



Research Article

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AN OPEN-LABEL, PROSPECTIVE CLINICAL STUDY TO EVALUATE THE EFFICACY OF CONSTAC IN THE MANAGEMENT OF CHRONIC CONSTIPATION

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ABSTRACT

An open-label, prospective, interventional study was carried out to evaluate the efficacy and safety of CONSTAC for the management of chronic constipation (CC). Adult patients with CC (n=247) were enrolled to receive a CONSTAC for maximum 60 days. The symptoms of constipation were evaluated by Longo's ODS score system, changes in stool form was assessed by the "Bristol stool form scale" and patients' quality of life was assessed by the Patient Assessment of Constipation-Quality of Life Questionnaire (PAC-QOL) before and after 15, 30, 60 days. Administration of CONSTAC showed a significant (p<0.05) reduction in pain during defecation from 2.23 (1.04) to 0.14 (0.35) and straining intensity from 1.47 (0.65) to 0.20 (0.15). At the end of therapy, there was significant improvement observed in defecation frequency per week from 3.00 (1.00) to 7.05 (0.23), extension of time in defecation from 2.10 (0.60) to 0.40 (0.51) and sensation of incomplete of evacuation from 1.98 (1.07) to 0.10 (0.31). Mean stool form score was significantly improved from baseline 02.92 (0.49) to 04.56 (0.81) (P<0.05) on Day 60. Mean PAC-QOL score and each of the subscales (worries and concerns, physical discomfort, psychosocial discomfort, and satisfaction) score significantly improved from baseline to end of therapy. Mild diarrhea was noted in 14 (5.66%) patient, so administration of CONSTAC was stopped on the same day. Mild nausea was noted in 23 (9.31%) of patients. Overall, patients showed an excellent tolerability to the study drug. It is an effective and safe herbal laxative formulation for constipation.

Key words: Chronic constipation, defecation, diarrhea, quality of life.

INTRODUCTION

Constipation is a very common gastrointestinal motility disorder and it is often chronic. It compromises economic burden, quality of life, social functioning, and the ability to perform activities of daily living.^{1,2} Chronic constipation has a prevalence of 14% and characterized by unsatisfying defecation associated with infrequent stools and difficult stool pass.^{3,4} Most cases of chronic constipation are primary or idiopathic, but some cases may be secondary to a number of medications or diseases.⁵ Primary chronic constipation is multifactorial and includes diet, colonic motility and absorption, anorectal motor and sensory function, and behavioral and psychological factors.⁶ Rome III criteria is one of the most widely accepted for diagnosis of constipation.⁷ Treatment of constipation includes patient education, dietary fiber supplementation, adequate fluid intake, and regular physical activity.⁸ Some studies suggested that modification such as dietary and aerobic are recommended to relieve symptoms, but effect is not obvious.^{9,10,11} Depending on chronicity and severity of constipation various drugs such as bulk-forming agents, stimulants, stool softeners and osmotic agents are used, but they are known to cause abdominal cramping, hypokalemia, flatulence, abdominal distension, and

alteration in electrolyte transportation which limit the long-term use of these drugs.^{8,12,13} Hence, there is a need to explore the drugs from other systems of medicine such as ayurveda for potential solutions to the problem of constipation. Nowadays, there is an increasing interest in medicinal herbs as precursor for pharmacological actives.^{14,15} CONSTAC is an Ayurvedic proprietary polyherbal formulation in powder form. All the ingredients of the formulation have been used for thousands of years and individual therapeutic efficacy of these herbs as laxative has also been reported in an ancient ayurvedic literature.^{16,17,18} Hence, an open-label, prospective, clinical study was performed to evaluate the efficacy and safety of "CONSTAC" in patients with chronic constipation.

Aim and Objective: The primary objective of the study was to evaluate the efficacy of "CONSTAC" in patients with Chronic constipation by assessing symptoms of constipation by Longo's ODS score system and changes in stool form assessed using the "Bristol stool form scale." Secondary objectives were to evaluate the patients' quality of life using the Patient Assessment of Constipation-Quality of Life Questionnaire and evaluate the safety of the study drug by assessing adverse events.

MATERIAL AND METHOD

Study design: This study was a prospective, open-label, non-comparative, single-arm, single-center, interventional study conducted in Healing Hands Clinic, Pune, India.

Study Drug: "CONSTAC" is an Ayurvedic proprietary polyherbal formulation in powder form. Composition of *Terminalia chebula* (Hirada), *Terminalia belerica* (Balhirada), *Terminalia belerica*, *Emblica officinalis*, *Plantago ovata*, *Glycyrrhiza glabra*, *Ptychotis ajowan*, *Foeniculum vulgare*, *Elliteria cardamomum*, *Coscos nucifera*, Castor oil. CONSTAC is manufactured at Good Manufacturing Practices approved plant.

Ethics committee approval and regulatory compliance: This study was conducted in accordance with the Schedule Y of Drugs and Cosmetics act, India and ICMR ethical guidelines for biomedical research on human participants. Each patient, provided the written informed consent before initiation of any study procedures. The study protocol and a copy of the informed consent document were reviewed and approved by the ethics committee.

Participant: Patients meeting the Rome III diagnostic criteria¹⁹ for constipation were included. Patients with a stool form score ranging from 1 to 3 on the "Bristol Stool Form Scale" were included. Patients with known colorectal cancer, anal abscess, anal fissure, rectocele, inflammatory bowel disease, megacolon or mechanical bowel obstruction, unknown cause of gastrointestinal bleeding or acute infection, history of alcohol or drug abuser, women who are pregnant, received herb therapy within one month prior to enrollment were excluded from the study.

Study intervention: Adult patients with chronic constipation were enrolled. Following written informed consent, the patient was recruited in the study if he/she fulfilled all the eligibility criteria. The patient received CONSTAC powder 2 tablespoon at night with a glass of warm water for maximum 60 days. The patient was called for follow up on Day 15, 30 and 60 after the baseline visit.

Statistical analysis: Statistical analysis of the study data was performed with statistical software SPSS 20.0. Data describing quantitative measures were expressed as median or mean (SD). Comparison of variables representing categorical data was performed using "Chi-square test" or "Fisher's exact test." Group means of dependent sample were compared by means of ANOVA (repeated-measures design, generalized linear model

procedure) or Wilcoxon sign rank test. Corresponding contrasts were tested using t-test for dependent samples and nonparametric test like "Wilcoxon Sign Rank" Test. P values below 0.05 (p<0.05) were considered significant.

RESULT

Total 247 patients included in the study, 185 (75.0%) were men while 62 (25%) were women and the mean age was 39.77 (13.08) years. Study treatment did not cause any significant change in vital signs like pulse rate, body temperature, respiratory rate, and the blood pressure.

Administration of CONSTAC showed a significant (p<0.05) reduction in mean pain during defecation from 2.23 (1.04) to 0.14 (0.35) on Day 60. Mean extension of time in defecation score significantly improved from 2.10 (0.60) to 0.40 (0.51) on Day 60. Mean defecation frequency per week score significantly improved from 3.00 (1.00) to 6.30 (1.17), 7.02 (0.24) and 7.05 (0.23) on Day 15, Day 30 and Day 60 respectively. There was a reduction in straining intensity mean score from 1.47 (0.65) to 0.63 (0.49) on Day 15, 0.14 (0.24) on Day 30 and 0.20 (0.15) on Day 60. Sensation of incomplete of evacuation mean score improved from 1.98 (1.07) to 0.87 (0.73) on Day 15, 0.42 (0.50) on Day 30 and 0.10 (0.31) on the Day 60. Mean activity reduction per week score improved from 2.61 to 1.65 (1.54) on Day 15, 1.07 (1.13) on Day 30 and 0.37 (0.87) on Day 60. Mean digitation score reduced from 2.63 (1.84) to 1.57 (1.63) on Day 15, 0.52 (0.71) on Day 30 and 0.10 (0.37) on Day 60. (Table 1)

Mean stool form score assessed on a Bristol stool form scale was improved on all the three follow-up visits, as shown in (Table 2)

The quality of life assessed on Patient Assessment of Constipation-Quality of Life Questionnaire. Mean PAC-QOL total scores, as well as scores for each of the subscales (worries and concerns, physical discomfort, psychosocial discomfort, and satisfaction) significantly improved (p<0.005) from baseline to end of therapy, as shown in (Table 3).

During study mild AEs were observed; diarrhea (n= 14/ 5.67%), nausea (n = 23/ 9.31%), abdominal bloating (n=9/ 3.64 %), and abdominal cramps (n=12/4.86%). All were resolved by medical management. No major complications or SAEs were observed during the study.

Table 1: Changes in mean score of Chronic constipation symptoms on Longo's ODS score

Study Visits	Defecation Frequency per week mean(SD)	Straining Intensity mean(SD)	Extension of time in defecation mean(SD)	Sensation of incomplete of evacuation mean(SD)	Recto/ perineal pain/ discomfort mean(SD)	Activity reduction per week mean(SD)	Digitations mean(SD)
Day 1 (n=247)	3.00(1.00)	1.47(0.65)	2.10(0.60)	1.98(1.07)	2.23(1.04)	2.61(1.84)	2.63(2.97)
Day 15 (n=247)	6.30(1.17)	0.63(0.49)	1.12(0.32)	0.87(0.73)	0.97(0.82)	1.65(1.54)	1.57(1.63)
Day 30 (n=153)	7.02(0.24)	0.14(0.34)	0.63(0.45)	0.42(0.50)	0.44(0.58)	1.07(1.13)	0.52(0.71)
Day 60 (n=48)	7.05(0.23)	0.20(0.15)	0.40(0.51)	0.10(0.31)	0.14(0.35)	0.37(0.87)	0.10(0.37)

*p<0.05, significant by student 't' test as compared to baseline (Day1)

Table 2: Improvement in mean score of stool form on Bristol stool form scale

Study Visits	Mean (SD)
Day 1 (n=247)	2.92 (0.49)
Day 15 (n=247)	4.45 (0.87)
Day 30 (n=153)	4.33 (0.79)
Day 60 (n=48)	4.56 (0.81)
*p<0.05, significant by student 't' test as compared to baseline (Day1)	

Table 3: Changes in mean score of PAC-QOL subscale scores

Study Visits	PAC- QOL Mean (SD)	Worries and concern Mean (SD)	Physical discomfort Mean (SD)	Psychosocial discomfort Mean (SD)	Satisfaction Mean (SD)
Day 1 (n=247)	2.67 (0.78)	2.54 (0.96)	2.83 (1.19)	2.36 (1.18)	1.56 (0.78)
Day 15 (n=247)	1.48 (0.70)	1.34 (1.21)	1.15 (1.09)	1.89 (1.05)	0.67 (0.3)
Day 30 (n=153)	0.58 (0.55)	0.73 (0.91)	0.89 (0.98)	0.98 (0.87)	- 0.24 (0.83)
Day 60 (n=48)	0.47 (0.50)	0.59 (0.87)	0.93 (1.17)	0.69 (0.75)	- 0.76 (0.91)
*p<0.005, significant by student 't' test as compared to baseline (Day1)					

Table 4: Composition of "CONSTAC" powder

Name of ingredient	Quantity in gm
<i>Terminalia chebula</i>	10 gm
<i>Terminalia bellerica</i> (Hirada)	10 gm
<i>Terminalia bellerica</i> (Balhirada)	8 gm
<i>Emblica officinalis</i>	10 gm
<i>Plantago ovata</i>	10 gm
<i>Glycyrrhiza glabra</i>	8 gm
<i>Ptychotis ajowan</i>	8 gm
<i>Foeniculum vulgare</i>	6 gm
<i>Elliteria cardamomum</i>	8 gm
<i>Coscos nucifera</i>	10 gm
Castor oil	2 gm

DISCUSSION

There are many therapeutic approaches for the treatment of chronic constipation. These therapeutic approaches includes patient education, dietary fiber supplementation, adequate fluid intake, regular physical activity, osmotic and stimulant laxatives, and new pharmacological therapies that have different mechanisms of action and side effects. Plants produce a wide range of bioactive principles and comprise a rich source of medicines.²⁰ CONSTAC is a polyherbal formulation in the form of powder. Composition of CONSTAC is shown in (Table 4).

Triphala is made by combining *Terminalia chebula*, *Terminalia bellerica*, *Emblica officinalis*. It gently cleanses the colon and relieves symptoms like anorectal blockage, sensation of incomplete evacuation, flatulence, and bloating.^{21,22} In CONSTAC powder we have used *Triphala*. Seeds of *Terminalia chebula* are used in traditional medicine and used as homeostatic, laxative, antitussive, diuretic, and cardiotoxic remedy.²³ A study proved that aqueous extract of *Terminalia chebula* seed improves constipation and increases the gastrointestinal transit ratio, which supports its traditional use in constipation.²⁴ *Emblica officinalis* is used to treat diseases such as anemia, fever, chronic ulcers, constipation, jaundice and asthma.²⁵ Marlett et al stated that *Plantago ovata* for improvement in stool consistency and high degree of subjective relief in constipated population.²⁶ *Glycyrrhiza glabra* Linn is active as an anti-allergic, anti-inflammatory, spasmolytic, mild laxative, antistress,

antidepressive, antiulcer, liver protective, estrogenic, emmenagogue, and antidiabetic substance, and is widely used in the Indian system of medicine.²⁷ *Foeniculum vulgare* is used as a laxative in the treatment of mild digestive disorders due to its gastrointestinal effects, namely stimulation of motility and, at higher concentrations, antispasmodic action.²⁸ It is a natural triglyceride containing mainly ricinoleic acid, which has a long history as a remedy because of its various biological effects, including an increase in propulsive intestinal motility. Study results show that Castor oil may be used for controlling symptoms of constipation.²⁹ The individual therapeutic efficacy of these herbs as laxative has also been reported in an ancient Ayurvedic literature.^{30,31,32} Though the exact mechanism of action of the CONSTAC is not clearly understood, the synergistic effect of the different types of laxative ingredients has possibly made it a balanced formulation of effective management of chronic constipation.

CONCLUSION

An ayurvedic proprietary polyherbal laxative formulation CONSTAC is significantly effective and safe herbal formulation in chronic constipation.

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REFERENCES

- O'Keefe EA, Talley NJ, Zinsmeister AR, Jacobsen SJ. Bowel disorders impair functional status and quality of life in the elderly: a population-based study. *J Gerontol A Biol Sci Med Sci*. 1995;50(4):M184–M189. <http://dx.doi.org/10.1093/gerona/50A.4.M184>
- Chang L. Review article: epidemiology and quality of life in functional gastrointestinal disorders. *Aliment Pharmacol Ther*. 2004;20(suppl 7):31–39. <http://dx.doi.org/10.1111/j.1365-2036.2004.02183.x>
- Suares NC, Ford AC. Prevalence of, and risk factors for, chronic idiopathic constipation in the community: systematic review and meta-analysis. *American Journal of Gastroenterology*. 2011;106:1582–91. <http://dx.doi.org/10.1038/ajg.2011.164>
- American College of Gastroenterology Chronic Constipation Task Force. An evidence-based approach to the management of chronic constipation in North America. *American Journal of Gastroenterology*. 2005;100(Suppl.1):S1–4. http://dx.doi.org/10.1111/j.1572-0241.2005.50613_1.x
- Tack J, Muller-Lissner S, Stanghellini V, et al. Diagnosis and treatment of chronic constipation – a European perspective. *Neurogastroenterology and Motility* 2011;23:697–710. <http://dx.doi.org/10.1111/j.1365-2982.2011.01709.x>
- Basilisco G, Coletta M. Chronic constipation: a critical review. *Dig Liver Dis*. 2013 Nov;45(11):886–93. <http://dx.doi.org/10.1016/j.dld.2013.03.016>
- Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. *Gastroenterology* 2006;130(5):1480–91. <http://dx.doi.org/10.1053/j.gastro.2005.11.061>
- Marshall JB. Chronic constipation in adults: How far should evaluation and treatment go?. *J Postgrad Med*. 1990;88:49–51, 54, 57–59, 63.
- Meshkinpour H, Selod S, Movahedi H, Nami N, James N, Wilson A. Effects of regular exercise in management of chronic idiopathic constipation. *Dig Dis Sci*. 1998;43:2379–2383. <http://dx.doi.org/10.1023/A:1026609610466>
- Young RJ, Beerman LE, Vanderhoof JA. Increasing oral fluids in chronic constipation in children. *Gastroenterol Nurs*. 1998;21:156–161. <http://dx.doi.org/10.1097/00001610-199807000-00002>
- Lingu I, Kulkarni PV, Tanna I, Chandola HM. Evaluation of diet, life style and stress in the etiopathogenesis of constipation in geriatric people. *Int.J. Res. Ayurveda Pharm*. 2012;3(6):879–883. <http://dx.doi.org/10.7897/2277-4343.03643>
- Rao SS. Constipation: Evaluation and treatment. *Gastroenterol Clin North Am* 2003;32:659–83. [http://dx.doi.org/10.1016/S0889-8553\(03\)00026-8](http://dx.doi.org/10.1016/S0889-8553(03)00026-8)
- Johnson DA. Treating chronic constipation: How should we interpret the recommendations. *Clin Drug Investig* 2006;26:547–57. <http://dx.doi.org/10.2165/00044011-200626100-00001>
- Munshi R, Bhalerao S, Rathi P, Kuber VV, Nipanikar SU, Kadbhane KP. An open-label, prospective clinical study to evaluate the efficacy and safety of TLPL/AY/01/2008 in the management of functional constipation. *J Ayurveda Integr Med* 2011;2:144–52. <http://dx.doi.org/10.4103/0975-9476.85554>
- Fasinu PS, Bouic PJ, Rosenkranz B. An Overview of the Evidence and Mechanisms of Herb–Drug Interactions. *Frontiers in Pharmacology*. 2012;3:69. <http://dx.doi.org/10.3389/fphar.2012.00069>
- Nadkarni KM. *Indian Materia Medica*. Vol 1. Mumbai: Bombay Popular Prakashan; 2007. p. 982–985.
- Srikantha Murty KR, editor. Bhavprakash of Bhavmishra. Vol. 1. Varanasi: Chaukhamba Shrikrishna Das Academy; 2008. p. 275.
- Anonymous. The Ayurvedic Formulary of India, Part 1, 2nd ed. New Delhi: Govt of India, Ministry of Health and Family Welfare, Dept of Indian Systems of Medicine; 2003. p. 110.
- Wong RK, Palsos OS, Turner MJ, et al. Inability of the Rome III criteria to distinguish functional constipation from constipation-subtype irritable bowel syndrome. *Am J Gastroenterol* 2010;105(10):2228–2234. <http://dx.doi.org/10.1038/ajg.2010.200>
- Badrul Alam. Antioxidant, Antimicrobial and Toxicity studies of the Different Fractions of Fruits of Terminalia bellerica Roxb. *Global Journal of Pharmacology*. 2011; 5(1):07–17.
- Pulok K. Mukherjee, Sujay Rai, Sauvik Bhattacharyya, Pratip Kumar Debnath, Tuhin Kanti Biswas, Utpalendu Jana, Srikanta Pandit, Bishnu Pada Saha, Pradip K. 2006. PAUL Clinical Study of 'Triphala'—A Well Known Phytomedicine from India. *IJPT* 5:51–54.
- Anonymous. The Ayurvedic Formulary of India, Part 1, 2nd ed. New Delhi: Govt of India, Ministry of Health and Family Welfare, Dept of Indian Systems of Medicine; 2003. p. 110.
- Lee HS, Won NH, Kim KH, Lee H, Jun W, Lee KW. Antioxidant effects of aqueous extract of Terminalia chebula in vivo and in vitro. *Biol Pharm Bull*. 2005;28(9):1639–1644. <http://dx.doi.org/10.1248/bpb.28.1639>
- Seyyed AMD, Ali Veisi, Mohammad Kazem Gharib Naseri, Peyman Mikaili Malays *J Med Sci*. 2011 Jul-Sep;18(3):18–26.
- Singh, D.P. R. Govindarajan and A.K. Rawat, 2008. High-performance liquid chromatography as a tool for the chemical standardisation of churna (Emblca officinalis Gaertn.): an ayurvedic Triphala—an Ayurvedic formulation. *Phytochem Anal.*, 19(2):164–168. <http://dx.doi.org/10.1002/pca.1032>
- Marlett JA, Li BU, Patrow CJ, Bass P. Comparative laxation of psyllium with and without senna in an ambulatory constipated population. *Am J Gastroenterol*. 1987 Apr;82(4):333–337.
- Gantait A, Pandit S, Nema NK, Mukherjee PK. Quantification of glycyrrhizin in Glycyrrhiza glabra extract by validated HPTLC densitometry. *J AOAC Int*. 2010 Mar-Apr;93(2):492–495.
- Klein S, Rister R, Riggins C. The complete German commission E monographs: therapeutic guide to herbal medicines. Austin: American Botanical Council; 1998.
- Arslan GG, Eser I. An examination of the effect of castor oil packs on constipation in the elderly. *Complement Ther Clin Pract*. 2011 Feb;17(1):58–62. <http://dx.doi.org/10.1016/j.ctcp.2010.04.004>
- Nadkarni KM. *Indian Materia Medica*. Vol 1. Mumbai: Bombay Popular Prakashan; 2007. p. 982–985.
- Srikantha Murty KR, editor. Bhavprakash of Bhavmishra. Vol.1. Varanasi: Chaukhamba Shrikrishna Das Academy; 2008. p.275.
- Anonymous. The Ayurvedic Formulary of India, Part 1, 2nd ed. New Delhi: Govt of India, Ministry of Health and Family Welfare, Dept of Indian Systems of Medicine; 2003. p.110.

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