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Anti-asthmatic effect of *Shirishadi* compound through nasal spray actuation

Divya Kajaria, Jyotishankar Tripathi[1], Shrikant Tiwari[1]

Department of Kayachikitsa, Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, [1]Department of Kayachikitsa, Ch. Brahm Prakash Ayurved Charak Sansthan, New Delhi, India

Abstract

Background: Increasing morbidity and mortality of Asthma placed it among the most dreaded diseases. Prediction says that asthma along with chronic obstructive pulmonary disease become third leading cause of death by the year 2020. Despite the availability of a wide range of antiasthmatic drugs, incidence of asthma is increasing alarmingly because the relief offered by these drugs is mainly symptomatic and short-lived. Moreover, their side effects are also quite distressing. Hence, a continuous search is needed to identify effective and safe remedies to treat bronchial asthma. **Aims:** The present clinical study was conducted to evaluate the efficacy of *Shirishadi* Polyherbal compound (given through nebulizer in Aerosol form) in the management of acute and chronic uncomplicated Bronchial Asthma and to propose a novel and safer Ayurvedic treatment modality. **Methods and Materials**: It is a randomized, open, control clinical trial in which the effect of the drug was compared with contemporary treatment and placebo medication (normal saline) in 60 adults with mild to moderate asthma. **Results:** There was a (t>0.001) found in pulmonary function tests (including FEV1, FVC and PEFR) in the group treated with polyherbal drug. Improvement remain constant in consecutive follow-ups signifies that there is no reverse broncho-constriction after discontinuation of the drug. **Conclusion**: This study signifies that polyherbal drug - *Shirishadi* compound may prove beneficial future alternative remedy for asthma, and its effect is similar to that of modern contemporary drug when given through nasal route.

Key words: Bronchial asthma, pulmonary functional test, *Shirishadi* polyherbal compound

Introduction

Asthma is a chronic disease characterized by recurrent attacks of breathlessness and wheezing, which vary in severity and frequency from person to person.[1] WHO estimates show that 300 million people currently suffer from asthma. Asthma deaths will increase in the next 10 years if urgent action is not taken.[2] Asthma cannot be cured, but proper diagnosis, treatment and patient education can result in good asthma control and management. Asthma occurs in all countries regardless of level of development. Over 80% of asthma deaths occur in low and lower-middle income countries. For effective control, it is essential to make medications affordable and available, especially for low-income families.[3,4]

Address for correspondence: Dr. Divya Kajaria,
Asst. Prof., Department of Kayachikitsa, Ch. Brahm Prakash Ayurved Charak Sansathan, Khera Dabar, Najafgarh, New Delhi - 110 073, India.
E-mail: divyakajaria@gmail.com

On the basis of similar clinical features, Bronchial Asthma can be correlated with *Tamaka Shwasa*, a disease described under the heading of five types of *Shwasa* in Ayurvedic classics. According to Ayurveda *Shwasa* is a *Kapha-Vataja* disease, which is originated from *Pittasthana*.[5] According to Ayurveda, formation of *Ama* is the seed for the development of future disease. The acute attack of disease appears whenever there is an obstruction of the normal passage of *Pranavayu*. Once the obstruction is removed, and *Vayu* start travelling in its normal path symptom, (breathlessness, cough etc.,) are abolished. Considering the Ayurvedic concept of treatment of *Tamaka Shwasa* it was decided to select an herbal Preparation "*Shirishadi* compound" for the management of bronchial asthma. The drug was decided to be given through nasal route followed by oral administration of the drug.

Administration of the drug through nasal route is known as *Nasya* in Ayurveda.[6] Ayurveda emphasis more on Nasal delivery of drug in diseases related to *Shira* and *Pranavaha Srotasa*. The channels carrying *Pranavayu* are known as *Pranavaha Srotasa*,

vitiation of *Pranavaha Srotasa* cause *Shwasa* (dyspnea). In the present trial, Nasal route of drug administration and its efficacy in the acute attack was assessed and compared with that of contemporary modern medicine. Desired to make some Ayurvedic preparation which is effective in controlling the acute attack of Asthma, having least toxic side effects, and efficacy equivalent to that of modern medicine inspire to plan the present research work.

Materials and Methods

Preparation of drug: *Shirishadi* compound

The plants *Albizia lebbeck* (L.) Benth., *Cyperus rotundus* Linn., and *Solanum xanthocarpum* Schrad and Wendl. were collected from the local market of Varanasi in equal quantity [Table 1]. Hydroalcoholic extraction (distilled water: ethanol = 2:1) of drugs was carried out by hot percolation method through Soxhlet apparatus. Thereafter, extracts were dried using a rotatory evaporator, and dried extract was again diluted to prepare a homogenous concentration of drug (1 mg/ml). Standardization of drug was done by using physical characterization, thin layer chromatography, and gas chromatography–mass spectrometry analysis.

Ayurvedic medication

For nebulization - Extract of *Shirishadi* compound 2.5 ml (1 mg/ml).
Oral drug - *Shirishyadi Ghana Vati* (500 mg).

Modern medication

For nebulization - a. Duoline (Levosalbutamol + Ipratropium Bromide) 2 mg in 1st sub group
b. Budecort 2 mg in 2nd sub group.
Oral drug - Tablet Deriphyllin Retard (115 + 35 mg).

Placebo therapy

For nebulization - Normal saline 2.5 ml
Oral drug - Sugar pills (inert placebo tablets).

Clinical trial

Human trial consist of Stage- I, II and III Clinical Study. The studies were carried out to determine the effective dose for the human being and to assess the safety and maximum tolerated dose in the human being.

Table 1: Contents of *Shirishadi* polyherbal compound

Name of the drug	Botanical name	Part used	Approximately quantity in 100 ml of extract (mg)
Shirisha	*Albizia lebbeck* (L.) Benth	*Twaka* (bark)	20
Nagarmotha	*Cyperus rotundus* Linn	*Kanda* (rhizome)	20
Kantkari	*Solanum xanthocarpum* Schrad and Wendl	*Panchanga* (whole plant)	20

Stage – I Clinical Study

For this study, five healthy individual were selected. 100 µl of water extract (prepared through decoction method) of *Shirishadi* mixture (*Shirishadi* Ayurvedic Nebulizer) dissolved in 1.5 ml of distilled water and was given twice in a day to five healthy individual for 5 days. Routine blood test, renal function test, and liver function test were done before and after administration of the drug.

No side effects as well as no abnormality in laboratory investigations was reported.

Stage-II Clinical Study

Multiple ascending dose determination study

Five patients of bronchial asthma were selected for this study and the drug was given in the following ascending doses:

- 100 µl of extract dissolved in 1.5 ml of distilled water B.D. for 2 days
- 200 µl extract dissolved in 1.5 ml of distilled water B.D. for 2 days
- 400 µl extract dissolved in 1.5 ml of distilled water B.D. for 2 days
- 600 µl extract dissolved in 1.5 ml of distilled water B.D. for 2 days
- 800 µl extract dissolved in 1.5 ml of distilled water B.D. for 2 days
- 1000 µl extract dissolved in 1.5 ml of distilled water B.D. for 2 days.

Followed by routine blood, renal function and liver function test. Spirometery and lung X-ray was also done.

Dose determination of drug

On the basis of results obtained from Stage II clinical study the dose of drug was decide as 5 mg/daily in two divided doses.

Stage-III Clinical Study

Total 60 cases of bronchial asthma aged 18 – 60 years were selected from Outdoor/Indoor patient department wing of Department of Kayachikitsa, Faculty of Ayurveda, IMS, BHU, Varanasi.

Exclusion criteria

Patients having bronchial carcinoma, emphysema, chronic pulmonary obstructive disease, pleural effusion, tuberculosis, cardiac asthma, status asthmatics were excluded.

Study Design

Randomized study (Simple Random Sampling/ Unrestricted Random Sampling).

Trial Methodology

Open clinical trial.

Grouping and posology

Total 60 clinically diagnosed patients of bronchial asthma were randomly divided into three groups:

Group 1

20 registered patients were administered *Shirishadi* Ayurvedic Nebulizer, 2.5 mg (2.5 ml) twice in a day for first 15 days and then S.O.S, followed by oral administration of *Shirishadi Ghana Vati* - 500 mg with lukewarm water, twice in a day for 1-month.

Group 2

20 registered patients divided into two sub groups (10 in each) and were given Duoline (Levosalbutamol + Ipratropium Bromide) 2 mg twice in a day in one group and 2 mg of Budecort twice in a day in another group for 15 days followed by oral administration of Tablet Deriphyllin Retard (115 + 35 mg), twice in a day for 15 days and then S.O.S.

Group 3

20 registered patients will be administered 2.5 ml normal saline twice in a day for 15 days and one sugar pill (inert sugar placebo tablet) twice day for 15 days and then S.O.S. In this group only mild asthmatic patient with no complication were chosen to avoid any discomfort for the patients.

Follow-up studies

- All patients of three groups were regularly followed once after 15 days for 45 days
- Improvement and other effects were noted down
- All patients were asked to undergo laboratory investigations before and after the treatment and during follow-up period.

Duration of trial

- Duration of nebulization: 15 days
- Duration of oral treatment: 30 days
- Total duration of treatment: 45 days.

Statistical analysis

One-way analysis of variance (ANOVA), *post-hoc* test, Chi-square, Friedman test, Paired *t*-test were applied. To assess the effect of drugs from the baseline to different follow-ups in qualitative variables increment in asymptomatic plus mild cases were undertaken.

Observations and Results

Effect of drug on dyspnea

Within the group, comparison by Friedman test shows a significant *P* value in G1 and G2 and between the group comparisons by Chi-square test shows significant *P* value in AT, F1 and F2. It's evident from the Table 2, that in G1, there is reduction in percentage of severe and agonizing cases from 42.4% and 26.3% (BT) to 26.3% and 5.3% (AT) and 15.8%, 5.3% at first follow-up (F1). In G2: Marked reduction is observed in the percentage of both severe and agonizing cases from 43.8% and 18.8% (BT) to 0.00%, which is greater than G1. Normal saline-treated group showed an increase in the percentage of severe and agonizing cases from 10.0% and 0.00% to 70.0% and 10.0%.

Effect of drug on cough

Within the group comparison by Friedman test shows a significant *P* value in G1 and G2 and between the group comparisons by Chi-square test shows significant *P* value in AT, F1, and F2. It's evident from the Table 3 that in G1, there is increase in percentage of asymptomatic cases from 0.00% (BT) to 15.8% (AT) with the reduction in moderate and severe cases from 47.4% and 36.8% to 21.1 and 10.5%, respectively. Marked reduction is observed in the percentage of both moderate and severe cases from 56.3% and 31.3% (BT) to 6.3% and 0.00% in G2. Normal saline-treated group showed increase in percentage of severe cases from 0.00% to 20.0% and reduction in percentage of moderate cases from 80.0% to 60.0% showing that severity of symptom increases after treatment with normal saline.

Effect of drug on expectoration

Within the group comparison by Friedman test shows a significant *P* value in G1 and G2 and between the group

Table 2: Effect of *Shirishadi* compound on dyspnea in bronchial asthma

Groups	Symptoms grading	Dyspnea Number of patients (%)				Within the groups comparison Friedman test
		BT	AT	F1	F2	
Group 1	Mild	0	0	1 (5.3)	1 (5.3)	χ^2=34.9
	Moderate	6 (31.6)	13 (68.4)	14 (73.7)	14 (73.7)	*P*<0.001
	Severe	8 (42.4)	5 (26.3)	3 (15.8)	3 (15.8)	
	Agonizing	5 (26.3)	1 (5.3)	1 (5.3)	1 (5.3)	
Group 2	Mild	0	5 (31.3)	5 (31.3)	5 (31.3)	χ^2=48.0
	Moderate	6 (37.5)	11 (68.8)	11 (68.8)	11 (68.8)	*P*<0.001
	Severe	7 (43.8)	0	0	0	
	Agonizing	3 (18.8)	0	0	0	
Group 3	Mild	1 (10.0)	0	0	0	
	Moderate	8 (80.0)	2 (20.0)	2 (20.0)	2 (20.0)	χ^2=4.00
	Severe	1 (10.0)	7 (70.0)	7 (70.0)	8 (80.0)	*P*=0.26
	Agonizing	0	1 (10.0)	1 (10.0)	0	*P*>0.05
Between the groups comparison Chi-square test		χ^2=10.7 *P*<0.05 df=4	χ^2=21.0 *P*<0.001 df=4	χ^2=22.4 *P*<0.001 df=4	χ^2=22.40 *P*<0.001 df=4	-

BT: Before treatment, AT: After treatment, F1: First follow-up, F2: Second follow-up

Table 3: Effect of *Shirishadi* compound on cough in bronchial asthma

Groups	Symptoms grading	Cough Number of patients (%)				Within the groups comparison Friedman test
		BT	AT	F1	F2	
Group 1	Absent	0	3 (15.8)	4 (21.1)	4 (21.1)	χ^2=42.48
	Mild	3 (15.8)	10 (52.6)	9 (47.4)	9 (47.4)	*P*<0.001
	Moderate	9 (47.4)	4 (21.1)	4 (21.1)	3 (15.8)	
	Severe	7 (36.8)	2 (10.5)	2 (10.5)	3 (15.8)	
Group 2	Absent	1 (6.3)	8 (50.0)	9 (56.3)	9 (56.3)	χ^2=43.64
	Mild	1 (6.3)	7 (43.8)	6 (37.5)	6 (37.5)	*P*<0.001
	Moderate	9 (56.3)	1 (6.3)	1 (6.3)	1 (6.3)	
	Severe	5 (31.3)	0	0	0	
Group 3	Absent	0	0	0	0	χ^2=4.38
	Mild	2 (20.0)	2 (20.0)	2 (20.0)	3 (30.0)	*P*=0.223
	Moderate	8 (80.0)	6 (60.0)	8 (80.0)	7 (70.0)	
	Severe	0	2 (20.0)	0	0	
Between the groups comparison Chi-square test		χ^2=1.73 *P*>0.05 df=4	χ^2=10.2 *P*<0.05 df=4	χ^2=11.2 *P*<0.05 df=4	χ^2=11.2 *P*<0.05 df=4	-

BT: Before treatment, AT: After treatment, F1: First follow-up, F2: Second follow-up

Table 4: Effect of *Shirishadi* compound on expectoration in bronchial asthma

Groups	Symptoms grading	Expectoration Number of patients (%)				Within the groups comparison Friedman test
		BT	AT	F1	F2	
Group 1	Absent	3 (15.8)	9 (47.4)	10 (55.6)	10 (52.6)	χ^2=27.38
	Mild	11 (57.9)	8 (42.1)	6 (33.3)	7 (36.8)	*P*<0.001
	Moderate	4 (21.1)	3 (10.5)	2 (11.1)	2 (10.5)	
	Severe	1 (5.3)	0	0	0	
	Severe	8 (44.4)	0	0	0	
Group 2	Absent	0	7 (43.8)	7 (43.8)	8 (50.0)	χ^2=46.63
	Mild	1 (6.3)	8 (50.0)	8 (50.0)	7 (43.8)	*P*<0.001
	Moderate	7 (43.8)	1 (6.3)	1 (6.3)	1 (6.3)	
	Severe	8 (50.0)	0	0	0	
Group 3	Absent	0	0	0	0	χ^2=9.00
	Mild	4 (40.0)	2 (20.0)	3 (30.0)	3 (30.0)	*P*=0.029
	Moderate	6 (60.0)	6 (60.0)	7 (70.0)	7 (70.0)	
	Severe	0	2 (20.0)	0	0	
Between the groups comparison Chi-square test		χ^2=10.3 *P*<0.05 df=4	χ^2=6.94 *P*>0.05 df=4	χ^2=9.25 *P*>0.05 df=4	χ^2=9.19 *P*>0.05 df=4	-

BT: Before treatment, AT: After treatment, F1: First follow-up, F2: Second follow-up

comparisons by Chi-square test shows significant *P* value in AT, F1, and F2. It's evident from the Table 4 that in G1, there is increase in percentage of asymptomatic cases from 15.8% (BT) to 47.4% (AT) with the reduction in moderate and severe cases from 21.1% and 5.3% to 10.5 and 0.00%, respectively. In G2, marked reduction is observed in the percentage of both moderate and severe cases from 43.8% and 50.0% (BT) to 6.3% and 0.00%. In G3, normal saline-treated group showed an increase in the percentage of severe cases from 0.00% to 20.0% and a reduction in the percentage of mild cases from 40.0% to 20.0%.

Effect of drug on wheezing

Within the group comparison by Friedman test shows a significant *P* value in G1 andG2 and between the group comparisons by Chi-square test shows significant *P* value in AT, F1, and F2 [Table 5]. In G1, there is increase in percentage of asymptomatic cases from 15.8% (BT) to 47.4% (AT) with reduction in moderate and severe cases from 21.1% and 5.3% to 10.5% and 0.00% respectively. In G2, marked reduction is observed in percentage of severe cases from 50.0% (BT) to 6.3% (AT), whereas percentage of moderate cases mildly

increase after treatment from 43.8% (BT) to 50.0% (AT), though the severity of symptom is greatly reduced in this group. In G3, normal saline-treated group showed increase in percentage of severe cases from 0.00% to 20.0% and reduction in percentage of mild cases from 40.0% to 20.0% showing that severity of symptom increases after treatment with normal saline.

Effect of drug on frequency of attack

Within the group comparison by Friedman test shows a significant *P* value in G1 and G2 and between the group comparisons by Chi-square test shows highly significant *P* value in AT, F1 and F2 [Table 6]. In G1, there is increase in percentage of asymptomatic and mild cases from 0.00% and 26.3% (BT) to 26.3% and 57.9% (AT) with the significant reduction in severe cases from 52.6% to 0.00%. In G2, there is increase in percentage of asymptomatic and mild cases from 0.00% and 18.8% to 56.3% and 43.8% with the significant reduction in percentage of moderate and severe cases from 43.8% and 37.8% to 0.00% and 0.00%. In G3, there is a mild

Table 5: Effect of *Shirishadi* compound on wheezing in bronchial asthma

Groups	Symptoms grading	Wheezing Number of patients (%)				Within the groups comparison Friedman test
		BT	AT	F1	F2	
Group 1	Absent	3 (15.8)	9 (47.4)	10 (55.6)	10 (52.6)	χ^2=48.0
	Mild	11 (57.9)	8 (42.1)	6 (33.3)	7 (36.8)	*P*<0.001
	Moderate	4 (21.1)	2 (10.5)	2 (11.1)	2 (10.5)	
	Severe	1 (5.3)	0	0	0	
	Severe	8 (44.4)	0	0	0	
Group 2	Absent	0	0	0	0	χ^2=45.17
	Mild	1 (6.3)	7 (43.8)	7 (43.8)	8 (50.0)	*P*<0.001
	Moderate	7 (43.8)	8 (50.0)	8 (50.0)	7 (43.8)	
	Severe	8 (50.0)	1 (6.3)	1 (6.3)	1 (6.3)	
Group 3	Absent	0	0	0	0	χ^2=6.00
	Mild	4 (40.0)	2 (20.0)	3 (30.0)	3 (30.0)	*P*<0.112
	Moderate	6 (60.0)	6 (60.0)	7 (70.0)	7 (70.0)	
	Severe	0	2 (20.0)	0	0	
Between the groups comparison Chi-square test		χ^2=10.9 *P*>0.05 df=4	χ^2=13.8 *P*<0.01 df=4	χ^2=16.8 *P*<0.01 df=4	χ^2=17.0 *P*<0.01 df=4	-

BT: Before treatment, AT: After treatment, F1: First follow-up, F2: Second follow-up

Table 6: Effect of *Shirishadi* compound on frequency of attack in bronchial asthma

Groups	Symptoms grading	Frequency of attack Number of patients (%)				Within the groups comparison Friedman test
		BT	AT	F1	F2	
Group 1	Absent	0	5 (26.3)	5 (26.3)	5 (26.3)	χ^2=53.48
	Mild	5 (26.3)	11 (57.9)	11 (57.9)	14 (73.7)	*P*<0.001
	Moderate	4 (21.1)	3 (15.8)	3 (15.8)	0	
	Severe	10 (52.6)	0	0	0	
Group 2	Absent	0	9 (56.3)	9 (56.3)	9 (56.3)	χ^2=40.76
	Mild	3 (18.8)	7 (43.8)	7 (43.8)	7 (43.8)	*P*<0.001
	Moderate	7 (43.8)	0	0	0	
	Severe	6 (37.5)	0	0	0	
Group 3	Absent	0	0	0	0	χ^2=6.00
	Mild	5 (50.0)	4 (40.0)	4 (40.0)	4 (40.0)	*P*=0.112
	Moderate	5 (50.0)	6 (60.0)	6 (60.0)	6 (60.0)	
	Severe	0	0	0	0	
Between the groups comparison Chi-square test		χ^2=3.47 *P*>0.05 df=4	χ^2=11.0 *P*<0.05 df=4	χ^2=11.0 *P*<0.05 df=4	χ^2=11.0 *P*<0.05 df=4	-

BT: Before treatment, AT: After treatment, F1: First follow-up, F2: Second follow-up

increase in the percentage of a moderate case after treatment with reduction in the percentage of mild cases.

Effect of drug on paroxysms of dyspnea

Within the group comparison by Friedman test shows a significant *P* value in G1 and G2 and between the group comparisons by Chi-square test shows highly significant *P* value in AT, F1 and F2. It's evident from the Table 7 that in G 1, there is increase in percentage of asymptomatic and mild cases from 0.00% (BT) to 84.2% and 15.8% (AT) with the reduction in moderate and severe cases from 26.3% and 73.7% (BT) to 0.00% (AT). In G2, there is an increase in the percentage of asymptomatic and mild cases from 0.00% and 0.00% to 62.5% and 37.5%. Significant reduction is observed in percentage of moderate and severe cases as 50.0% (BT) reduces to 0.00%. In G3, there is no significant observable change found in patients treated with normal saline.

Effect of drug on peak expiratory flow rate

The mean score of peak expiratory flow rate (PEFR) before treatment in G1, G2, and G3 was 120,138 and 141, respectively. There is highly significant increase in mean score after treatment in GI (210) and G2 (194), $P < 0.001$. There is a decrease in mean score of PEFR in Group 3 [Table 8]. Within the group comparison by Paired *t*-test shows a significant difference in mean score between BT-AT, BT-F1, AT-F1, and AT-F2, $P < 0.001$ in G1. In G2 significant difference is found in BT-AT, BT-F1, BT-F2, $P < 0.001$ with insignificant change in

Table 7: Effect of *Shirishadi* compound on paroxysms of dyspnea in bronchial asthma

Groups	Symptoms grading	Paroxysms of dyspnea Number of patients (%)				Within the groups comparison Friedman test
		BT	AT	F1	F2	
Group 1	Absent	0	16 (84.2)	17 (89.5)	17 (89.5)	χ^2=52.90
	Mild	0	3 (15.8)	2 (10.5)	2 (10.5)	*P*<0.001
	Moderate	5 (26.3)	0	0	0	
	Severe	14 (73.7)	0	0	0	
Group 2	Absent	0	10 (62.5)	10 (62.5)	6 (37.5)	χ^2=44.00
	Mild	0	6 (37.5)	6 (37.5)	8 (50.0)	*P*<0.001
	Moderate	8 (50.0)	0	0	2 (12.5)	
	Severe	8 (50.0)	0	0	0	
Group 3	Absent	0	2 (20.0)	0	0	χ^2=6.00
	Mild	5 (50.0)	5 (50.0)	7 (70.0)	7 (70.0)	*P*=0.112
	Moderate	3 (30.0)	3 (30.0)	3 (30.0)	3 (30.0)	
	Severe	2 (20.0)	0	0	0	
Between the groups comparison Chi-square test		χ^2=0.00 *P*>0.05 df=4	χ^2=26.5 *P*<0.001 df=4	χ^2=28.3 *P*<0.001 df=4	χ^2=31.3 *P*<0.001 df=4	-

BT: Before treatment, AT: After treatment, F1: First follow-up, F2: Second follow-up

Table 8: Effect of *Shirishadi* compound on PEFR in bronchial asthma

Groups	PEFR Mean±SD				Within the group comparisonpaired *t*-test				
	BT	AT	F1	F2	BT-AT	BT-F1	AT-F1	BT-F2	AT-F2
Group 1	120±38.0	210±69.6	207±65.6	197±61.8	90±58.4	87.3±54.9	77.6±49.7	2.63±9.3	12.3±13.3
					t=6.71	*t*=6.92	*t*=6.80	*t*=1.22	*t*=4.03
					P<0.001	*P*<0.001	*P*<0.001	*P*>0.05	*P*<0.001
Group 2	138±72.2	194±80.0	141±60.7	138±58.1	55.6±29.6	3.12±31.9	52.51±32.76	0.62±24.3	56.2±32.0
					t=7.50	*t*=0.39	*t*=6.41	*t*=0.10	*t*=7.02
					P<0.001	*P*>0.05	*P*<0.001	*P*>0.05	*P*<0.001
Group 3	141.0±44.3	134±48.9	134±48.8	131±43.8	6.5±10.5	7.0±9.48	0.50±6.85	10.0±11.54	3.50±14.5
					t=1.94	*t*=2.33	*t*=0.23	*t*=2.73	*t*=0.761
					P>0.05	*P*<0.05	*P*>0.05	*P*<0.05	*P*>0.05
Between the group comparison one-way ANOVA	*F*=0.44 *P*>0.05	*F*=2.12 *P*≥0.05	*F*=3.50 *P*≤0.05	*F*=3.15 *P*<0.05					
Post-hoc test significant pairs (*P*<0.05)	None	None	(1, 3) (2, 3)	(1, 3) (2, 3)					

BT: Before treatment, AT: After treatment, F1: First follow-up, F2: Second follow-up, PEFR: Peak expiratory flow rate, ANOVA: Analysis of variance, SD: Standard deviation

AT-F1, AT-F2, $P > 0.005$. In G5 insignificant change is found between BT-AT, BT-F1and BT-F2.

Between the groups comparison by one-way ANOVA shows insignificant *P* value in AT, whereas significant *P* value in F1 and F2. *Post-hoc* test shows significant pair (1,3), (2,3) in F1 and F2.

Effect of drug on forced vital capacity

The mean score of forced vital capacity (FVC) before treatment in G1 and G2 and G3 was 1.55, 1.18, and 1.07, respectively. There is a significant increase in mean after treatment in GI (2.16) and G2 (2.10), $P < 0.001$. There is an insignificant change in mean score of FVC found in Group 3.

Within the group comparison by Paired *t*-test shows a significant increase in mean score in FVC between BT-AT, BT-F2, $P < 0.001$ in G1. In G2 also a significant difference is found between BT-AT, BT-F1, BT-F2, AT-F1, and AT-F2, $P < 0.001$. In Group 5, insignificant change is found between BT-AT, BT-F1, and BT-F2.

Between the groups comparison by one-way ANOVA shows highly significant *P* value in AT, F1 and F2. *Post-hoc* test shows significant pair (1,3), (2,3) in AT, F1 and F2 [Table 9].

Effect of drug on forced expiratory volume

The mean score of forced expiratory volume in 1 s (FEV1) before treatment in G1, G2 and G3 was 1.45, 1.13, and 1.14, respectively. There is a significant increase in mean after treatment in GI (2.09), and G3 (1.60), $P < 0.001$. There is an insignificant change in mean score of FEV1 found in Group 3.

Within the group comparison by Paired *t*-test shows a significant increase in mean score in FEV1 between BT-AT, BT-F2, AT-F2, $P < 0.001$ in G1. In G2 also a significant difference is found between BT-AT, BT-F1, BT-F2, AT-F1, and AT-F2, $P < 0.001$. In Group 3 insignificant change is found between BT-AT, BT-F1, and BT-F2. Between the groups comparison by one-way ANOVA shows highly significant *P* value in AT, F1, and F2. *Post-hoc* test shows significant pair (1,3), (2,3) in AT, F1, and F2 [Table 10].

Discussion

The clinical studies on subjective, objective, and laboratory parameters have revealed that patients treated with Duoline and Budecort Nebulizer had shown significant improvement initially but after prolonged use the progress become constant along with the drug dependence. Moreover, patients treated with Budecort showed some side effects such as leg cramps, dizziness, palpitation, acidity, and nervousness. The most striking fact observed in patients treated with modern medicine was a high rate of recurrence in symptoms. After completion of the course of medicine, patient gets the symptom of the disease reappeared within 10–15 days. Moreover, no improvement was observed in recurrence of the attack on exposure to allergens.

In the patients of bronchial asthma, treated with Ayurvedic nebulizer statistically significant improvement on various parameters was recorded after the course of the therapy. The patients showed faster relief in symptoms with no apparent toxic effects. The improvement in pulmonary function remained constant even after 1-month of discontinuation of drugs, that is, there was no rebound broncho-constriction. There was ≥20% improvement in PEER, measured just after the administration of the drug. The group treated with Ayurvedic medicine showed significant improvement in PFT evidenced by marked increase in FEV1, FVC and PEFR.

According to Acaraya Charaka *Shirisha* (*A. lebbeck*) is best *Vishaghna* that is, it is best antitoxin. It is selected for its *Vishaghna* property. Acharya Charaka told that the indigested food act as a toxin in the body (*Amavisha*).[7] *Shirisha* is known for having antiallergic,[8] antihistaminic and mast cell stabilizing properties[9] anti-inflammatory[10,11] and antioxidant[12] activity for which it is selected. *Nagarmotha* (*C. rotundus*) is known as best *Samgrahaka*, *Deepana*, and *Pachana* drug.[13]

Table 9: Effect of *Shirishadi* compound on forced vital capacity in bronchial asthma

Groups	FVC Mean±SD				Within the group comparison paired *t*-test				
	BT	AT	F1	F2	BT-AT	BT-F1	AT-F1	BT-F2	AT-F2
Group 1	1.55±0.53	2.16±0.55	2.17±0.49	2.18±0.50	0.60±0.44	10.3±42.1	9.70±42.2	0.62±0.55	0.0016±0.27
					t=5.90	*t*=1.06	*t*=1.00	*t*=4.90	*t*=0.25
					P<0.001	*P*>0.05	*P*>0.05	*P*<0.001	*P*>0.05
Group 2	1.18±0.75	2.10±0.80	1.49±0.71	1.54±0.73	0.92±0.32	0.31±0.47	0.61±0.43	0.36±0.42	0.56±0.35
					t=11.4	*t*=2.50	*t*=5.71	*t*=3.4	*t*=6.26
					P<0.001	*P*<0.05	*P*<0.001	*P*<0.001	*P*<0.001
Group 3	1.07±0.53	1.03±0.48	1.04±0.43	1.02±0.45	0.003±0.13	2.70±0.16	0.001±7.47	0.004±0.17	0.0006±9.7
					t=0.914	*t*=0.50	*t*=−0.46	*t*=0.79	*t*=0.194
					P>0.05	*P*>0.05	*P*>0.05	*P*>0.05	*P*>0.05
Between the group comparison one-way ANOVA	*F*=1.00 *P*>0.05	*F*=6.63 *P*<0.001	*F*=0.88 *P*≤0.001	*F*=8.01 *P*<0.001					
Post-hoc test significant pairs (*P*<0.05)	None	(1, 3) (2, 3)	(1, 3) (2, 3)	(1, 3) (2, 3)					

BT: Before treatment, AT: After treatment, F1: First follow-up, F2: Second follow-up, ANOVA: Analysis of variance, SD: Standard deviation, FVC: Forced vital capacity

Table 10: Effect of *Shirishadi* Ayurvedic compound on FEV in bronchial asthma

Groups	FEV1 Mean±SD				Within the group comparison paired *t*-test				
	BT	AT	F1	F2	BT-AT	BT-F1	AT-F1	BT-F2	AT-F2
Group 1	1.45±0.60	2.09±0.61	2.06±0.63	1.9±0.60	0.61±0.48	0.58±0.50	0.003±0.12	0.50±0.50	0.10±0.12
					t=5.50	*t*=5.00	*t*=1.17	*t*=4.38	*t*=3.79
					P<0.001	*P*<0.001	*P*>0.05	*P*<0.001	*P*<0.001
Group 2	1.13±0.42	1.60±0.57	1.36±0.49	1.40±0.47	0.46±0.31	0.22±0.31	0.24±0.30	0.26±0.21	0.20±0.26
					t=5.9	*t*=2.8	*t*=3.13	*t*=3.5	*t*=3.07
					P<0.001	*P*<0.01	*P*<0.001	*P*<0.001	*P*<0.001
Group 3	1.14±0.51	1.10±0.49	1.09±0.54	1.16±0.42	0.003±0.009	0.004±0.22	0.002±0.14	0.0009±0.21	0.006±0.14
					t=1.2	*t*=0.62	*t*=–0.62	*t*=0.13	*t*=1.36
					P>0.05	*P*>0.05	*P*>0.05	*P*>0.05	*P*>0.05
Between the group comparison one-way ANOVA	*F*=2.39 *P*>0.05	*F*=5.31 *P*<0.001	*F*=6.50 *P*≤0.001	*F*=5.49 *P*<0.001					
Post-hoc test significant pairs (*P*<0.05)	None	(1, 3) (2, 3)	(1, 3) (2, 3)	(1, 3) (2, 3)					

*BT: Before treatment, AT: After treatment, F1: First follow-up, F2: Second follow-up, ANOVA: Analysis of variance, SD: Standard deviation, FEV1: Forced expiratory volume

It is also known to have antioxidant and anti-inflammatory properties.[14,15] *Kantakari* (*S. xanthocarpum*) is a potent drug used in the ailment of *Pranavaha Srotas Dusti* (*Shwasa*, *Kasa*). It has potent bronchodilator effect[16] with antimicrobial[17] and anti-inflammatory[18,19] properties. *Shirishadi* compound is mainly selected to evaluate the anti-allergic property of the drug and its action in atopic asthma and according to Ayurveda it is supposed to act on *Rasagata Ama*, increase the *Rasagni*.

As there was no significant change found in patients treated with normal saline, it can be said the effect produced by Ayurvedic drug was existent and not apparent or placebo effect. Reduction in erythrocyte sedimentation rate and eosinophil count was more prominent when the drugs was given through oral route than nasal administration of drug, suggesting that systemic effect of the drugs was more effective when given through oral route.[20]

Conclusion

It can be concluded that polyherbal compound *Shirishadi* has potent antiasthmatic activity. It can be further concluded that this polyherbal compound can be used as "Therapeutic Agents" in the management of an acute attack of asthma as well as chronic persistent asthma. The trial gives a direction for searching new route of herbal drug administration. In spite of limitations, the present study conducted entirely from the new angle. The study has yielded several useful observations and result which would definitely open new vistas for the future research workers of Ayurveda in general and respiratory disorders as particular.

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हिन्दी सारांश

नेजल स्प्रे प्रवर्तन के माध्यम से शिरीषादि योग का एण्टी अस्थमेटिक प्रभाव

दिव्या काजरिया, ज्योतिशंकर त्रिपाठी, श्रीकांत तिवारी

लगातार बढ़ती हुयी अवस्थादर एवम् मृत्युदर ने ब्रोंकियल अस्थमा को भयानक/खतरनाक व्याधियों की श्रृखंला में शामिल कर दिया है। अनुमानों के अनुसार २०२० तक ब्रोंकियल अस्थमा एवम् COPD विश्व की तीसरी सबसे द्यातक व्याधि होगी। यद्यपि ब्रोंकियल अस्थमा के उपचार हेतु विस्तृत श्रृखंला में आधुनिक दवाईयाँ उपलब्ध हैं, तथापि इसका प्रसार एवम् व्यापकता बढ़ती जा रही हैं, जिसका मुख्य कारण सम्भवतः ये है कि इन दवाइयों का प्रभाव मुख्यतः लाक्षणिक एवम् तत्कालीन होता हैं। इसके साथ ही इन दवाईयों से होने वाले दुष्प्रभाव भी काफी तकलीफ देहक होते हैं। अत एव ये अत्यन्त आवश्यक है कि ब्रोंकियल अस्थमा के उपचार हेतु एक प्रभावी एवम् सुरक्षित उपचार की खोज की जाये। उपस्थित नैदानिक अध्ययन का मुख्य उद्देश्य शिरीषादि योग का प्रयोग (Aerosol के रूप में Nebulizer के द्वारा किया गया) तीव्र एवम् चिरकारी उपद्रव रहित ब्रोंकियल अस्थमा में उपयोगिता की जाँच करना है। एवम् एक नवीन तथा सुरक्षित उपचार विधि को प्रस्तावित करना भी है। यह एक Randomised, open placebo-control अध्ययन है जिसमें कि शिरीषादि योग की उपयोगिता की तुलना Placebo (Normal Saline) एवम् आधुनिक औषधियों से की गयी हैं। इस अध्ययन के लिये कुल ६० रोगियों का चयन किया गया था जो कि Mild से Moderate ब्रोंकियल अस्थमा से पीडित थे। उपस्थित नैदानिक अध्ययन में जिन रोगियों का उपचार शिरीषादि योग से किया गया था, उनके Pulmonary Function tests (FEV, FVC PEFR सम्मिलित) में Significant (P>0.001) सुधार पाया गया। एवम् ये सुधार सभी Follow-ups में भी स्थाई बने रहे। जिससे ये सुनिश्चित होता है कि दवाई छोड़ने के बाद भी फिर से broncho-constriction नहीं हुआ। इस अध्ययन से ये सिद्ध होता है कि शिरीषादि योग का उपयोग ब्रोंकियल अस्थमा के उपचार हेतु आधुनिक दवाईयों के समान ही लाभकारी सिद्ध हो सकता हैं।