Indian Journal of Traditional Knowledge
Vol 23(2), February 2024, pp 109-118
DOI: 10.56042/ijtk.v23i2.6532

A multi-centre study to evaluate the effect and safety of a classical Ayurveda medicine *Vyaghri Haritaki* in bronchial asthma

Milind Suryawanshi[a], Vinod Bihari Kumavat[b], Pradeep Dua[c], Babita Yadav[c], Shruti Khanduri[c], Pallavi Mundada[c,*], Richa Singhal[c], Rakesh Kumar Rana[c], Bharti[d] & Narayanam Srikanth[c]

[a]Regional Ayurveda Research Institute, KDK College Rd, Near Gharkul Parisar, Nandanvan, Nagpur, Maharashtra 440 009

[b]Regional Ayurveda Research Institute, Indira Colony, Jhotwara Road, Jaipur, Rajasthan 302 016

[c]Central Council for Research in Ayurvedic Sciences, Opposite 'D' Block, Janakpuri, New Delhi 110 058

[d]Central Ayurveda Research Institute, Road No.66, West Punjabi Bagh, Punjabi Bagh, New Delhi, Delhi 110 026

[*]E-mail: pallavimundada86@gmail.com

Received 01 November 2023; revised 26 December 2023; accepted 30 January 2024

Bronchial asthma (vis-à-vis *Tamaka Swasa* in Ayurveda) is a chronic inflammatory disorder of the airway. Multiple Ayurvedic formulations are prescribed by Ayurveda physicians for *Tamak Swasa*. *Vyaghri Haritaki* is one such commonly prescribed poly herbal classical Ayurvedic formulation. A multicentre single-arm study was conducted at three Ayurveda Research Institutes in India to explore the effect and tolerability of *Vyaghri Haritaki*, a classical Ayurvedic medicine, on bronchial asthma (*Tamaka Swasa*). One forty seven patients between 18 and 60 years diagnosed with bronchial asthma showing a positive test of reversibility of airway obstruction were enrolled. Patients with peak expiratory flow rate (PEFR) < 50% and/ or forced expiratory volume in the first second (FEV1) < 50% of the predicted value and other major co-morbidities were excluded. 10 g *Vyaghri Haritaki* twice a day with lukewarm water was given for 12 weeks (84 days). Changes in the clinical symptoms (Asthma Control Questionnaire), quality of life (St. George Respiratory Questionnaire), respiratory function (peak expiratory flow rate and forced expiratory volume in one second), and haematological and biochemical parameters were compared before and after the treatment. Data of 142 participants were analysed which revealed significant improvement in PEFR [Baseline 301.7 litre/minute and 84th Day 334.85 litre/minute ($p<0.001$)], FEV1 [Baseline 1.83 litres and 84th Day 2.12 litres ($p<0.001$)], Asthma Control Questionnaire [Baseline 2.95 and 84th Day 1.43 ($p<0.001$)], and the total score of the St. George Respiratory Questionnaire [Baseline 50.46 and 84th Day 30.74 ($p<0.001$)]. No adverse events were reported during the study. *Vyaghri Haritaki* may prove beneficial in improving the pulmonary function, overall symptoms, and quality of life of patients with bronchial asthma which is well tolerated.

Keywords: *Avaleha*, FEV1, PEFR, Polyherbal, Respiratory disorders, *Tamak Swasa, Vyaghri haritaki*

IPC Code: Int Cl.[24]: A61K 36/00, A61K 9/00

Bronchial asthma is a chronic condition that impairs the well-being of the patients in social, physical, and psychological contexts. More than 339 million people are living with asthma globally. According to the Global Burden of Diseases, Injuries, and Risk Factors Study 2015 (GBD 2015), among the top 20 conditions causing disability, asthma was at 23rd rank globally as a cause of disease burden when measured by disability-adjusted life years (DALYs)[1]. WHO estimates state that in 2016, 24.8 million DALYs and 417,918 deaths were attributable to asthma at the global level; and the low- and lower-middle income countries are the most affected ones[2]. In India, out of total 1.31 billion population, about 6% children and 2% adults have asthma[3]. As per the National Family Health Survey (NFHS-4) 2015-16, prevalence of self-reported asthma in women and men aged 15-49 years is 2% and 1% respectively which is almost same as compared to NFHS-3 in 2005-06[4].

Bronchial asthma is among the most prevalent chronic inflammatory airway diseases characterised by bronchial hyper reactivity and airway obstruction[5]. Most common clinical presentation includes recurrent attacks of breathlessness and wheezing, that vary in severity and frequency in every patient. Other associated common symptoms are cough, tightness in chest, fatigue, irritability, pain in chest or abdomen and tachycardia. The attacks may frequently occur

*Corresponding author

throughout a day when flared up. Symptoms may worsen with increased physical activity or at night. Important patho-physiological event in bronchial asthma is frequent inflammation of the air passages in lungs that affects the sensitivity of the nerve endings in the airways making them easily irritated. While an attack of bronchial asthma, the lining of the air passages swells resulting in narrowing of airways thus reducing the flow of air in and out of the lungs[6].

Most important symptom of Asthma, breathlessness is generally considered as a normal phenomenon by the patients for a long time resulting in under-reporting of the disease. Generally, diagnosis of bronchial asthma is made on the basis of clinical history, physical examination, and pulmonary function tests, including reversibility testing and measurement of bronchial reactivity[7]. Since obstruction of airways is recurrent and reversible, the goal of treatment of bronchial asthma is mostly confined to control the symptoms effectively for a long time. The therapeutic agents for asthma are either symptoms-modifying, symptom preventers or disease modifying[8]. Long-term treatment of bronchial asthma through conventional medicine is generally focused on enhancing their quality of life by preventing frequent attacks and reducing the severity of symptoms when they occur. Antiasthma therapies involve inhaled corticosteroids and bronchodilators for rapid symptomatic relief of acute attacks as basic treatment, along with preventive measures and patient education[9].

In Ayurveda, the respiratory system is referred to as *Pranavaha Srotas,* and *Swasa* has been described as one of major disorders of this *Pranavaha Srotas*. The symptom *Swasa* literally means difficulty in breathing. *Tamaka Swasa* is one among five types of *Swasa* described in Ayurveda. It is mentioned that *Swasa* is difficult to treat and if not treated timely can lead to death[10]. *Tamaka Swasa* is mainly caused by vitiated *Vata* and *Kapha* but the pathology originates from sites dominated by *Pitta* and ultimately the pathology gets manifested through *Pranavaha Srotas*[11].

Vyaghri Haritaki is a classical Ayurvedic polyherbal formulation which can be consumed in the form of linctus or electuary[12]. It is one of the commonly prescribed Ayurvedic medicines since ancient times for symptomatic relief in chronic bronchial Asthma. However, the scientific documentation for validation of its effect and safety among the patients with bronchial asthma was not available. So, this study was done to evaluate the effect of *Vyaghri Haritaki* on clinical symptoms, quality of life and respiratory functions of patients with bronchial asthma vis-à-vis *Tamaka Swasa*. This study also assessed the safety of this Ayurveda intervention among the study participants through evaluating the biochemical parameters before and after the study period.

Methodology

Study setting and design

This was an open label single arm multicentre pilot study conducted at three peripheral institutes of Central Council for Research in Ayurvedic Sciences (CCRAS) *viz*., Regional Ayurveda Research Institute, Vijayawada, Regional Ayurveda Research Institute, Jaipur and Regional Ayurveda Research Institute, Nagpur during July 2011 and September 2012.

Ethics approval and trial registration

The Institutional Ethics Committee of each participating centre had approved this study. The study was conducted in compliance with the Declaration of Helsinki and existing GCP guidelines. All eligible patients were screened after getting informed consent. The study was registered in Clinical Trial Registry of India CTRI/2012/04/002584.

Participants

Inclusion and exclusion criteria

Patients diagnosed to have stable bronchial asthma (as per GINA Guideline) for at least 6 weeks prior to screening for the study (no upper limit for the duration of illness was set), between 18 and 60 years, with positive test of reversibility were included for the study. The positive reversibility was defined as either improvement of 60 L/min or ≥ 20% in peak expiratory flow rate (PEFR) 10 min after the inhalation of 200 mcg of salbutamol by symptomatic patients, and in asymptomatic patients provocation with 5-10 min of physical exercise followed by reversal upon inhalation of 200 mcg of salbutamol, improvement of 60 L/min or ≥ 20% fall in PEFR when assessed after 10 min].

Patients with PEFR < 50% and/or forced expiratory volume in the first second (FEV1) < 50% of the predicted value, or evidence of malignancy, or uncontrolled diabetes mellitus (defined as blood sugar fasting >250 mg/dL), or poorly controlled hypertension defined as ≥ 160/100 mm Hg, or on

prolonged (≥ 6 weeks) medication with corticosteroids, bronchodilators, mast cell stabilizers, antidepressants, anticholinergics, etc, or suffering from major systemic illness necessitating long term drug treatment (rheumatoid arthritis, tuberculosis, psycho-neuro-endocrinal disorders, etc.), or those having past history in the last 6 months of any condition resulting cardiac compromise (e.g. atrial fibrillation, acute coronary syndrome, myocardial infarction, stroke or severe arrhythmia), or clinical evidence of heart failure, concurrent serious hepatic disorder or Renal disorders, Severe Pulmonary Dysfunction or smoker/alcoholics and/or drug abusers, or pregnant or lactating women were excluded from the study.

The participants whose treatment adherence was less than 80% were withdrawn from the study. The participants whose disease worsened and met the exclusion criteria were also withdrawn from the study and were referred to appropriate health care facility for their condition.

Trial drug

Vyaghri Haritaki (API Part-II-Vol–I: Pg 35-37) an Ayurvedic classical formulation was procured from a GMP certified pharmaceutical company. The dose of 10 g *Vyaghri Haritaki* twice a day with lukewarm water for 12 weeks (84 days) was given. The ingredients of *Vyaghri Haritaki* are *Solanum xanthocarpum* (4.8 kg whole plant), *Terminalia chebula* (100 fruits in number approximately 1.2 kg), *Zingiber officinalis* (96gm Rhizome), *Piper longum* (96 g Fruit), *Piper nigrum* (96 g Fruit), *Cinnamomum zeylanicum* (48 g Stem Bark), *Elettaria cardamomum* (48 g fruits), *Cinnamomum tamala* (48 g Leaf), *Mesua ferrea* (48 g Stamen), Jaggery (4.8 kg) and Honey (2.288 litres)[12].

Outcome measures

Changes in the clinical symptoms of bronchial asthma and *Tamak Swasa*, Asthma Control Questionnaire (ACQ), and investigations *viz.*, PEFR and FEV1 were assessed after every 2 weeks. Further St. George Respiratory Questionnaire (SGRQ-C) was assessed at baseline (before treatment) at 84th day (after treatment) and after 2 weeks of post treatment follow-up. The ACQ is a questionnaire consisting of seven questions. Its scores range from 0 (well controlled) to 6 (extremely poorly controlled). A score of 1.5 or more indicates that a patient has inadequate asthma control[13]. SGRQ-C is a COPD-specific version of the St. George respiratory questionnaire which measures impact on overall health, daily life, and perceived well-being in patients with obstructive airways disease[14].

Ayurvedic parameters that were assessed included *Prakriti i.e.,* the inherent constitution of the three humours (*dosha*), *Ahara Shakti i.e.,* capacity of a person to eat and digest the food comfortably, *Vyayama Shakti i.e.,* capacity of a person to perform physical activity and incidence of the cardinal symptoms of *Tamak Swasa. Prakriti* was assessed only at baseline and the remaining parameters were assessed at baseline and during each follow-up through pre-structured interviews with self developed questionnaires. The *Ahara Shakti* and *Vyayama Shakti* were categorised as *Pravara* (Excellent) *Madhyam* (Moderate) and *Avara* (Less) based on a self-developed scale. The following series of symptoms of *Tamaka Swasa* were also assessed for their incidence during each visit - Rhinorrhoea *(Pīnasa),* rattling sound in chest (*Ghurghurakam*), exceedingly severe attack of dyspnoea causing suffocation (*Prāṇaprapīḍakam Tīvra śwāsa*), severe cough (*kāsate*), Hoarseness of voice (*Kanthodhwaṃsa*), difficulty in expectorating the phlegm and feels relieved after expectoration (*Śleṣmaṇyam Unmuchyamane Tu Bhriṣam Bhavati Dukhitah*), difficulty in talking (*Kricchacchknoti Bhāṣitum*), unable to sleep (*Nā chāpi Labhate Nidrā*), Getting relief only in sitting position (*Āsīno Labhate Saukhyam*), pain in lateral side of the chest (*Pārśva śūla*), lack of taste (*Aruci*), severe restlessness (*Bhrisha Artimāna*), eye balls are always prominent (*Ucchṛitāksho*), sweating over forehead (*Lalāta Sweda*), dryness in mouth (*Visūṣkāsyatā*), fainting during attack (*Pramoha*), gets repeated attacks of dyspnea (*Muhuśwāso Muhuścha*ivāvdhamyate), vomiting (*Vamathu*), fever (*Jwara*), excessive thirst (*Tṛṣṇā*), aggravation of symptoms on cloudy day (*Meghāt Vardhate*), aggravation of symptoms on exposure of wind (*Prāgvātam Vardhate*), aggravation of symptoms on intake of cold water (*Śītodaka vardhate*), aggravation of symptoms in cold weather (*Śītaṛitu vardhate*), aggravation of symptoms on intake of food items that increase the humour '*kapha'* (*Śleṣmala Āhāra vardhate*), relief in symptoms with rise in temperature through intake of hot food items, hot environment) etc. (*Saukhyam Ūṣṇam*).

For assessment of safety of the trial intervention, incidence of adverse drug reactions and any adverse events were recorded and clinical assessment was

performed biweekly at each visit *i.e.,* at 0 day (baseline), 14th, 28th, 42nd, 56th, 70th and 84th day. Haematological and biochemical parameters like serum haemoglobin, total leucocyte count (TLC), erythrocyte sedimentation rate (ESR), absolute eosinophil count, fasting blood sugar, blood urea, serum uric acid, serum creatinine, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), serum proteins, serum bilirubin, serum alkaline phosphatase (ALP) were assessed before and after treatment.

Tolerability of the trial intervention was assessed based on the number of participants withdrawn from the study because of treatment adherence less than 80%.

Statistical analysis

The data on continuous parameters has been presented as Mean (SD) and compared using paired sample t-test. The data on nominal variables has been presented as n (%). The dichotomous data has been compared using Mc-Nemar test. A p-value of <0.05 has been considered as significant. Statistical analysis was done using SPSS 15.0.

Results

Total 147 patients could be enrolled in the study at all three centres, out of which 134 completed the study and 13 were dropouts. Last Observation Carried Forward (LOCF) method of imputation was applied to impute the data of patients whose data for 14th day visit was available. Data of patients who dropped out between baseline and 14th day visit were excluded from the analysis. Therefore, data of 142 patients was considered for analysis.

Demographic data of the patients (Table 1) revealed that most of the patients (27.5%) belonged to 27-35 years age group and the mean age was 38.54±10.72 years, 52.8% patients were women, 78.2% were married, 83.1% were literate and 76.8% patients were above poverty line, 54.9% patients were non-vegetarians, 95.8% of the patients were not addicted to smoking, tobacco chewing or alcohol. 78.2% patients complained of disturbed sleep at baseline. 98.6% patients were allergic to some agent out of which most of them were allergic to dust. 63 (42.85%) patients had family history of bronchial asthma. Assessment of Ayurvedic parameters at baseline revealed that 72 (50.7%) patients had *pitta-kaphaja prakriti*. Mean duration of illness (bronchial asthma) was 5.08 years.

Assessment of efficacy

Proportion of patients having *Pravara* (excellent) *Ahara Shakti* improved from 9.2% before treatment to 32.4% and proportion having *Pravara Vyayama Shakti* improved from 3.5% before treatment to 18.3% after treatment. The incidence of all the symptoms of *Tamak Swasa* decreased after treatment (p<0.05) (Table 2). Similarly the incidence of all cardinal signs and symptoms of bronchial asthma also reduced after the treatment (p<0.05) (Table 3).

There was significant increase in PEFR (Litre/Minute) after treatment [Mean (SD) being 334.85 (85.64)] as compared to baseline [Mean (SD) being

Table 1 — Demographic profile of the patients

Values are expressed as Mean (SD) or n (%)

Age	38.54 (10.721)
Sex	
Female	75 (52.8)
Marital Status	
Married	111 (78.2)
Socio-economic status	
Above poverty line	109 (76.8)
Below poverty line	33 (23.2)
Addiction	
Smoking	3 (2.1)
Tobacco	2 (1.4)
Alcohol	1 (0.7)
None	136 (95.8)
Sleep pattern	
Normal	31 (21.8)
Disturbed	111 (78.2)
Bowel habits	
Regular	103 (72.5)
Irregular	39 (27.5)
Allergens	
Dust	122 (93.8)
Moulds	1 (0.8)
Food	2 (1.5)
Others	5 (3.8)
Emotional stress	
Average	77 (54.2)
Moderate	63 (44.4)
Too much	2 (1.4)
Height (m)	2.64 (12.453)
Weight (kg)	60.34 (10.961)
Respiratory Rate (per minute)	19.66 (3.674)
Pulse Rate (per minute)	77.9 (6.948)
Sharirik Prakriti	
Vataja	8 (5.6)
Pittaja	5 (3.5)
Kaphaja	15 (10.6)
Vata-Pittaja	35 (24.6)
Vata-Kaphaja	3 (2.1)
Pitta-Kaphaja	72 (50.7)
Sannipataja	4 (2.8)

Table 2 — Assessment of Ayurvedic parameters before and after treatment

Ayurvedic parameters (n = 142)	Baseline	84th day	p-value
Ahara Shakti			
Pravara	13 (9.2)	46 (32.4)	
Madhayama	112 (78.9)	87 (61.3)	
Avara	17 (12.0)	9 (6.3)	
Vyayama Shakti			
Pravara	5 (3.5)	26 (18.3)	
Madhayama	122 (85.9)	114 (80.3)	
Avara	15 (10.6)	2 (1.4)	
Symptoms			
Getting relief only in sitting position	140 (98.6)	54 (38.0)	<0.001
Lack of taste	97 (68.3)	23 (16.2)	<0.001
Severe restlessness	105 (73.9)	13 (9.2)	<0.001
Fever	33 (23.2)	5 (3.5)	<0.001
Rattling sound in chest	140 (98.6)	62 (43.7)	<0.001
Severe cough	136 (95.8)	82 (57.7)	<0.001
Hoarseness of voice	110 (77.5)	64 (45.1)	<0.001
Difficulty in talking	96 (67.6)	30 (21.1)	<0.001
Sweating over forehead	80 (56.3)	14 (9.9)	<0.001
Gets repeated attacks of dyspnea	138 (97.2)	51 (35.9)	<0.001
Aggravation of symptoms on cloudy day	132 (93.0)	90 (63.4)	<0.001
Unable to sleep	119 (83.8)	38 (26.8)	<0.001
Rhinorrhoea	97 (43.7)	80 (56.3)	0.001
Exceedingly severe attack of dyspnoea causing suffocation	56 (39.4)	8 (5.6)	<0.001
Fainting during attack	39 (27.5)	26 (18.3)	0.011
Pain in lateral side of the chest	117 (82.4)	40 (28.2)	<0.001
Aggravation of symptoms on exposure of wind	117 (82.4)	71 (50.0)	<0.001
Difficulty in expectorating the phlegm and feels relieved after expectoration	88 (62.0)	14 (9.9)	<0.001
Aggravation of symptoms on intake of cold water	141 (99.3)	108 (76.1)	<0.001
Aggravation of symptoms in cold weather	141 (99.3)	134 (94.4)	0.016
Aggravation of symptoms on intake of food items that increase *kapha dosha*	139 (97.9)	126 (88.7)	0.002
Excessive thirst	89 (62.7)	34 (23.9)	<0.001
Relief in symptoms with rise in temperature (hot food intake or hot environment)	139 (97.9)	130 (91.5)	0.035
Eye balls are always prominent	30 (21.1)	4 (2.8)	<0.001
Dryness in mouth	47 (33.1)	10 (7.0)	<0.001
Vomiting	20 (14.1)	1 (0.7)	<0.001

Values are expressed as n (%), Compared using Mc-Nemar test, (*) A p-value of <0.05 has been considered as significant

Table 3 — Effect of the treatment on chief complaints

Sr. No.	Chief complaints (n = 142)	Baseline	84th day	p-value
1	Breathlessness	142 (100)	114 (80.3)	
2	Paroxysm of breathlessness	123 (86.6)	45 (31.7)	<0.001
3	Wheezing	140 (98.6)	58 (40.8)	<0.001
4	Cough	133 (93.7)	78 (54.9)	<0.001
5	Expectoration of sputum	123 (86.6)	54 (38.0)	<0.001
6	Tightness in the chest	124 (87.3)	39 (27.5)	<0.001
7	Skin allergy	9 (6.3)	1 (0.7)	0.008
8	Worsening of breathlessness in night	120 (84.5)	32 (22.5)	<0.001
9	Awakening in the night	126 (88.7)	34 (23.9)	<0.001

Compared using Mc-Nemar test
Values are expressed as n (%)
(*) p-value of <0.05 has been considered as significant.

301.70 (65.23)] (p<0.001) (Fig. 1). Similarly, FEV_1 (litres) improved significantly (p<0.001) after treatment [Mean (SD) being 2.12 (0.52)] as compared to baseline [Mean (SD) being 1.83 (0.48)] (Fig. 2).

The score of Asthma Control Questionnaire reduced significantly after treatment [Mean (SD) being 1.43 (0.64)] as compared to baseline [Mean (SD) being 2.95 (1.32)] (p<0.001) (Fig. 3). Further, significant decrease was also observed in the score of all domains of St. George Respiratory Questionnaire. Symptoms-related domain improved from [Mean (SD) being 69.43 (14.72)] at 84th day as compared to baseline [Mean (SD) being 70.86 (14.87)] (p=0.010); activity related domain also improved on 84th day [Mean (SD) being 26.78 (19.49)] as compared to baseline [Mean (SD) being 47.15 (26.19)] (p<0.001);

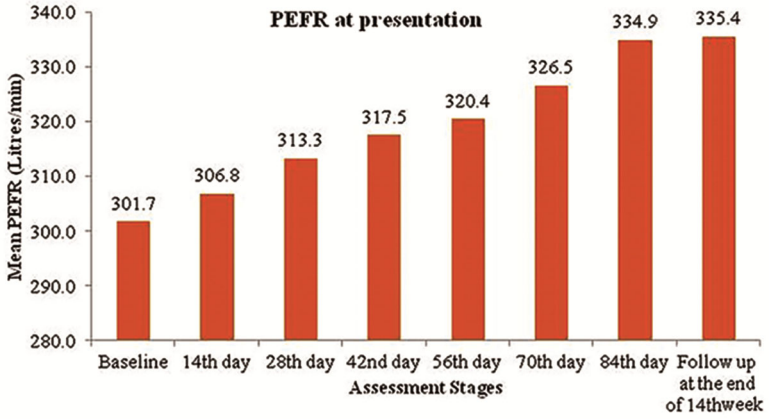

Fig. 1 — Effect of the treatment on PEFR (Ltr/min) at presentation

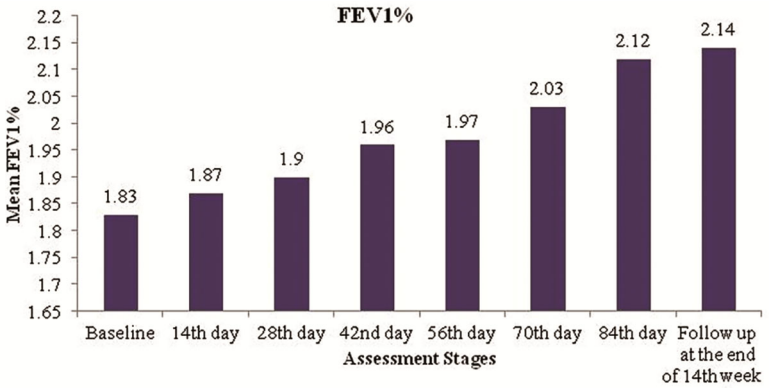

Fig. 2 — Effect of the treatment on FEV_1%

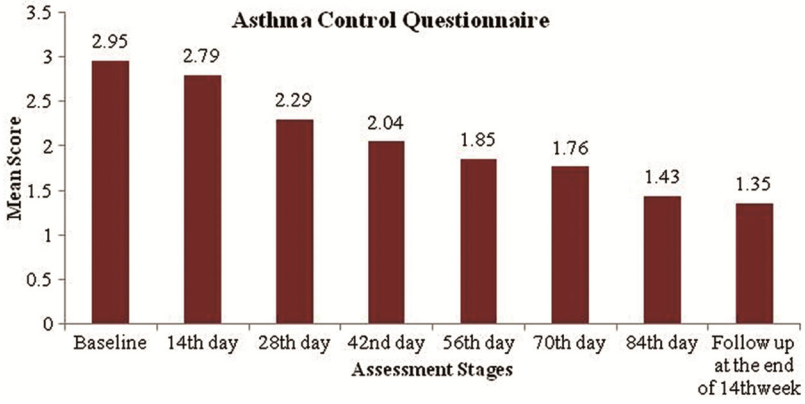

Fig. 3 — Effect of the treatment on Asthma Control Questionnaire

and score of impact related domain was [Mean (SD) being 20.76 (17.19)] on 84th day but was [Mean (SD) being 45.59 (21.09)] at baseline ($p<0.001$). The total score of the SGRQ after the treatment period also improved from [Mean (SD) being 30.74 (16.06)] at 84th day from [Mean (SD) being 50.46 (20.26)] at baseline ($p<0.001$) (Fig. 4 and Table 4).

The mean Absolute Eosinophil Count at baseline was [Mean (SD) being 506.5 cells/µL (767.88)] which reduced to [Mean (SD) being 480.7 cells/µL (1044.75)] ($p=0.522$) at 84 days. Though this change was not statistically significant, it is of clinical relevance as the change was in accordance with symptomatic relief observed among the patients.

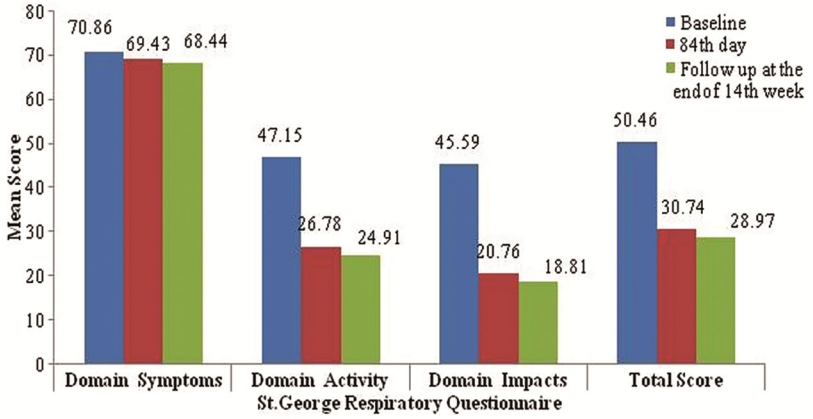

Fig. 4 — Effect of the treatment on St. George Respiratory Questionnaire

Table 4 — Effect of the treatment on outcome measures

Assessment Stage	PEFR at presentation (Litre/min.)	FEV_1 (Litre)	Asthma Control Questionnaire	St. George Respiratory Questionnaire			
				Domain symptoms	Domain activity	Domain impacts	Total score
Baseline	301.70 (65.23)	1.83 (0.48)	2.95 (1.32)	70.86 (14.87)	47.15 (26.19)	45.59 (21.09)	50.46 (20.26)
14th day	306.80 (85.11)	1.87 (0.51)	2.79 (2.26)				
28th day	313.31 (87.99)	1.90 (0.52)	2.29 (0.58)				
42nd day	317.51 (84.51)	1.96 (0.52)	2.04 (0.58)				
56th day	320.43 (81.15)	1.97 (0.49)	1.85 (0.60)				
70th day	326.49 (86.35)	2.03 (0.50)	1.76 (0.61)				
84th day	334.85 (85.64)	2.12 (0.52)	1.43 (0.64)	69.43 (14.72)	26.78 (19.49)	20.76 (17.19)	30.74 (16.06)
Follow up at the end of 14th week	335.43 (84.90)	2.14 (0.50)	1.35 (0.66)	68.44 (14.70)	24.91 (18.87)	18.81 (17.36)	28.97 (15.89)
$t-value	7.887	9.379	10.871	2.607	13.944	15.360	16.370
p-value	<0.001*	<0.001*	<0.001*	0.010*	<0.001*	<0.001*	<0.001*

Values are expressed as Mean (SD), $ Compared using paired t-test at baseline and 84th day, *p-value of <0.05 has been considered as significant.

Assessment of safety

No adverse events were reported throughout the study period. Further, 91% participants completed the study duration with more than 80% compliance to trial intervention. The statistical analysis of the safety parameters of 142 participants was done which showed that there were statistically significant differences in the values of some parameters after treatment. However, there was no clinically significant difference in any of the haematological and biochemical parameters. The small rise in mean haemoglobin was statistically significant [Mean (SD) at baseline 11.3 (2.69) and 11.6 (2.36) at 84th day] ($p<0.001$) because of large sample size. The Total Leucocyte Count decreased after treatment [Mean (SD) at baseline 8625.3 (1958.59) and 8167.5 (1667.78) at 84th day] ($p=0.007$). Similarly, serum creatinine value [Mean (SD) at baseline 0.85 (0.164) and 0.81 (0.196) at 84th day] ($p=0.007$) and SGOT value [Mean (SD) at baseline 21.9 (7.36) and 20.4 (6.37) at 84th day] ($p=0.026$) also decreased after treatment (Table 5).

Discussion

The findings related to the demographic distribution of the disease in this study are consistent with other reports. In a cross-sectional multi centre study conducted by the Global Asthma Network (GAN) to know the prevalence of symptoms of asthma in children and adults, it was reported that the mean age of adults was 37.6±6.4 years and 50.2% adults with bronchial asthma were females in India[15]. Further, the findings of socio-economic status of the study participants in the present study are also consistent with another study conducted to explore the factors associated with asthma and the contribution of those factors in socioeconomic inequality in the prevalence of asthma in India. This study is based on the descriptive statistics applied to the data from the 75th round of National Sample Survey (NSS),

Table 5 — Effect of the treatment on safety parameters

Lab parameters (n = 142)	Baseline	84th day	t-value$	p-value
Haemoglobin (g/dL)	11.3 (2.69)	11.6 (2.36)	3.918	<0.001*
TLC / cu.mm.	8625.3 (1958.59)	8167.5 (1667.78)	2.759	0.007*
ESR (mm at the end of 1st h)	27.3 (22.63)	24.6 (21.21)	1.518	0.131
Absolute Eosinophil Count (cells/µL)	506.5 (767.88)	480.7 (1044.75)	0.642	0.522
Blood Sugar Fasting (mg / dL)	83.4 (11.20)	83.4 (9.99)	0.021	0.983
Blood Urea (mg/dL)	20.6 (6.47)	20.4 (5.41)	0.329	0.742
Serum Uric Acid (mg/dL)	4.3 (1.14)	4.2 (0.95)	1.353	0.178
Serum Creatinine (mg/dL)	0.85 (0.164)	0.81 (0.196)	2.718	0.007*
SGOT (IU/L)	21.9 (7.36)	20.4 (6.37)	2.254	0.026*
SGPT (IU/L)	25.4 (13.16)	25.5 (11.47)	0.085	0.933
Total protein (g/dL)	7.17 (0.673)	7.24(0.803)	0.939	0.349
S. albumin (g/dL)	4.31 (0.373)	4.28 (0.444)	1.102	0.272
S. globulin (g/dL)	2.86 (0.659)	2.94 (0.536)	1.533	0.128
Conjugated Bilirubin (mg/dL)	0.21 (0.146)	0.42 (2.50)	0.992	0.323
Serum Alkaline Phosphatase (U/L)	144.7 (50.79)	147.9 (57.98)	0.870	0.386

Values are expressed as mean (SD), $Compared using paired t-test, *p-value of <0.05 has been considered as significant

collected by the National Sample Survey Organization (NSSO) during 2017-18 and reported that, asthma was more concentrated among individuals from higher socioeconomic status[16].

According to the summary of Group for the Respect of Ethics and Excellence in Science (GREES) Asthma Report, the outcome measures recommended for statistical and clinical interpretation while conducting clinical trials for anti-asthmatic drug development include symptoms, lung function, reduction in concomitant medication and exacerbations, quality of life and measures of inflammation[8].

The study results show consistent decrease in symptoms throughout the study period (Fig. 1 & 2). All the symptoms especially, paroxysm of breathlessness, wheezing, cough, expectoration of sputum, tightness in the chest, worsening of breathlessness at night, awakening in the night, reduced considerably at the end of study period. The mean score of ACQ improved by 51% after treatment. The lung function improved consistently till the treatment period as well as in the post treatment follow-up period (Fig. 3 & 4). There was 11% improvement in the mean PEFR and 16% improvement in FEV1 after treatment. The quality of life of the study participants improved by 39% after treatment, as per the mean difference of the total score of SGRQ-C. Mean Absolute Eosinophil Count decreased significantly after the treatment period. Even though, the average duration of illness of the study participants was 5.08 years, quality of life of the patients improved significantly after 84 days intervention of *Vyaghri Haritaki* as compared to baseline (Fig. 4). From the treatment history recorded at baseline and at each follow-up, it was observed that need for rescue medication in the form of conventional medicines like broncho-dilators, corticosteroids, anti-histaminics, etc. reduced greatly at the end of the study period. The haematological and biochemical parameters were also almost similar before and after the intervention period and no adverse event was observed during this study.

Vyaghri Haritaki has been previously explored for its effect on bronchitis[17] among children and adults. It was also proven beneficial in symptomatic improvement of patients of chronic sinusitis[18]. This efficacy can be attributed to the fact that almost all the ingredients of *Vyaghri Haritaki* are of *laghu* (action of creating lightness) and *ruksha* (action of increasing dryness), *Ushna veerya* (hot in potency) and *katu* (pungent taste) and *madhur vipak* (effects of sweet taste after digestion)[19]. The main ingredients of *Vyaghri Haritaki* are *Kantakari* (*Solanum xanthocarpum*) and *Haritaki* (*Terminalia chebula*) have been experimentally proven to have anti-tussive[20] activity and positive effect on airway dilation[21], anti-asthmatic effect[22], anti-inflammatory,[23] anti-allergic[24] and immune-modulatory[25] activities. The other herbal ingredients that are some spices and honey act as bio-availability enhancers[26] along with disease specific therapeutic effects[27].

So the results of the present study are encouraging and randomised controlled trials to evaluate the efficacy of *vyaghri haritaki* in chronic bronchial asthma may be designed.

Limitations

This is single arm study and so the observed effect of *Vyaghri Haritaki* on the disease condition cannot

be endorsed unless compared with control arm in a randomised clinical trial. However, tolerability and effect on critical variables of the disease condition can be inferred from the results of this study.

Conclusion

The classical Ayurveda medicine *Vyaghri haritaki* has shown significant improvement in lung function tests *viz.,* FEV1, PEFR along with subjective scores of symptoms. The drug was well tolerable by the patients of bronchial asthma. *Vyaghri Haritaki* is also effective in improving all the disease specific symptoms of bronchial asthma as well as *Tamaka Swasa*. Hence, this commonly prescribed Ayurvedic formulation may be further studied through randomised controlled trials with larger sample size to prove its efficacy in bronchial asthma.

Acknowledgement

The authors thank Dr. G K Swamy who contributed in smooth conduction of the study at one of the study centres. We are grateful to the technical teams (research fellows and office assistants) at all the study centres who helped in execution of trial. We also thank the drug cell for making the quality assured trial drug available. The authors are grateful to the heads of the study centres and former heads of the Council for their guidance and support during this study.

Funding

Central Council of Research in Ayurveda Sciences, under Ministry of AYUSH, Government of India, New Delhi

Conflict of Interest

All the authors declare that they have no conflict of interest. However, the authors are employees at the funding agency which is a Government organization.

Author Contributions

PD, BY, SK & RKR conceptualised the study, BY & RS designed the protocol, VBK & MNS did fund acquisition and execution of study, RKR, B & NS supervised the study execution, PM drafted and edited the manuscript, BY & RS reviewed and finalised the manuscript. All authors have contributed in the study inception, designing, execution, analysis and/or writing of manuscript. All the authors have reviewed and approved the manuscript prior to submission.

References

1 Singh S K, Gupta, J, Sharma, H, Pedgaonkar S P & Gupta N, Socio-economic correlates and spatial heterogeneity in the prevalence of asthma among young women in India, *BMC Pulm Med,* 20 (190) (2020). https://doi.org/10.1186/s12890-020-1124-z

2 World Health Organisation, Chronic Respiratory Diseases: Asthma, (20th May 2020). Available from https://www.who.int/ en/news-room/fact-sheets/detail/asthma (Accessed 16th April 2022)

3 Singh V, Despite barriers regular patient education programmes are increasing the acceptability of inhaler treatment, *The Global Asthma Report* 2018 (Global Asthma Network), (2018), p. 60. Available from http://globalasthmareport.org/management/india.php#:~:text=Despite%20barriers%2C%20regular%20patient%20education,facilities%20for%20rich%20and%20poor. (Accessed 16th April 2022)

4 International Institute for Population Sciences, India and ICF (India National Family Health Survey NFHS-4 2015-16, Mumbai, India), (2017) p. 345. Available at http://dhsprogram.com/pubs/pdf/FR339/FR339.pdf (Accessed 16th April 2022)

5 Ukena D, Fishman L & Niebling W B, Bronchial asthma: Diagnosis and long-term treatment in adults, *Dtsch Arztebl Int,* 105 (21) (2008) 385-394.

6 World Health Organisation, Chronic Respiratory Diseases: Asthma, (15th May 2020). Available from https://www.who.int/news-room/q-a-detail/chronic-respiratory-diseases-asthma (Accessed 16th April 2022)

7 Agarwal R, Dhooria S, Aggarwal A N, Maturu V N, Sehgal I S, *et al*., Guidelines for diagnosis and management of bronchial asthma: Joint ICS/NCCP (I) recommendations, *Lung India*, 32 (Suppl 1) (2015) p. S3-S42.

8 Holgate S T, Bousquet J, Chung K F, Bisgaard H, Pauwels R, *et al.,* Summary of recommendations for the design of clinical trials and the registration of drugs used in the treatment of asthma, *Respir Med*, 98 (6) (2004) 479-487.

9 Vora A C, Bronchial asthma, *J Assoc Physicians India*, 62 (3 Suppl) (2014) 5-6.

10 Anonymous, Madhavanidana (Rogavinischayam), 12th chapter 15th sloka, English translation by Prof Srikantha Murthy, (Choukamba orientalia, Varanasi), 2001, fourth edition.

11 Anonymous, Charaka Samhitha, 17th chapter 55th sloka, English translation by Bhagavandhas, R K Sharma (Choukhamba Sanskrit series, Varanasi) 2002, Third edition.

12 Anonymous, The Ayurvedic Pharmacopoeia of India e-book version, Part-II , Vol-1 3:6, (CCRAS, New Delhi), First edition

13 P M O'Byrne, H K Reddel, G Eriksson, O Östlund, S Peterson, *et al*., *Eur Respir J*, 36 (2) (2010) p. 269-276.

14 Meguro M, Barley E A, Spencer S & Jones P W, Development and validation of an improved COPD-specific version of the St George's Respiratory Questionnaire, *Chest* 132 (2006) 456-463

15 Singh S, Salvi S, Mangal D K, Singh M, Awasthi S, *et al*., Prevalence, time trends and treatment practices of asthma in India: The Global Asthma Network study, *ERJ Open Res,* 8 (2) (2022) 00528-2021.

16 Rashmi R, Kumar P, Srivastava S & Muhammad T, Understanding socio-economic inequalities in the prevalence

of asthma in India: An evidence from national sample survey 2017-18, *BMC Pulm Med*, 21 (1) (2021) 372.

17 Ram J P & Baghel M S, Clinical efficacy of Vyaghriharitaki Avaleha in the management of chronic bronchitis, *Ayu*, 36 (1) (2015) 50-55.

18 Dave P, Kunjal H, Vaghela D & Dhiman K S, Role of *Vyaghri Haritaki* Avaleha and Anu Taila Nasya in the management of *Dushta Pratishyaya* (Chronic Sinusitis), *Int J Ayurvedic Med*, 7 (1) (2016) 49-55.

19 Sreedharan A & Suryawanshi N, Review of evidence based study on *Vyaghri Haritaki* Avaleha with special reference to certain respiratory disorders, *Nat J Res Ayurved Sci,* 9 (1) (2021) 1-11.

20 Nosalova G, Jurecek L, Chatterjee U R, Majee S K, Nosal S, *et al*., Antitussive activity of the water-extracted carbohydrate polymer from *Terminalia chebula* on citric acid-induced cough, *Evid Based Complement Altern Med*, 2013 (650134) (2013). doi:10.1155/2013/650134

21 Duan S, Cui X Y, Wang X Y, Shan C B & Ma C M, Combination of *Ephedra sinica* stems and *Terminalia chebula* fruits produces new ephedrine derivatives in vivo that diminish the permeability to BBB while retaining airway dilation and hepatoprotective effects, *J Ethnopharmacol*, 285 (114837) (2022). doi: https://doi.org/10.1016/j.jep.2021.114837

22 Vadnere G P, Gaud R S & Singhai A K, Evaluation of anti-asthmatic property of *Solanum xanthocarpum* flower extracts, *Pharmacologyonline*, 1 (2008) 513-522.

23 More S K, Lande A, Jagdale P G, Adkar P & Ambavade S D, Evaluation of anti-inflammatory activity of *Solanum xanthocarpum* Schrad and Wendl (Kaṇṭakāri) extract in laboratory animals, *Anc Sci Life*, 32 (4) (2013) 222-226. doi:10.4103/0257-7941.131976

24 Singh O M & Singh T P, Phytochemistry of *Solanum xanthocarpum*: An amazing traditional healer, *J Sci Ind Res,* 69 (10) (2010) 732-740.

25 Aher V D, Immunomodulatory effect of alcoholic extract of *Terminalia chebula* ripe fruits, *J Pharm Sci Res*, 2 (9) (2010) 539-544.

26 Kesarwani K, Gupta R & Mukerjee A, Bioavailability enhancers of herbal origin: An overview, *Asian Pac J Trop Biomed*, 3 (4) (2013) 253-266.

27 Abbas A S, Ghozy S, Minh L H N, Hashan M R, Soliman A L, *et al*., Honey in bronchial asthma: From folk tales to scientific facts, *J Med Food*, 22 (6) (2019) 543-550.