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EFFICACY OF *BHARANGIMOOLA ARKA* NEBULIZATION IN *TAMAKA SHVASA* (ACUTE EXACERBATION OF BRONCHIAL ASTHMA) - A CASE SERIES STUDY

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Abstract : ***Background:*** *Tamaka Shvasa*(~Bronchial asthma) is a disorder which is manifested due to the vitiation of humor *Prana Vata* . Being a disease which requires an emergency management, an effort is put forth to give an immediate relief through administering *Bharngimoola Arka* nebulization. ***Objectives:*** The main aim of the study was to assess the efficacy of *Bharangimoola Arka* nebulization in reducing the symptoms of *Vegavasta* of *Tamaka Shvasa* (Acute exacerbation of Bronchial Asthma). ***Materials and Methods:*** It was an open label, single center, prospective, clinical study conducted in 30 patients of acute exacerbation of Bronchial Asthma. Nebulization with 5ml of *Bharangimoola Arka* was administered 8th hourly for 3 times. Results: There was statistically highly significant difference in breathlessness (Z = -4.820, *p*= 0.000) after treatment. Breathlessness was reduced in 27, increase in none and no change in 3 patients. FVC% improvement was recorded as highly significant with Mean BT 1.64 and Mean AT 2.03 which is statistically highly significant (t = -5.857, p<0.05). FEV_1% improvement was recorded as highly significant with Mean BT 1.41 and Mean AT 1.67 which is statistically highly significant (t = -5.090, p<0.05). ***Conclusion:*** This study provides good evidence which shows the significant effect of Bharangimoola *Arka* in reducing the symptoms like Breathlessness, Wheeze and Cough etc in Acute exacerbation of Bronchial asthma.

Keywords: *Arka*, *Ayurveda*, *Bharangimoola*, Bronchial asthma, *Clerodendrum serratum* (Linn.), Nebulization, *Tamaka Shvasa*.

INTRODUCTION

Tamaka Shvasa is one among five variety of *Shvasa* which manifests due to predominant of *Kapha –Vata Doshas*. [5] During the state of attack, dyspnoea becomes so severe, that patient feels as if he is entering into darkness and hence called *Tamaka*. Its prevalence of the same is increased over the past two decades is due to pollution, rapid environment changes, adaptation of newer dietetic preparation and tremendous psychological stress.[1] It is estimated around 15-20 million people are asthmatics and it was seen as one of the leading cause of morbidity and mortality in rural India.[2]

Among different treatment modalities, the administration of drug is through nasal route, as *Nasya* and using the drug in the form fumes as *Dhoomapana*.[3] Present day the management of acute stage of the same is done by Nebulization, which is a process that involves suspension of fine vaporized liquid droplets in air otherwise known as aerosol.[4]This study is carried out with the same aspire to establish the efficacy of herbal preparation in acute Exacerbation of Bronchial Asthma. The drug *Bharangi* (*Clerodendrum serratum Linn.*) possesses *Ushna Veerya* by which it pacifies both *Kapha* and *Vata.* [6] In *Arka Prakasha*, *Bharangimoola* is mentioned as drug of choice for *Tamaka Shvasa* in the form of *Arka*.[7] It is a aromatic plant from which aqueous extract of active principles can be taken out easily. After conducting pilot study using different medicated *Arka* like *Vasa* (*Adhatoda vasica*), better

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efficacy was observed from *Bharngimoola Arka*, so this study is up taken.

MATERIALS AND METHODS

After taking consent from institutional ethical clearance and the written consent from the patients with acute presentation were recruited from IPD unit of general medicine, SDM College of Ayurveda and Hospital, Hassan through purposive sampling. The self structured proforma consisting of clinical symptoms of *Tamaka Swasa* and Acute Exacerbation in Bronchial Asthma as per criteria mentioned in GINA-Global Initiation for Asthma are administered to the patients to include into the study. [8]

Assessment criteria:

Clinical features of patients were assessed before and after three episodes of Nebulization. Grading for the signs and symptoms is as follows

0 – No symptoms, 1 – Mild – while walking, can lie down, 2 – Moderate- while at rest, prefers sitting, 3 – Severe –while at rest, sits upright.

Spirometry parameters were observed before and after Nebulization.

Inclusion & Exclusion criteria:

Patients with mild-moderate acute exacerbation, who are conscious and well oriented, of both gender and age between 16 – 60 years were included for study. Whereas the patients with severe exacerbation, emphysema, chronic airway limitation, with history of tuberculosis and cardiac involvement, other complicated respiratory diseases having any organic lesion such as tumor or any anatomical defect in airway, cyanosis and uncontrolled hypertension and diabetes mellitus were not included for the study.

Method of Preparation of Drug:

Required quantity of water is added to the root of drug for soaking and kept it overnight. Next day morning it is poured into the *Arka Yantra* (~distillation apparatus) and boiled after adding remaining water. The vapor generated is condensed and collected in a receiver, which was stored in amber colour bottle.

INTERVENTION

Patients with acute exacerbation were given with 5ml *Bharangimoola Arka* in the form of Nebulization 8th hourly for three times. The dose of 5 ml was fixed on the basis of pilot study conducted in 20 patients. Pre and post Spirometry and peak expiratory flow rate was measured.

Spirometry parameters were observed before and after the 1st dose of nebulization. Peak expiratory flow rate was observed before and after 2nd and 3rd dose of nebulization. Both Spirometry and Peak expiratory flow rate were recorded after 20 min of administration of nebulization and clinical features of patients were assessed before and after 3 episodes of Nebulization(NHLBI, Fig 3-11).

STATISTICAL METHODS

Analysis of data is done by statistical package for social sciences, (SPSS) version 20. Completed 30 patients were taken for statistical analysis. Wilcoxon signed rank test is done to analyze the significance of change in Subjective parameters. For objective parameters repeated measures ANOVA was done for analyzing the significance of change. Paired t test was done for analyzing the significance of some of the objective parameters

OBSERVATIONS AND RESULTS

1. In study 43.3% of patients were in the age group of 16-26 years. The sample includes 33.3% labor workers, 26.7% Students. 23.3% were of housewives. 10% and 6.7% are professionals and business men respectively.

2. In the present study, 70.0% of patients have aggravation of symptoms due to smoke, 90.0% due to dust and 80.0% were recorded by seasonal changes. Where as it is observed that in the present study 50% of the patients found relief for the symptoms due to the change of the climate, 43.3% are in sitting posture and 26.7% due to intake of hot water.

3. In the present study, maximum of 66.7% patients were recorded having history of illness within 5 years. Out of total 30 patients, 43.3% of patients were recorded as duration of attack between 7 days to 1 month, maximum of 43.3% of patients have the time of occurrence of attack during early morning hours.

4. Statistically significant reduction was observed in following symptoms, breathlessness ($Z = -4.820$, $p = 0.000$, $n=27$), wheeze ($Z = -$

4.772, *p*= 0.000, n=25), difficulty in speech (Z = -3.207, *p*= 0.001, n=11), cough (Z = -3.051, *p*= 0.002, n=10), sputum production (Z = -2.236, *p*= 0.025, n=5) and chest tightness (Z = -3.873, *p*= 0.000, n=15) **(Table 1)**

5. Following is the effect of therapy on pulmonary function test and related parameters:

A repeated measures ANOVA with a Greenhouse – Geisser correction determined that mean PEFR has been increased significantly after treatment {F (1.679, 48.702) = 9.839, p < 0.05}. Post hoc tests using the Bonferroni correction 0.008 revealed that treatment elicited an increase in PEFR from 1st dose BT(Before treatment) to 1st dose AT(After treatment) (3.213 vs. 3.803, respectively), from 1st dose AT to 2nd dose BT (3.803 vs. 3.055, respectively), from 2nd dose BT to 2nd dose AT (3.055 vs. 3.622, respectively), from 2nd dose AT to 3rd dose BT (3.622 vs. 3.238, respectively) and from 3rd dose BT to 3rd dose AT (3. 238 vs. 3.878, respectively) which was statistically highly significant. On comparing the effect of treatment in between treatments it was found that treatment was statistically significant after each episodes of nebulization. **(Table 2,3)**

Statistically highly significant improvement observed in all parameters of Spirometry (Pulmonary Function Test). FVC% improvement was recorded which is significant with Mean BT 1.64 and Mean AT 2.03 which is statistically highly significant (t = -5.857, p<0.05). FEV_1% improvement was recorded as highly significant with Mean BT 1.41 and Mean AT 1.67 which is statistically highly significant (t = -5.090, p<0.05). **(Table 4)**

DISCUSSION

The disease which is produced due to aggravation of all the three *Dosha* as a result of specific etiological factors, which is difficult to cure and can kill a patient instantaneously is the reference available under disease *Shvasa*. This disease originates from the site of *Pitta*, and is caused by the simultaneous aggravation of *Kapha*

Table 1: Effect of therapy on signs and symptoms of *Tamakashvasa.*

Parameters	Negative Rank			Positive Rank			Ties	N	Z value	P value	R
	N	MR	SR	N	MR	SR					
Breathlessness |BT – AT	27	14.00	378.0	0	.00	.00	3	30	-4.820	.000	HS
Wheeze BT – AT	25	13.00	325.0	0	.00	.00	5	30	-4.772	.000	HS
Speech BT – AT	11	6.0	66.0	0	.00	.00	19	30	-3.207	.001	S
Cough BT – AT	10	5.50	55.0	0	.00	.00	20	30	-3.051	.002	S
Sputum production BT – AT	5	3.00	15.00	0	.00	.00	25	30	-2.236	.025	S
Chest tightness BT – AT	15	8.00	120.00	0	.00	.00	15	30	-3.873	.000	HS

(a) BT Before treatment (b) AT – After treatment (c) HS – highly significant (d) S – Significant (e) NS – not significant
(f) N – total number g) MR – mean rank (h) SR – sum of ranks (i) Wilcoxon Signed Rank Test (Post hoc) (J) R-Remark

Table 2: Effect of Therapy on PEFR in *Tamakashvasa* Patients

Parameters	N	Mean	GREEN HOUSE - GEISSER			Green house – geisser Error df	Remarks
			Df	f value	p value		
PEFR 1st DOSE BT	30	3.213	1.679	9.839	.001	48.702	HS
PEFR 1st DOSE AT		3.803					
PEFR 2nd DOSE BT		3.055					
PEFR 2nd DOSE AT		3.622					
PEFR 3rd DOSE BT		3.238					
PEFR 3rd DOSE AT		3.878					

HS – highly significant, df – degree of freedom, Repeated Measures ANOVA, BT – before treatment, AT – after treatment

Table 3:.Pair wise comparison for PEFR at different intervals of treatment

Parameters		Mean difference	P value	Remarks
PEFR 1st DOSE BT	PEFR 1st DOSE AT	-.591	.002	S
PEFR 1st DOSE AT	PEFR 2nd DOSE BT	.748	.021	NS
PEFR 2nd DOSE BT	PEFR 2nd DOSE AT	-.566	.000	HS
PEFR 2nd DOSE AT	PEFR 3rd DOSE BT	.383	.000	HS
PEFR 3rd DOSE BT	PEFR 3rd DOSE AT	-.639	.000	HS

(a). PEFR – Peak expiratory flow rate (b). HS – highly significant (c). df – degree of freedom, Repeated Measures ANOVA, (d). N – total number (e). BT – before treatment (f). AT – after treatment

Table 4: .Effect of therapy on Spirometry parameters in *Tamaka shvasa* Patients.

Parameters	Mean BT	Mean AT	Mean difference	SD	SE	't' value	'p' value	Remark
FVC %	1.64	2.03	-0.39	0.361	0.066	-5.857	.000	HS
FEV1 %	1.41	1.67	-0.26	0.278	0.051	-5.090	.000	HS

HS – highly significant b) NS – not significant c) BT – before treatment d) AT – after treatment e) SD – standard deviation f) SE – standard error g) FVC- forced vital capacity h) FEV1- forced expiratory volume in 1 second

Table 5: Results of standardization parameters for *Bharangimoola Arka*

Parameter	Results n = 3 %w/w
Specific gravity	0.998
Viscosity	1.00793
Refractive Index (At 32ºC)	1.3317
Volatile Matter	0.02
pH	6.73
Boiling Point	102º-103ºC

and *Vayu*. If this is not properly treated at appropriate time or if the patient indulges in unwholesome regimens during the disease being exacerbated become fatal like the deadly snake-venom.

This can manifest either in *Vega* or *Avega Avastha***,** in this study has been taken with the aims of evaluating efficacy of *Bharangimoola Arka* Nebulization in reducing the symptoms of acute exacerbation of the same.

As per a study in allied sciences Nebulization therapy in acute stage of asthma is more beneficial as lung has larger surface area which increases rate of absorption and drug delivery of proteins derivative in lung tissue is more active.

Here 17 patients were under oral allopathic medicine and 13 patients were using the inhalers. Among them 6 patients are using nebulization for 1 year and 5 patients were using more than 5 years respectively. Common complaints observed on regular usage of nebulaization are tiredness, loss of appetite and tremors.

There is some limitation of using drugs from other system such as, the side effects are related to plasma concentrations of theophyline are nausea, vomiting, and headaches due to PDE inhibition and at higher concentrations to cardiac arrhythmias and seizures due to adenosine A_1-receptor antagonism.[9]

It was an open label, single center, prospective, clinical study conducted in 30 patients of acute exacerbation of Bronchial Asthma. In 16 to 26 years age group patients are prone to indulge in irregular dietary habits which leads to the hampering of the *Agni* in the site of *Pitta*, in turn results in formation of *Ama* (undigested material) causing vitiation of *Kapha* leading to difficulty in breathing. Many of the patients were employees, agriculturists and other type of workers like carpenter, driver etc are having the high risk of exposure to dust, irregular dietary habits which is known to produce respiratory diseases. Most of the females in this study were housewives, who also have exposure to house dust and also presented with history of habit of day sleep.

In this disease *Vata* moving in the reverse order and pervades the channels afflicts the neck and head, and stimulates *Kapha* to cause following signs and symptoms due to obstruction. Hence the therapies will be beneficial which causes downward movement of *Vata*, as the snow melts over the creepers in the mountain range on account of the hot rays of the sun, the stable *Kapha* in the body gets dissolved on account of the heat generated by oliation and fomentation therapies.

That liquefied *Kapha* should be eliminated by administering emesis therapy[10]. And also the residual *Dosha* which are still remained in channels can be eliminated by the administering medicated fumes[11].

As modification of Nebulization with 5ml of *Bharangimoola Arka* was administered 8 hourly for 3 times. On observation the number of patients who got the attacks after 1st episode of nebulization is 13 patients, but the number of patients after 2nd dose of nebulization is 20. The time duration between the administration of each nebulization was fixed to 8 hours, for some of the patients (n=) who had got attack within 8 hours, another episode of nebulization had been administered prior to the time, considering the time of medication for *Tamaka Shvasa* as *Muhur Muhu*.

The symptom breathlessness, tightness of chest, wheeze and cough was reduced significantly (p value =.000. (p value .002) N= 30) respectively after nebulization by facilitating the movement of *Pranavayu* by liquefies the tenacious sputum in the *Srotus*(channels).

*S*tatistically significant (p value .001) reduction in speech difficulty was observed by controlling the *Vega Avastha* of *Tamaka Shvasa*.

The initial mean score of PEFR, FVC & FEV1 is 3.213, 1.64, and 1.41 respectively and is increased to 3.878, 2.03, and 1.67. These values show marked improvement after the treatment. It suggests significant reduction in airway obstruction. [12]

The photochemical compounds present in the root of *Clerodendrum serratum (Linn.)* on preliminary test have proven to be positive for Carbohydrates, Phenolics, Tannins and Terpenoids. Generally, among carbohydrates components D-mannitol has been found in the roots of the Plant in many of the earlier studies. [13]

The phenolic compound, Tannins and Terpenoids have the anti inflammatory action in Asthma which have been proved previously [14]. The bronchial tubes become swollen and narrowed and mucus is secreted into the tubes from glands in the walls of the tubes. Inflammation of the bronchial tubes and their plugging with mucus makes difficulty in breathing. It is well known that acute inflammation of the bronchial tubes occurs during the Asthma attacks. Since the *Bharangimoola (Clerodendrum serratum (Linn.))* contains the phyto chemical constituents like Phenols, Tannins and Terpenoids, when it is administered into lung field directly by nebulization, due to its Anti Inflammatory action succeed to restrict the underlying pathology instantly.(Table 5) The anti-inflammatory effects of phenolic compounds are related to the ability in modulating the expression of pro-inflammatory genes, such as NOS, cyclooxygenase, lipoxygenase but also by acting throughout nuclear factor (NF-êB) signaling and mitogen-activated protein kinase and activating the Nrf2/Keap1 pathway. [15]

In another way oxidative stress initiates a number of pathologic processes, including airway inflammation and also in exacerbation of pulmonary disease. The role of any particular phenolic antioxidant is directly associated with the capacity of the hydrogen radical donation from the phenolic group and the presence of an unpaired electron in the aromatic ring. The ethanolic root extract of *C. serratum* showed significant anti-inflammatory activity in carrageenan - induced oedema in rats, and also in the cotton pellet model in experimental mice, rats and rabbits at concentrations of 50, 100 and 200 mg/kg.[16]

Also Terpenoids are also responsible for anti-inflammatory activity; rarely it can also cause allergic reactions. Also Icosahydropicenic Acid (IHPA) a new pentacyclic triterpenoid saponin was first isolated from roots of *Bharangi*. IHPA at the dose of 100mg/kg showed significant showed significant protection of mast cell degeneration (59.62%) as compared to standard sodium cromoglycate (64.48%). The compound also revealed significant inhibitory activity on histamine induced gout tracheal chain preparation.[17]

Presence of Saponin and D mannitol processing of antihistamine and anti allergic effect respectively, Apigenin-7-glucoside(flvaonide) acts as anti inflammatory and antimicrobial agent which all constituents of Bharngi Moola.[18]

Phytochemisty of root was observed in a study was presence of Saponins, D-mannitol, Stigmasterol, olinolic acid, quaretaroic acid, Serratagenic acid, sitosterol, Clerosterol identified as 5, 25-stimastedien -3b 0, Clerodone as 3b – hydroxyl-lupan12-one, B –sitosterol, Lupenol, A steroidal glycoside, Pphytosterols, Ferulic acid, Arabinose, Scutellatin, Baicalein, Serratin and Urosolic acid.[19] However in present study the interpretation of the GCMS graph of Arka was not fulfilled, further study can be carried out for detecting the chemical constituents present in the *Bharangimoola Arka*. And also to know the

prolonged action and also side effects of the drug, on long term usage study can be carried out in larger samples in near future.

CONCLUSION

The *Bharangimoola Arka* Nebulization has shown significant effect on symptoms like breathlessness and wheeze, & moderate effect on symptoms like cough, chest tightness and speech. Even though *Bharangimoola Arka* administration is indicated internally, it has proved its efficacy in the mode of nebulization. According to the severity of exacerbation repeated administration of the medicine caries a value. The administration of *Bharangimoola Arka* is proved to be safe as it didn't show any side effects for any of the patients during the study.

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