patients suffering from chronic constipation were recruited and were randomized into two groups with twenty five patients in each group. All the patients were evaluated at initiation of study and at intervals of two weeks basis for a period of one month.

The efficacy was evaluated using various parameters such bowel movements, pain on defecation, hard stool, blood stained stools and bloating sensation. The parameters used to evaluate bowel movements were change in frequency, consistency and color of the feces. Pain at defecation

score was evaluated using four point scale where in 0 = No pain, 1= mild pain, 2 = moderate pain and 3 = severe pain. Hard stool, blood stained stools and bloating sensation parameters were evaluated by presence or absence of symptoms. Safety evaluation included hematology (Hb, WBC, ESR and Platelet counts), clinical chemistry (creatinine) and cardiovascular (pulse and BP) parameters. Adverse effects, as volunteered by the patients, were recorded in the case record forms. The predefined primary end points were clinical recovery from constipation and associated symptoms and predefined secondary end points were incidence of any adverse events and the overall compliance.

STATISTICAL ANALYSIS

Statistical analysis was performed using unpaired t test for increase in the frequency of stools between the group comparisons. Fisher's exact test was used for evaluating the presence or absence of symptom which included parameters like hard stool, bloating sensation and blood stained stools. Repeated measures of ANOVA using Friedman test for non parametric parameters or repeated measures of ANOVA for parametric parameters followed by Dunnett's multiple comparison test. The minimum level of significance was fixed at $p < 0.05$. Statistical analysis was performed using GraphPad prism software version 4.03.

RESULTS

Out of 106 patients screened, 50 new patients with constipation were recruited. Intention to treat analysis included 50 patients Group-A twenty four (17 males and 7 females) patients with a mean age of 48.1 ± 17.2 years received Triphala. Group B twenty six (12 males and 14 females) patients with a mean age of 42.4 ± 14.4 years received Placebo. The patients in both groups received the assigned treatment for a period of 4 weeks. Patients treated with Triphala showed significant improvement in relief of various clinical symptoms. No significant difference was observed in the patients treated with Placebo (Table 1).

Table 1 Symptomatic improvement with respect to increase in frequency of stools and pain on defecation

Sl No.	Signs and Symptoms	Week	Group A (Triphala)	Group B (Placebo)	Significance
1.	Increase in frequency of stools as compared to initial values.	2	2.00 ± 0.93	1.21 ± 0.94	p<0.008
		4	2.20 ± 0.95	1.23 ± 0.88	p<0.002
2.	Pain on defecation	Initial	1.96 ± 1.04	2.08 ± 0.70	a p<0.001
		2	0.58 ± 0.78 ^a	1.72 ± 0.61 ^b	b NS
		4	0.00 ± 0.00 ^a	1.68 ± 0.69 ^b	
a: Significance as compared to the initial values in drug A(Triphala); b: Significance as compared to the initial values in drug B(Placebo); NS: Not significant.					

Similarly effect of Triphala caplets on relief of clinical symptoms in patients was significant (Table 2).

Table 2: Effect of Triphala caplets on relief of clinical symptoms in patients

Sl No.	Signs and Symptoms	Week	No. of patients showing symptoms		Significance
			Group A (Triphala)	Group B (Placebo)	
1.	Hard stools	2	10	25	p<0.0001
		4	1	21	p<0.0001
2.	Bloating sensation	2	4	26	p<0.0001
		4	1	19	p<0.0001
3.	Blood stained stools	2	3	9	p<0.0001
		4	0	9	p<0.0001

In both the groups 3 patients in each did not complete the study. Hematological parameters assessed after 2 and 4 weeks did not show any variations and were within normal limits in both the groups. Comparison between the two groups did not show statistical significance (Table 3) as well there was no effect on co-morbid conditions.

Table 3: Effect of Triphala on hematology, clinical chemistry, pulse rate and blood pressure

SL. No.	Signs and Symptoms	Drug	Treatment			Significance
			Initial	Week 2	Week 4	
1.	Hemoglobin (gm/dl)	A	11.23 ± 1.17	11.14 ± 1.15	11.34 ± 1.07	NS
		B	10.99 ± 1.15	11.11 ± 0.79	11.20 ± 0.85	NS
2.	WBC count /cu.mm)	A	9055 ± 1936	9647 ± 1407	10470 ± 1202	NS
		B	8983 ± 2372	9703 ± 1611	10710 ± 1530	NS
3.	ESR (mm/h)	A	22.62 ± 12.71	21.95 ± 6.99	23.33 ± 6.11	NS
		B	24.04 ± 10.48	24.83 ± 7.30	25.58 ± 5.24	NS
4.	Platelets(lakhs/cu.mm)	A	2.32 ± 0.76	2.21 ± 0.54	2.21 ± 0.37	NS
		B	2.23 ± 0.51	2.22 ± 0.35	2.23 ± 0.33	NS
5.	Creatinine (mg/dl)	A	1.00 ± 0.50	0.94 ± 0.06	0.94 ± 0.07	NS
		B	0.91 ± 0.15	0.94 ± 0.07	0.93 ± 0.08	NS
6.	Pulse (/min)	A	76.18 ± 4.70	76.45 ± 4.78	76.09 ± 5.33	NS
		B	76.38 ± 4.84	75.81 ± 4.69	75.62 ± 4.50	NS
7.	Systolic BP (mm Hg)	A	123.4 ± 10.14	122.6 ± 8.61	121.8 ± 8.29	NS
		B	127.3 ± 10.82	126.7 ± 11.80	125.9 ± 9.68	NS
8.	Diastolic BP (mm Hg)	A	79.00 ± 6.26	78.18 ± 4.09	77.91 ± 5.11	NS
		B	81.50 ± 6.33	80.17 ± 4.21	79.25 ± 4.08	NS

Drug A: Triphala , Drug B:Placebo, NS: Not significant

DISCUSSION

The present study was designed to evaluate the efficacy and safety of Triphala in constipation over a period of four weeks. Patients treated with Triphala showed significant improvement in relief of various clinical symptoms. No significant difference was observed in the patients treated with Placebo. Similarly effect of Triphala caplets on relief of clinical symptoms in patients was significant. The overall impression by the patient in the Triphala treated group showed marked improvement in 1 patient and cure in 20 patients. The overall impression by the investigator in the Triphala treated group showed moderate improvement in 1 patient, marked improvement in 2 patients and cure in 18 patients. In Placebo treated group, majority of patients showed no change after treatment and in few cases the symptoms became worse. Based on the outcome it was observed that treatment with Triphala is safe and effective in patients with chronic constipation. This study needs to be validated with larger study involving greater number of subjects for longer duration and follow-ups. The outcome of the study has a pronounced effect regarding to the direct cost of therapy as treatment with Triphala is economical and can be considered an effective and safe option in the Indian population.

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