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Result of a Comparative RCT for the Assessment of Effectiveness and Safety Profile of the Two Siddha Medicines *(Nilavarai Chooranam* and *Sivathai Chooranam)* in the Treatment of Functional Constipation

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ABSTRACT Constipation is one of the digestive system issue prevalent in apparently common populations. The aim of this study was to investigate the efficacy and safety of the *Sivathai Chooranam* and *Nilavarai Chooranam* in patients with functional constipation. This study was a comparative (RCT) randomized controlled clinical trial. The participants (N=60) diagnosed with functional constipation were enrolled into 2 arms; Group A- *Nilavarai Chooranam* (Control Arm) and Group B - *Sivathai Chooranam* (Experimental Arm). Each group received prescribed quantities for 21 days medicines and patients were pursued for 1-week post-treatment for safety and to identify relapse incidents if any. The Bristol Stool Form Scale, Modified Longo Score, and Constipation Assessment Scale were used to evaluate efficacy as the study's main outcome measures on Day 0 (baseline), as well as Days 7, 14, 21, and 28 of the experiment. The secondary objectives were to evaluate the change in life quality, which was derived by using a questionnaire and safety profile of the study drugs. Finally, the data were analyzed using inferential and descriptive statistical tests. During the whole phase of the study, any adverse events (AEs) or serious adverse events (SAEs) were not registered. The results of this study exhibited that "*Sivathai Chooranam*" is an effectual, harmless, and Siddha Plant based laxative medicine in the treatment of functional constipation and superior (with no reported cases of relapse) to *Nilavarai Chooranam* in improving quality of life. Therefore, *Sivathai Chooranam* can be used as a safe treatment option for constipation management.

INTRODUCTION

Around the world, reports on the prevalence of constipation based on the Rome III criteria range from 8.2 percent to 32.9 percent (Tamura et al. 2016). Constipation is a familiar gastro-intestinal Health problem in evidently healthy populations and also in patients with a variety of contributing diseases that have a roughly universal prevalence of 12-19 percent (Peppas et al. 2008). According to physicians, constipation is defined as three or less than three bowel movements per week. Constipation is associated with symptoms of lower abdominal discomfort, distension, or bloating (Johanson et al. 1989). The most common form of constipation is Functional Constipation (Sung 2008; Rao 2003). Functional Constipation is also known as Idiopathic Chronic Constipation. The Rome III Criteria provides a more complete and reproducible definition of functional constipation (Longstreth et al. 2006; Barimani et al. 2021). Functional constipation significantly affects the quality of life, causes psychological distress, increases health care costs, and impacts productivity. A study which was conducted in North India involving 4,767 participants has found the prevalence of constipation 11 percent, based on this study, it is estimated that around 130 million Indians are suffering from constipation (Quigley and Hunt 2012; A Special WDHD Supplement (WGO) 2012). However, it is observed that at least 65 percent of patients suffering from constipation do not seek imme-

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diate medical advice, or who use over the counter (OTC) laxatives (Johanson and Kraslstein 2007; Pare et al. 2001).

Classical Siddha literature mentions constipation as "*Malachikkal*", "*Malakattu*" (Kuppusamy and Uthamarayan 1992). Even though constipation has not been described as a distinctive disease, it is described as a symptom or indication associated with other gastro -intestinal disorders and other diseases in many Siddha literatures.

According to '*Siddha Vaithya Thirattu'* (Kuppusamy and Uthamarayan 1992), the drug *Sivathai Chooranam*- a Siddha formulation has been specifically indicated for *Malakattu* (constipation). Even though various Siddha formulations are available for the treatment of constipation, The objective of this study is to determine whether the Siddha drug "Sivathai Chooranam" is more effective and safer than "Nilavarai Chooranam" in the management of the aforementioned functional constipation.

Objectives

The primary objective of this trial was to compare the effectiveness of Sivathai Chooranam and Nilavarai Chooranam in the treatment of functional constipation. The purpose of this study was to identify the most effective Siddha therapy plan for treating functional constipation. (Manickavasagam et al. 2021).

Examining the effectiveness of Sivathai and Nilavarai Chooranam in treating functional constipation and utilizing a questionnaire to measure research participants' quality of life are the secondary objectives (Manickavasagam et al. 2021).

MATERIAL AND METHODS

The study was carried out at the Siddha Out-Patient Department of SCRU Siddha Clinical Research Unit, which is located at Safdarjung Hospital, New Delhi. The duration of the study was from 12 January 2021 to 11 May 2021. The Ethics Committee of Safdarjung Hospital has approved the study protocol and related documents. Before enrolled into the study, all patients were educated about the nature and purpose of the study and written informed consent with their mother language was acquired. Research procedures related to this study, were strictly followed in adherence with AYUSH GCP and Indian Council for Medical Research (ICMR) Guidelines. The study was enrolled in the Clinical Trial Registry of India (CTRI), and the registration Number CTRI/2019/02/017831.

Study Design

The study was an exploratory and comparative clinical trial on patients suffering with functional constipation. Patients were allotted by using simple randomization technique into two groups in a 1:1 ratio, Group A-*Nilavarai Chooranam* (Control arm and Group B-*Sivathai Chooranam* (Experimental arm) to Blocks in Microsoft Excel. The allocation duty was performed by Statistician. The study period was consisting of 4 weeks, 1 week of screening, 2 weeks of treatment, and 1 week of follow-up (Manickavasagam et al. 2021).

Eligibility Criteria

Participants were enrolled in to the study those who eligible to all the following criteria (i) Subjects of both sexes; (ii) Age range between 19-65 years; (iii) People meeting the Rome III Diagnostic Criteria. Besides the above-mentioned criteria, inclusion and exclusion measures were considered while enrolling the participants in the study. Patients were included based on criteria (at least 2 or 3) like straining, passing lumpy stools, feelings of incomplete evacuation, the feeling of anorectal obstruction/blockage, manual manoeuvres to enable for at least 25 percent of defecations, patients passing lesser than three defecations per week, patient with stool form score ranging 1-2 Bristol Stool Form Scale, people willing to undergo intervention and complete Modified Longo ODS Score. Patients were excluded who were undergoing certain medications or presented with medical history considered as an exclusion criteria scale (Manickavasagam et al. 2021).

Study Treatment

Participants were randomized to receive 2gm of *Nilavarai Chooranam* in Group A (control arm) and 2gm of *Sivathai Chooranam* in Group B (Experimental arm) with honey once daily at bedtime (post-evening meal, before sleep) for 21 days. Patients were pursued for 7 days to record the safety and to identify release incidents if any, post-treatment period. The study design is picturized in Figure 1.

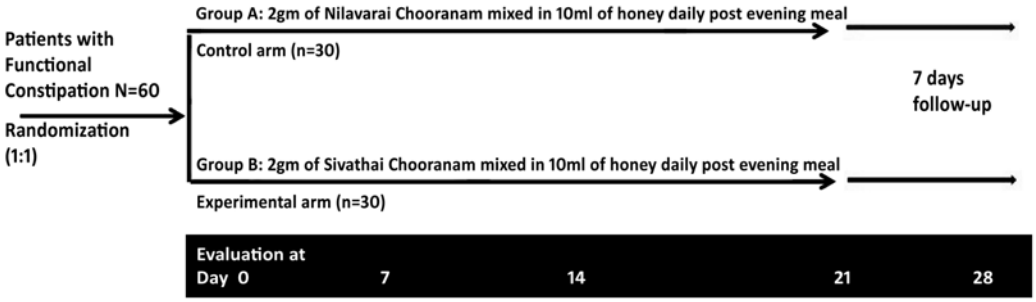

Fig. 1. Study design displaying treatment allocation for each arm

For each visit, the patients given a zip-lock bag with 20 g of the trial medicine's powder (14 gm for 1 week and 6 gm excess powder, adequate to last for a 3-day gap period). For a duration of 21 consecutive days, participants were advised to take the study prescription every day before bed. The study participants were not given any particular dietary advice for constipation.

Procurement of Trial Medicines

The trial medicines were procured from the GMP-certified manufacturer, in Chennai, Tamil Nadu (Indian Medical Practitioners Co-operative Pharmacy and Stores Ltd [IMPCOPS]). The composition of both *Nilavarai and Sivathai* are Tabulated in Tables 1a and 1b separately.

Outcome Measures

The primary outcome measure was to estimate the efficacy of *Sivathai Chooranam* and *Nilavarai Chooranam* for Functional Constipation (at least a 30% increase in bowel movement) using the Bristol Stool Form Scale, Modified Longo ODS Score and Constipation Assessment Form.

Secondary outcome measures were to to compare the efficacy of *Sivathai Chooranam* with *Nilavarai Chooranam* and to assess the safety profile of the *Trial medicines*. The study also calculated the change in the quality of life of participants using a questionnaire (Marquis et al. 2005).

Efficacy Evaluations

By using the Bristol stool form scale and Modified Longo score, major symptoms associated with functional constipation were measured (Lewis and Heaton 1997). The patient was given a diary card to keep track of the consistency of their faeces every morning at home.

The BSFS recorded stool consistency, scores ranging from type 1 to 7, where types 1 and 2 indicated harder stool; type 3 to 5 normal stool, and higher scores type 6 and 7 indicated liquid stool. Modified Longo score ranges from 0-40 (higher score indicates more severe symptoms).

CAS was questionnaires to be assessed based on Diary completed by patients. CAS score ranges from 0-30 (higher score indicates more severe symptoms)

The patient's symptoms were assessed for overall improvement by using the BSFS, Modified Longo score, and CAS at 0 Day (baseline), 7th Day, 14th, and 21st Day during the study visit.

A self-reported questionnaire was used to measure the patient's quality of life, score ranges from 0- 4 (lower score indicates a better quality of life). The questionnaire was administrated on day 0 (baseline) and Day 28.

Safety Evaluation

The routine blood tests for all patients (alanine transaminase [ALT], aspartate aminotransferase [AST], thyroid profile, and serum electrolytes) were done prior to randomization for screening and to establish the eligibility criteria. Routine blood test for all patients was done post-completion treatment, to know the adverse event if any.

Post-treatment (Day 21), patients were followed up for 7 days (until Day 28) to identify relapse symptoms of functional constipation if any. All the patients were monitored unfavourable any events (AE & SAE) throughout the study.

Statistical Analysis

All data were collected in a digital database and were statistically analysed with software. The demographic characteristics were analyzed by descriptive statistics. The comparison between Two arms (Group A and B) performed with student's t-test. A p-value of <0.05 which was considered statistically significant. GraphPad Prism 7.0 software was used for Statistical analysis

RESULTS

The allocation of participants included in the study (N=60) is briefed in Figure 2. A total of 157 patients were screened and 64 were enrolled in the study (Group A: 30, and Group B: 30) as 4 patients withdrew (2 each) before the start of treatment. Totally 60 patients were completed the study. Out of 60 participants, 24 were female and 36 were male. The participants' average age varied from 20 to 62.

All participants who involved in the study gave written informed consent, then they were included into the study if they met out the eligibility criteria. Prior to enrolment all the patients were educated to register their improvement by Longo's ODS score system, Bristol stool form scale, Efficacy Assessment parameter and quality of life by Questionnaire (PAC-QOL). The follow-up visits of patient were scheduled during the 7th, 14th,21^{st,} and 28th days after the initial visit.

Out of the 157 total screened patients, 93 patients were excluded based on inclusion/exclusion criteria. The signs and symptoms that were most frequently seen during communication during screening visits were lumpy, hard stools, straining during faeces, the sensation of an imperfect bowel evacuation, and anorectal obstruction.

Based on the Modified Longo Scale, Bristol Stool Form Scale, and Constipation Assessment Scale, study results were assessed at each visit. On each visit, the patient's and the investigator's global assessments of overall improvement were done. Drug tolerability and Drug compliance were assessed on every study visit.

The comprehensive analysis of the parameters is provided below, comparing Group B, Sivathai Chooranam (the experimental arm), and Nilavarai Chooranam (the control arm) in terms of overall efficacy and safety.

Bristol Stool Formation Score

The BSFS scale was used to measure the total stool consistency scale, which is shown in Table 2. This scale was previously used to evaluate study participants, and those with stool form scores between 1 and 2 on the Bristol Stool Form Scale were included in the study. On Days 0 (p=0.025), 14, 21, and 28 (p0.0001), it was discovered that groups A and B's BSFS differed considerably from each other. Day 0 results showed that 19 partici-

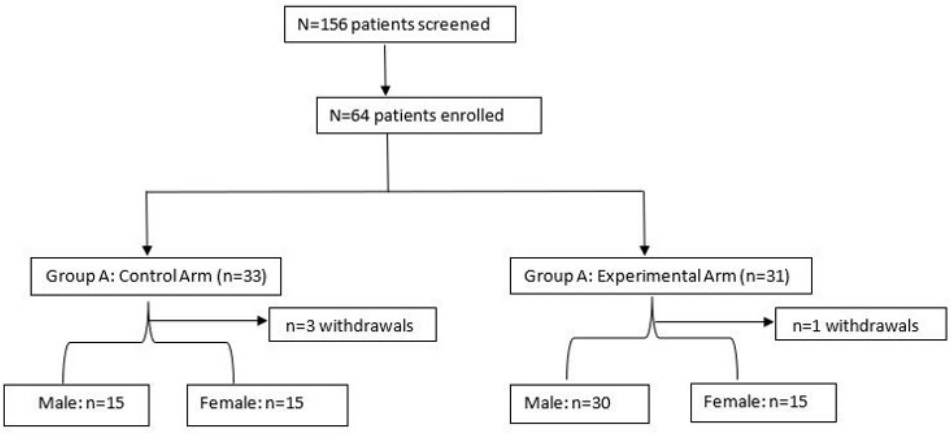

Fig. 2. Subject disposition displaying screening and treatment allocation of participants

Table 1: Demographic and baseline characteristics of the patients

Characteristic	*Group A*	*Group B*	*Total*	*P value*
Sex, n (%)				
Male	15	15	30	
Female	15	15	30	
Age- years				
(Mean ±SD)	35.03 (11.40)	35.37 (10.39)	35.20 (10.81)	p>0.05
Working, n (%)	22	19	41	NA
House Wife	5	9	14	
Student	3	2	5	
Income Group:				
High	1	0	1	
Middle	3	4	7	
Low	26	26	52	NA

Table 2: Changes in stool consistency on Bristol Stool formation score

Days	*Study groups*	*Very constipated*	*Constipated*	*Normal*	*Inflammation*	*Total*
Day 0	Group A	14 (53%)	14 (47%)		NA	30
	Group B	25 (83%)	5 (17%)		NA	30
	Total	41 (68%)	19 (32%)		NA	60
Day 7	Group A	1 (3%)	19 (64%)	10 (33%)	0	30
	Group B	1 (3%)	11 (37%)	16 (53%)	2 (7%)	30
	Total	2 (3%)	30 (50%)	26 (44%)	2 (3%)	60
Day 14	Group A	None	20 (67%)	10 (33%)	0	30
	Group B	None	5 (17%)	23 (77%)	2 (7%)	30
	Total	None	55 (50%)	42 (44%)	2 (3%)	60
Day 21	Group A	None	17 (57%)	13 (43%)	0	30
	Group B	None	1 (3%)	20 (67%)	9 (30%)	30
	Total	None	18 (30%)	33 (55%)	9 (15%)	60
Day 28	Group A	None	14 (53%)	16 (47%)	0	30
	Group B	None	1 (3%)	26 (87%)	3 (10%)	30
	Total	None	15 (25%)	42 (70%)	3 (5%)	60

pants (32%) and 41 individuals (68%) were both severely constipated. The majority of the participants, 25, were from Group B (83 %); nevertheless, the proportion of constipated participants in Group B was higher, with 14 (47 %) participants.

The consistency of the stools was noted on all of the planned days, namely Days 7, 14, 21, and 28. Only 2 patients (1 in each group) initially reported having highly constipated feces on Day 7 of the intervention. The remaining 59 participants in Group A included 10 (33%) who reported having normal stool production scores and 19 (64%) who reported being constipated. In Group A, none of the individuals mentioned inflammation. Out of the 59 participants who were still in Group B, 11 (37%) reported being constipated, and 16 (53%) reported having stools with normal stool production scores. In Group B, two (7%) subjects mentioned inflammation.

On Day 28, none of the participants (both groups) were observed to be very constipated. Group B participants showed a marked improvement wherein only 1 (3 %) participant out of 30 was observed to be constipated. Rest, 26 (87%) participants observed normal stool formation and 3 (10%) reported inflammation. Amongst Group A, 14 (53 %) participants were reported to be constipated whereas 16 (47%) participants reported normal stool formation. None of the participants in this group showed signs of inflammation.

Changes in the Mean Score of Modified Longo ODS Score: Modified Longo ODS Score was amongst the other scale analyzed to assess the efficacy of the interventional products and data is presented in Table 3. On Day 0, the Modified Longo ODS Score was assessed for both groups and revealed 16.27 (SD: 1.92) and 15.7 (SD: 1.93), respectively. The mean scores showed a gradual improvement on consecutive visits on 7th Day, 14th, 21st and 28th Day. On Day 7th the mean score was 13.57 (SD: 2.26) and 6.33 (SD: 4.80) in Group A and

Table 3: changes in mean score of modified Longo ODS

Duration in days	*Mean score*		*Standard Deviation (SD)*	
	Group A	*Group B*	*Group A*	*Group B*
Day 0	16.27	15.7	1.92	1.93
Day 7	13.57	6.33	2.26	4.80
Day 14	11.4	2.47	3.04	3.36
Day 21	9.53	0.63	4.97	1.63
Day 28	9.06	0.33	5.43	1.09

B correspondingly. On Day 28, the mean score improved to 9.06 (SD: 5.43) and 0.33 (SD: 1.09) with respect to Groups A and B, bring to light better outcomes in Group B.

Changes in the Mean Score of the Efficacy Assessment Scale for Constipation (CAS): Further, to evaluate the efficacy CAS was also analysed during the study tenure and presented in Table 4. On Day 0, the CAS was assessed for both groups and revealed 16.73 (SD: 2.36) and 16.73 (SD: 2.13) scores, correspondingly.

Table 4: Changes in mean score of efficacy assessment scale for constipation (CAS)

Duration in days	*Mean score*		*Standard Deviation*	
	Group A	*Group B*	*Group A*	*Group B*
Day 0	16.73	16.73	2.36	2.13
Day 7	14.70	7.53	2.78	5.61
Day 14	11.83	3.53	3.51	4.37
Day 21	9.40	1.00	5.62	2.02
Day 28	9.00	0.40	5.40	1.22

The mean scores showed a gradual improvement on consecutive visits on 7th Day, 14th, 21st and 28th. On 7th Day, the mean score was 14.70 (SD: 2.78) and 7.53 (SD: 5.61) in Group A and B respectively. On Day 28, the mean score improved to 9.00 (SD: 5.40) and 0.40 (SD: 1.22) with respect to Groups A and B, show up better outcomes in Group B.

Patient Assessment of Constipation -Quality of Life (PAC-QOL) Before and After Treatment: To evaluate the overall QOL PAC-QOL was evaluated, and data is given in Table 5. To analyze the overall improvement in the Questionnaire was assessed at baseline (Day 0) and Day 28 with lower scores indicating a better quality of life. After receiving the experimental drug for 21 days, the patients were informed to stop the consumption of

Table 5: Patient assessment of constipation -quality of life (PAC-QOL) before and after treatment
Duration in days Mean ±SD

	Group A				*Group B*			
	Physical discomfort (1-4)	*Psychosocial discomfort (5-12)*	*Worries and discomfort (13-23)*	*Satisfaction (24-28)*	*Physical discomfort (1-4)*	*Psychosocial discomfort (5-12)*	*Worries and discomfort (13-23)*	*Satisfaction (24-28)*
Day 0	18.5± 1.58	36.40± 3.40	50.67± 3.65	20.43±3.45	19.23± 0.77	37.00± 3.07	53.76± 1.89	23.83±1.46
Day 28	11.53± 4.30	21.76± 9.62	28.83±12.54		4.03± 0.18	8.1± 0.31	12.30± 3.45	

study medicines. Patients were monitored (without the administration of trial drug) for a recurrence of functional constipation symptoms from day 22 to day 28. None of the participants mentioned a return of their functional constipation symptoms.

On Day 0, the satisfaction score was 20.43±3.45 and 23.83±1.46 with respect to Groups A and B. On the same day, for Group A, other parameters viz Physical discomfort (1-4), Psychosocial discomfort (5-12), and worries and discomfort (13-23) the scores were 18.5±1.58, 36.40±3.40, and 50.67±3.65 respectively which improved to 11.53±4.30, 21.76±9.62, and 28.83±12.54 respectively on Day 28th. On the same day, for Group B other parameters viz Physical discomfort (1-4), Psychosocial discomfort (5-12), and worries and discomfort (13-23) the scores were 18.5±1.58, 36.40±3.40, and 50.67±3.65 respectively which improved to 19.23±0.77, 37.00±3.07, 53.76±1.89 respectively on Day 28th. Overall, Group A showed better satisfaction scores; however, upon analysing other parameters the results revealed improved outcomes in Group B.

Changes in Laboratory Parameter Mean Values at the End of the Study Treatment

The laboratory readings were taken at the beginning of the trial to determine eligibility require-

Table 6: Mean change in values of laboratory parameters from baseline to the end of study treatment

Parameters	*Baseline Mean ± Std. Dev.*		*End of the Treatment (Day 21) Mean ± Std.Dev.*	
Complete Hemogram	*Group A*	*Group B*	*Group A*	*Group B*
Haemoglobin	13.67± 1.79	13.50± 1.68	13.83± 2.67	14.06± 1.82
TLC (Total Leucocyte Count)*	6946.66 ±2022.41	6970±2221.54	5627.66±1114.75	6222.66±1511.77
Differential Leucocyte Count	58.3± 8.36	57.53± 7.62	55.9± 5.75	57.96± 6.67
Neutrophil*				
Lymphocyte*	33.03± 8.74	35.46± 8.70	35.96± 5.39	34.9± 6.39
Eosinophils*	3.7± 2.69	3.16± 1.14	3.23± 1.04	3.06± 0.94
Monocytes*	5.43± 1.13	4.90± 1.56	4.56± 1.61	4.06± 0.98
Basophils*	0	0	0	0
Erythrocyte Sedimentation Rate (ESR)*	22.66± 13.91	31.86± 20.70	15.73± 9.30	17.90± 13.20
Blood Glucose Random	89.00± 8.47	93.71± 15.84	98.15± 21.4	102.93± 11.87
Liver Function Test (LFT), Serum				
Bilirubin, Total	0.87± 0.43	0.73± 0.42	0.78± 0.40	0.69± 0.23
Bilirubin, Direct	0.31± 0.13	0.27± 0.12	0.26± 0.13	0.22± 0.06
Bilirubin, Indirect	0.57± 0.31	0.46± 0.3	0.51± 0.27	0.47± 0.18
SGOT(AST), Serum	29.56± 15.50	29.73± 12.15	23.66± 6.08	24.30± 6.73
SGPT(ALT), Serum	34.60± 32.01	36.43± 24.11	10.73± 3.52	11.46± 25.62
Alkaline Phosphatase (ALP), Serum	89.28± 26.39	92.4± 19.96	71.46± 16.33	78.10± 22.14
Gamma Glutamyl Transferase (GGT)*	27.70± 31.52	25.62± 17.59	25.53± 11.6	25.3± 11.7
Albumin, Serum	4.41± 0.21	4.37± 0.27	4.08± 0.47	4.36± 0.90
Globulin	3.33± 0.44	3.20± 0.48	3.13± 0.30	3.11± 0.41
A/G Ratio	1.34± 0.21	1.32± 0.2	1.32± 0.17	1.35± 0.19
Kidney Profile, Serum				
Urea	20.98± 5.96	21.41± 6.29	23.73± 8.02	22.29± 5.21
Creatinine	0.78± 0.14	0.74± 0.14	0.77± 0.12	0.79± 0.13
Uric Acid, Serum	5.29± 1.70	5.41± 1.46	4.26± 1.02	4.37± 1.27
Protein, Total	7.78± 0.36	7.70± 0.44	7.23± 0.62	7.24± 0.69
Sodium	140.22± 12.56	139.39± 3.20	138.91± 1.91	139.03± 1.89
Potassium	3.95± 0.45	3.98± 0.40	4.07± 0.33	4.0± 0.33
Chloride	103.66± 1.76	103.23± 1.31	103.46± 1.69	103.70± 1.91
Calcium, Serum	9.14± 0.35	9.18± 0.41	9.05± 0.41	9.21± 0.31
Immunoassay: TSH FT3 FT4				
3rdGen. (TSH Ultrasensitive)	3.17± 1.41	2.39± 1.11	3.25± 1.29	3.26± 1.24
Free Triiodothyronine (FT3)	2.76± 0.35	2.92± 0.38	2.84± 0.47	2.56± 0.36
Free Thyroxine (FT4)	2.76± 0.35	2.92± 0.30	1.187± 0.18	1.19± 0.07

ments and at the conclusion of the study to determine safety. Table 6 displays the laboratory parameter data. Patients from all trial groups (n = 60) reported that the study medication was very well tolerated. At the conclusion of the course of treatment, there were no statistically significant changes in any of the laboratory safety markers (for example, complete blood count, erythrocyte sedimentation rate, percent Hb, LFT, RFT, serum electrolytes, thyroid profile).

Safety Evaluation

In both groups, there were no adverse events (AEs) or serious adverse events (SAEs) reported during the study.

DISCUSSION

Globally, constipation is regarded as a chronic medical concern that impacts the overall health status and standard of life (Fang et al. 2021). Patients those suffering with functional constipation, also have the depression about their health condition (Barimani et al. 2021).Throughout the world, 32.1 percent of people who having constipation complaints are taking complementary and alternative medicines for their issue (Van Tilburg et al. 2008). The results of this study exhibited that "*Sivathai Chooranam*" is an effectual, harmless, and Siddha Plant based laxative medicine in the treatment of functional constipation and superior (with no reported cases of relapse) to *Nilavarai Chooranam* in improving quality of life. Overall, these therapies were observed to be an effective intervention and can be useful in the management of constipation in patients. In all the Groups, no adverse drug reaction was reported. Therefore, this Siddha intervention can be used as a reliable method to treat functional constipation, especially in Group B patients who consumed "*Sivathai Chooranam*". No relapse was observed in most of the patients in Group B during the monitoring period (that is, days 22-28).

In the current study, the researchers discovered that Sivathai Chooranam was superior to Nilavarai Chooranam in terms of positive assessment and conformity on improvement in the regularity of bowel movements and stool form. In Siddha literature, Sivathai Chooranam, a polyherbal medication for flatulence and particularly constipation, is referenced.

Even though the thorough mechanism of action of the *Sivathai Chooranam* is not clearly understood, the synergistic action of the various types of laxative ingredients has possibly made it a balanced formulation for the effective treatment of Functional constipation (Kolhe et al. 2018).

One of the key components of Sivathai Chooranam, the Sivathai (Operculina turpethum), has historically been used to ease bowel movement. Numerous secondary metabolites, such as saponins, flavonoids, glycosides, and phenolics, are present in it. Turpethein is mostly to blame for Operculina turpethum's laxative effects. (Gupta and Ved 2017).

Kadukkai (*Terminalia chebula*), *Nellikkai* (*Phyllanthus emblica*) and *Thandrikkai* (*Terminalia bellirica*). These herbs help to pacify three doshas (*Vatham, Pitham, Kabam*) and have rejuvenating effects.

Triphala was used in clinical trials to treat patients with gastrointestinal issues, and it was found to improve the frequency, yield, and consistency of stools while reducing constipation, stomach pain, hyperacidity, and flatulence. Triphala's high quantities of flavonoids and antioxidant properties were said to be responsible for this therapeutic effect. In 2022, Saini et al. said Phytochemicals present in *Triphala* such as quercetin and gallic acid promote the growth of gut microbiota such as *Bifidobacteria* and *Lactobacillus* species.While preventing the growth of unwanted gut inhabitants like E. coli, bifidobacteria and lactobacillus species are promoted. Additionally, the lactic acid bacteria have an enzyme called tannase that may break down Triphala's plant tannins, which include gallic acid. For instance, the human gut bacteria convert triphala-derived polyphenols like chebulinic acid into compounds called urolithins that may be able to reduce oxidative damage. (Singh et al. 2008; Peterson et al. 2017).

Numerous trillions of microbes make up the gut microbiome, which is referred to as the "virtual organ of the body" due to its significance in preserving host homeostasis. Disruptions in the gut microbiota were referred to as "dysbiosis," which has been more and more linked to a variety of disease states, including functional gastrointestinal disorders like constipation and irritable bowel syndrome. Disturbances in the gut microbiome may affect intestinal physiology and motility and contribute to the

onset of constipation, according to preclinical and clinical studies. (Rodriguez et al. 2020).

All active ingredients in *Sivathai Chooranam* contain flavonoids. Flavonoids play a vital role in the body by inhibiting gastrointestinal inflammation, via direct or indirect mechanisms.

Gut microbiota and host tissue extensively metabolize dietary flavonoids and flavonoid metabolites help to modulate gut immune function (Pei et al. 2020). The exact mechanism of how *Sivathai Chooranam* plays important roles in controlling intestinal movement is unclear yet. Further studies are needed to elucidate the specific pharmacological action of Sivathai Chooranam on functional constipation.

Both the interventions were evaluated to be efficacious as analyzed through various parameters viz Bristol Stool Form Scale (BSFS), Modified Longo Scale (MLS), and Constipation Assessment Scale (CAS). These scales revealed improved outcomes in both groups; however, Group B showed better outcomes indicating the superiority of Group B over the control group (Group A).

CONCLUSION

A Siddha proprietary polyherbal laxative formulation "*Sivathai Chooranam"* is remarkably successful in treating functional constipation. After using the medication for one to two weeks, the symptoms of functional constipation were also prevented from returning until the fourth week. This study offers proof that "Sivathai Chooranam" can be administered safely and effectively to treat functional constipation.

RECOMMENDATIONS

The following recommendations were given to health authorities, based on the observations of the study:

1. As results disclose there can be a big scope and great potential for Siddha proprietary polyherbal laxative formulation "*Sivathai Chooranam"* for effective in functional constipation management.
2. Further, double-blinded, placebo-controlled, randomized multicentric clinical trials with large sample sizes will give the clarity of the above findings.

CONFLICTS OF INTEREST

There is no conflict of interest of none of authors involved in this study.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

On 08.02.2021, the Institutional Human Ethical Committee of the Siddha Clinical Research Unit at Safdarjung Hospital in New Delhi granted ethical permission for the experiment.

Before being included in the study, each subject was given written informed permission and declared their willingness to participate.

AUTHORS CONTRIBUTIONS

Dr. R. Manickavasagam contributed hypothesis and written the initial draft of the manuscript, designed the study, and assisted in the interpretation of data. Dr. A. Aishwarya enrolled patients in the study and contributed to the manuscript development. Prof Dr. K. Kanakavalli mentored and guided the overall study.

TRIAL REGISTRATION

CTRI/2019/02/017831 is the Clinical Trial Registry of India (CTRI) registration number.

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