COMPARATIVE STUDY ON THE SUBSTITUTES USED IN AYURVEDA WITH SPECIAL REFERENCE TO SUBSTITUTES FOR PUSHKARAMULA (*INULA RACEMOSA* HOOK.F.) VIZ., KUSHTA (*SAUSSUREA LAPPA* DECNE.) AND ERANDAMULA (*RICINUS COMMUNIS* L.); A CLINICAL STUDY

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ABSTRACT

Ayurvedic literature introduced several substitutes for the herbs which are either not available or which are not accessible for various reasons. On review of more than 35 texts and their commentaries it is found that there are more than 350 substitutes in the Ayurvedic texts from ancient to modern times. Kushta is known to therapeutics since Vedic period (2000 BC). Puskaramula and Erandamula were introduced to Ayurvedic Materia Medica by Agnivesa (500 BC). While mentioning the substitutes of Pushkaramula, Yogaratnakara quoted Kushta and Erandamula as the substitutes. Earlier author studied the pharmacognostical similarities between the three plants. Therefore, in the present study it is decided to conduct a comparative study using the root powders of these three herbs in subjects (n=90) suffering with Tamaka Swasa (Bronchial Asthma) divided into three groups. The results are suggestive that all the trial herbs have comparable therapeutic benefits in the subjects of Tamaka Swasa. While Kushta and Puskaramula have chemical as well as therapeutic similarity, Erandamula and pushkaramula shared only therapeutic similarity though chemically dissimilar. This paper emphasizes the need for the identification of cost effective substitutes basing on the text in place of endangered or extinct medicinal plants.

Key Words: Pushkaramula; Kushta EM = Erandamula

INTRODUCTION

‘Ayurveda’ - the knowledge of life sciences is full in medical knowledge. The chronology of Samhita granthas, Sangraha granthas, Yoga granthas and Nighantu granthas reflect the Ayurveda of respective times. On careful review we come across gradual increase in number of herbs used. In the process of adding new herbs, some confusion is also added in the form of multiple synonyms, multiple varieties etc. This has led to the controversy in the identity of some herbs. More over, migration of Vaidas from forest areas to the urban areas resulted in dependancy upon shepherds and forest dwellers etc for the medicinal plants. Later, the controversy increased because, various people dwell in different areas with different cultures might have used the same name to denote different herbs. Thenceforth, substitutes as well as controversial herbs made their way into traditional practice. Where ever there is an availability issue or a cost issue, physicians were trying for suitable alternative.

Seers like Bhavamisra (16 AD) and Yogaratnakara (17 AD) did try to establish the comprehensive list of substitutes (Abhavapratinithi Dravyas or Alabdhapratinithi Dravyas) along with certain guidelines for substitution. However, in the present scenario (2005) Prevention of Food Adulteration Act 1954 considers **substitute** as the synonym for **adulterant**. For example, usage of *Carum carvi* for *Cuminum cyminum* or vice versa will attract the charges of Adulteration/Substitution. Therefore the author prepared a comprehensive data-base on the substitutes delineated in the Ayurvedic Texts¹ and decided to study the comparative clinical effects at least one original herb vs substitute(s). Hence the present study on the comparative clinical efficacy of the substitutes for Puskaramula / PM (*Inula racemosa* Hook. f.) viz., Kushta / KS (*Saussurea lappa* (Decne.) C.B.Clarke.) and Erandamula / EM (*Ricinus communis* L.)²⁶. Author earlier studied and reported the chemical similarity

between PM (*Inula racemosa* Hook. f.) and KS (*Saussurea lappa* CB Clarke)². It is also noted that Yogaratnakara mentioned both KS and EM as substitutes for PM. But, EM (*Ricinus communis* Linn.) neither has chemical similarity nor therapeutic similarity with PM. Therefore, it is decided to find out the comparative therapeutic benefits of these three herbs in a common indication like Tamaka Swasa (Bronchial Asthma) to test the concept of substitution. The comparative properties of the three trial herbs are provided in the table 1a.

Review of literature on the pharmacological similarities of trial herbs

The similarity in the pharmacological activity of the trial herbs is provided in Table 1b. All the three herbs have a common activity i.e., anti-inflammatory activity.

Review of Disease (Asthma) literature

Asthma is defined as a chronic inflammatory disorder of the airways characterized by reversible airflow obstruction causing cough, wheeze, tightness in the chest and breathlessness. Asthmatics fall between the ranges of 100 to 150 million people around the globe. The highest prevalence is reported from China and Malaysia. Worldwide deaths from this condition have reached over 180,000 annually. As per WHO Fact sheets, India has an estimated 15-20 million of asthmatics.¹³

It is estimated that, 2.5% of adults have a clinical diagnosis of asthma. In case of children, the asthma figures rose to 15% with an episode of wheezing characteristic within the previous year, 5% of them diagnosed as suffering from asthma, 1% with severe disabling asthma. It is useful to classify asthma as early-onset or extrinsic asthma, which occurs usually in atopic children and resolves in 80%. Late-onset asthma or idiopathic non-atopic adult asthma is chronic in the majority of cases.¹²

It is produced by the inflammation of the bronchial wall involving eosinophils, mast cells and lymphocytes, together with the cytokine and inflammatory products of these cells, inducing hyper-sensitiveness of the bronchi so that they narrow more readily in response to a wide range of stimuli. In brief, asthma may be described as presenting with either of the following three stages viz., air limitation, air-way hyper-responsiveness & airway inflammation.

The principles for the management of patients with asthma, according to the guidelines of British Thoracic Society and International Consensus Report on the Diagnosis and Management of Asthma is as follows:

- Avoidance - measures to be taken to prevent/ reduce exposure to allergic agents.
- Hyposensitisation - subcutaneous injection of extracts of allergens (single allergen only). This form of therapy has largely been banned in Britain.

Management of Chronic persistent asthma

Inhaled corticosteroids are the most effective and widely used form of anti-inflammatory therapy for use in patients with asthma. Metered Dose Inhaler (MDI) is widely used technique to administer the bronchodilators or corticosteroids. In spite of different drugs and measures, neither there is a single oral agent, which will reduce the frequency of asthma attacks/ episodes nor an effective non-steroidal respiratory anti-inflammatory drug in the modern pharmacology.

On the other hand it is noticed that several traditional / indigenous herbal drugs are being successfully used in the management of bronchial asthma and are found to be of some definite advantage viz.,

- Avoidance of side-effects of corticosteroids
- Enhancement of immunity
- Relief from symptoms/ frequent episodes for a longer time.
- Better compliance.

Ayurvedic texts quoted Bronchial Asthma as Svasa or Tamakasvasa. This condition is denoted as a result of exposure to dust, clouds etc along with other causative factors. This is caused by vata obstructed by kapha in the pranavaha srotas. Tamakasvasa if associated with fever is called as Pratamaka while without fever is called as Samtamaka i.e., Chronic Bronchitis and Chronic Allergic Bronchial Asthma respectively. This condition is claimed to be yapya according to Caraka. The treatment includes Virecana and Nasya under Sodhana procedures. Several Samana dravyas like Yastimadhu, Vasa, Kantakari, Puskaramula, kustha etc were found in the texts.

MATERIAL & METHODS

The powdered samples of the roots of Pushkaramula (*Inula racemosa*), Kushta (*Saussurea lappa*) and Erandamula (*Ricinus communis*) have formed the materials for the study while 90 subjects (divided into 30 subjects in each group) suffering from Tamaka Swasa (Bronchial Asthma) have formed the subjects [in the age group of 16-65 years] of the present study.

Aims & objectives of the study

Primary – To evaluate the comparative efficacy of Puskaramula and its substitutes Kustha and Erandamula in the management of Tamakasvasa (Bronchial Asthma).

Secondary – Symptomatic relief from Bronchial Asthma & Clinical improvement in the condition of the patients after using the trial drugs for 12 weeks.

Study Design

- Open, Labeled, comparative, Randomized
- Prospective clinical trial

Subject recruitment and screening

Study Subjects - Mild to moderate Chronic Allergic Bronchial Asthma (NAEPP1997 revised guidelines) Subjects belonging to both the sex.

Recruitment The Subjects were recruited from the OPD of Sri Dhanwantary Ayurvedic College & Hospital, Chandigarh and Seth Tarachand Hospital, Pune.

Inclusion & Exclusion criteria for study subjects

Inclusion criteria

- Subjects having mild to moderate Chronic Allergic Bronchial Asthma (NAEPP 1997 revised guidelines) belonging to both sex (atopic & non-atopic) are eligible.
- Subjects capable of understanding and signing an informed consent.
- Subjects between 16 to 65 years.
- Subjects medically stable and with normal LFT, RFT and Haemogram values.
- Subjects should not be in acute attack of Bronchial Asthma.

Exclusion criteria

- Subjects suffering from very severe/very chronic form of asthma
- Subjects with concurrent pulmonary disease (pulmonary hypertension, cystic fibrosis, sarcoidosis, bronchiectasis, hypersensitivity pneumonitis, restrictive lung disease etc.)
- Pregnant or Lactating mothers and females planning to get conceived in near future.
- Subjects suffering from any psychological condition that will influence the conduct of the study or interpretation of results.
- Subjects with systemic diseases, like diabetes mellitus, venereal diseases and HIV.
- Subjects not willing to sign informed consent
- Subjects not willing to come for follow-up when required
- Subjects participating in any other clinical trials.

Therapeutic or Clinical end points

Therapeutic End Points: Treatment with the trial drugs for 12 weeks with or without improvement in the clinical condition of trial subjects.

Clinical End Points

- Relief of symptoms of Bronchial Asthma.
- Decrease in the frequency of attack.
- Decrease in the background modern medicines like Bronchodilators/steroids.

Dosage Schedule

All the trial drugs were given in a dose of 2.5 g b.i.d. (with or without modern standard Tt) with honey thrice in a day.

Parameters for the Assessment of safety & efficacy

Safety parameters LFT, RFT, Haemogram

Efficacy parameters**Subjective**

- Global Asthma Control Score
- QoL assessment

- VAS score (subject as well as physician evaluation)

- Assessment symptoms of Asthma (viz., dyspnoea, cough & wheezing)

Objective

- IgE
- AEC
- Spirometry

Table 1a: Properties of trial drugs²⁶

Properties	Puskaramula	Kustha	Eradamula
Rasa	Katu, Tikta		Katu, Tikta
Guna	Usna, Tiksna, Laghu, Snigdha		Usna, Tiksna, Laghu, Snigdha
Virya	Usna	Usna	Usna
Vipaka	Katu	Katu	Katu
Prabhava	Hrdya	Vrsya	Vrsya
Karma	Kapha-vatahara, Hikkani-grahana, Svasahara, Kasahara, Jvarahara, Sophaghna	Vata-kaphahara, Kusthaghna, Sukrala, Kanduhara, Svasahara, Rasayana	Kapha-vatahara, Jvarahara, Sophaghna
Indications	Hricchula, Hrdroga, Parsvasula, Hikka, Svasa, Kasa, Sotha & Jvara	Vatarakta, Visarpa, Kushta, Swasa, Kasa, Vataroga	Vataroga, Sotha, Jvara
Part used	Root (Mulam)	Root (Mulam)	Root (Mulam)
Dosage	2.5 - 5 g of powder	2.5 - 5 g of powder	2.5 - 5 g of powder
Anupana	Honey	Honey	Honey

Table 1b: Pharmacological activities of trial drugs¹⁸

Activity	Puskaramula	Kustha	Eradamula
Anti-inflammatory activity	Extracts shown significant anti-inflammatory activity against exudative phase of inflammation when tested against carrageenin induced rat paw oedema (Singh, N. et al., 1976).	--	Root extract investigated against carrageenin, 5-hydroxytryptamine (5HT)-, dextran-, bradykinin- and prostaglandin E1 (PGE1)-induced rat hind paw oedema. Extract (0.15 g/kg) given orally 2 hr before injection of above phlogistic agents exhibited anti-inflammatory activity against all the agents except PGE1; efficacy of extract was: carrageenin > bradykinin > 5-HT > dextran (Indian J. Pharmacol. 1990, 22, 239).
Bronchodilatory activity	Alcoholic extract showed marked protective effect against bronchospasm induced by histamine, 5-HT, Zea maize, Holoptelia and Acacia arabica. The extract blocked the contraction induced by both histamine and 5-HT and the response was graded in nature (50, 100 & 150 mg/ml of the bath solution). Inula has similar antispasmodic effect on rat uterus as seen as guinea pig ileum. It blocked the response of different doses (0.05, 0.1, 0.2, & 0.4 mg/ml) of 5-HT in the dose range of 50 - 200 mg/ml.	Delactonized oil and some lactone fractions of the oil exhibited spasmolytic and broncho-dilatory effects (Chopra, 1958; Dutta, 1960).	
Anti-histamine activity	The aqueous alcoholic extract of the roots was found to have potent anti-5-HT- and antihistamine activities as revealed by blockade of histamine - induced contractions of isolated tracheal chain of guinea pig. The drug also offered marked protection against bronchospasm induced by histamine. 5-HT and pollens of Zea maize, Holoptelia sp., and A. arabica in guinea pigs. The beneficial effects of L. racemosa in bronchial asthma appear to be due to its anti-histaminic, anti-5-HT and antiallergic properties.	Alkaloids from root have a strong inhibitory effect on histamine-induced bronchospasm and intestinal spasm in guinea pigs. Chemical extracts from this herb have antispasmodic, bronchodilatory, and blood pressure lowering effects similar to, but weaker than papaverine (Oxygen for life, 1997).	--

Table 2: Number of Male and Female Subjects in the study

	Male	Female
Number	46	44
Percentage	51.11%	48.89%

Table 3: Mean Age of Each group involved in the study

Group	Avg age	SD
Gr 1	39.43	(+) 13.85
Gr 2	47.03	(+) 13.93
Gr 3	43.57	(+) 14.60
	43.34	(+) 13.81

Table 4: Effect of kustha on IgE

IgE	Present (%)	Absent (%)
Before Treatment	73.33 (n=22)	26.67 (n=8)
After Treatment	26.67 (n=8)	73.33 (n=22)

Table 5: Effect of erandamula on IgE

IgE	Present (%)	Absent (%)
Before Treatment	63.33 (n=19)	36.67 (n=11)
After Treatment	30 (n=9)	70 (n=21)

Table 6: Effect of puskaramula on AEC

AEC	Present (%)	Absent (%)
Before Treatment	73.33 (n=22)	26.67 (n=8)
After Treatment	36.67 (n=11)	63.33 (n=19)

Table 7: Effect of kustha on AEC

AEC	Present (%)	Absent (%)
Before Treatment	63.33 (n=19)	36.67 (n=8)
After Treatment	30 (n=9)	70 (n=21)

Table 8: Effect of erandamula on AEC

AEC	Present (%)	Absent (%)
Before Treatment	73.33 (n=22)	26.67 (n=8)
After Treatment	10 (n=3)	90 (n=27)

Table 9: Effect of puskaramula on severity of asthmatic attack

Asthmatic Attack	Severity %		
	Mild	Moderate	Severe
Before Treatment	20	60	20
After Treatment	86.67	13.33	00

Table 10: Effect of kustha on severity of asthmatic attack

Asthmatic Attack	Severity %		
	Mild	Moderate	Severe
Before Treatment	23.33	63.33	13.33
After Treatment	83.33	16.67	00

Table 11: Effect of puskaramula on severity of asthmatic attack

Asthmatic Attack	Severity %		
	Mild	Moderate	Severe
Before Treatment	26.67	53.33	20
After Treatment	86.67	13.33	00

Table 12: Spirometric evaluation of trial subjects

Parameter	Group 1	Group 2	Group 3
FEV ₁			
Before treatment	2.44 + 0.54	2.27 + 0.38	2.32 + 0.27
After treatment	2.43 + 0.53	2.20 + 0.40	2.29 + 0.28
PEF			
Before treatment	6.54 + 1.38	6.18 + 1.26	6.28 + 1.26
After treatment	6.67 + 1.33	6.26 + 1.32	6.25 + 1.27
FVC			
Before treatment	3.53 + 1.01	3.56 + 1.31	3.52 + 1.30
After treatment	3.24 + 0.77	2.92 + 0.55	2.98 + 0.53
FEV ₁ /FVC			
Before treatment	0.72 + 0.15	0.70 + 0.18	0.71 + 0.17
After treatment	0.76 + 0.08	0.76 + 0.08	0.75 + 0.07

Table 13: Reduction in usage of Inhalers etc in Group 1

Use of Inhalers	Yes (%)	No (%)
Before Treatment	60	40
After Treatment	23.33	76.67

Table 14: Reduction in usage of Inhalers etc in Group 2

Use of Inhalers	Yes (%)	No (%)
Before Treatment	66.67	33.33
After Treatment	20	80

Table 15: Reduction in usage of Inhalers etc in Group 3

Use of Inhalers	Yes (%)	No (%)
Before Treatment	70	30
After Treatment	16.67	83.33

Chart 1: Number of male & female patients in the study

Chart 2

Chart 3

Chart 4

RESULTS

Total 105 subjects belonging to both sexes, between the age group of 16-65 years were recruited into the study through randomization chart 35 each into three groups (Group-1, Group-2 & Group-3). Out of them, 90 subjects who completed the total study duration (3 months) 30 subjects in each group were finally assessed for understanding the comparative effect of the respective herbs in each group. There were 44 females and 46 males (vide Table 2 & Chart 1). The mean age of the completed subjects (n=90) is 43.34 years (+3.81) - (vide Table 3).

The mean age (both male and female together) of Group 1 is 39.43 years (+ 13.85), while that of Group 2 is 47.03 years (+ 13.93) and that of Group 3 is 43.57 years (+ 14.60).

Out of 90 subjects in three groups together, there were 16, 14 and 16 male in Group 1, 2 and 3 respectively while female were 14, 16 and 14 respectively in Group 1, 2 and 3. The mean age of male subjects in Group 1 is 36.69 years (+ 14.86) while that in Group 2 is 45.57 years (+ 15.24) and that in Group 3 is 39.38 years (+ 14.66). The mean age of female subjects in Group 1 is 42.57 years (+ 9.79) while that in Group 2 is 47.50 years (+ 13.75) and that in Group 3 is 46.71 years (+ 13.12).

Comparative Effect of Trial Drugs on Symptoms of Bronchial Asthma

Dyspnoea (breathlessness)

Dyspnoea was present in 90 % (n = 27) of subjects in **Group 1** at the baseline. After 12 weeks of drug administration the presence of dyspnoea was reduced and found to be present in 26.67% (n = 8) of subjects. But severity of symptom is considerably reduced in all the subjects who were administered with the interventional drug.

Dyspnoea was present in 86.67 % (n = 26) of subjects in **Group 2** at the baseline. After 12 weeks of drug administration the presence of dyspnoea was reduced and found to be present in 20% (n = 6) of subjects. But severity of symptom is considerably reduced in all the subjects who were administered with Puskaramula.

Dyspnoea was present in 93.33 % (n = 27) of subjects in **Group 3** at the baseline. After 12 weeks of drug administration the presence of dyspnoea was reduced and found to be present in 23.33% (n = 7) of subjects. But severity of symptom is considerably reduced in all the subjects who were administered with kustha.

Scoring of Dyspnoea on VAS

When the severity of Dyspnoea was scored over a 10 points Visual Analogue Scale, It was found that at baseline the mean score was 7 (+ 1.37), which was reduced to 2 (+1.10) after administration of trial drug in group-1 for 12 weeks. The

reduction in the severity was found to be statistically significant ($p < 0.001$).

When the severity of Dyspnoea was scored over a 10 points Visual Analogue Scale, It was found that at baseline the mean score was 7 (+ 1.33), which was reduced to 2 (+1.10) after administration of trial drug in group-2 for 12 weeks. The reduction in the severity was found to be statistically significant ($p < 0.001$) in all the three groups.

When the severity of Dyspnoea was scored over a 10 points Visual Analogue Scale, It was found that at baseline the mean score was 7 (+ 1.33), which was reduced to 2 (+1.10) after administration of trial drug in group-3 for 12 weeks. The reduction in the severity was found to be statistically significant ($p < 0.001$) in all the three groups.

There is a significant change between the baseline mean score and VAS score at the end of the study in each group ($p < 0.001$). However, the VAS score does not show significant variation when a comparison is made between the three groups ($p > 0.01$). That means there was intra group significance but not inter group significance. Almost all the groups showed comparable efficacy on dyspnoea. The details are present in Chart 2.

Cough

Cough was present in 80 % ($n = 24$) of subjects in **Group 1** at the baseline. After 12 weeks of drug administration the presence of dyspnoea was reduced and found to be present in 13.33% ($n = 4$) of subjects. But severity of symptom is considerably reduced in all the subjects who were administered with the interventional drug.

Cough was present in 73.33 % ($n = 22$) of subjects in **Group 2** at the baseline. After 12 weeks of drug administration the presence of dyspnoea was reduced and found to be present in 10% ($n = 3$) of subjects. But severity of symptom is considerably reduced in all the subjects who were administered with the interventional drug.

Cough was present in 70 % ($n = 21$) of subjects in **Group 3** at the baseline. After 12 weeks of drug administration the presence of dyspnoea was reduced and found to be present in 10% ($n = 3$) of subjects. But severity of symptom is considerably reduced in all the subjects who were administered with the interventional drug.

The percentage of relief from cough in three groups is statistically as well as clinically significant when comparison is made between baseline and end of the study ($p < 0.001$ in each group). However, there was no significant difference between the groups in percentage of relief ($p > 0.05$) showing that all the three interventional drugs have similar effect or comparable effect.

Wheezing

Wheezing was present in 90 % ($n = 27$) of subjects in **Group 1** at the baseline. After 12 weeks of drug administration the presence of dyspnoea was reduced and found to be present in 26.67% ($n = 8$) of subjects. But severity of symptom is considerably reduced in all the subjects who were administered with the interventional drug.

Wheezing was present in 86.67 % ($n = 26$) of subjects in **Group 2** at the baseline. After 12 weeks of drug administration the presence of dyspnoea was reduced and found to be present in 20% ($n = 6$) of subjects (Vide Table 15). But severity of symptom is considerably reduced in all the subjects who were administered with Puskaramula.

Wheezing was present in 93.33 % ($n = 27$) of subjects in **Group 3** at the baseline. After 12 weeks of drug

administration the presence of dyspnoea was reduced and found to be present in 23.33% ($n = 7$) of subjects. But severity of symptom is considerably reduced in all subjects who were administered with kustha.

The percentage of relief from wheezing in three groups is statistically as well as clinically significant when comparison is made between baseline and end of the study ($p < 0.001$ in each group). However, the difference between the groups in percentage of relief is non significant ($p > 0.05$) showing that all the three interventional drugs have similar effect or comparable effect.

Effect of trial drugs on Serum IgE

Serum IgE was found elevated in 53.33 % ($n = 16$) of subjects in **Group 1** at the baseline. After 12 weeks of drug administration the IgE levels were found elevated in 33.33% ($n = 10$) of subjects. The mean average of serum IgE at baseline and end of the study was found to be 553.23 (+ 215.51) IU/mL and 279.11 (+188.97) IU/mL respectively ($p < 0.001$).

Serum IgE was found elevated in 73.33 % ($n = 22$) of subjects in **Group 2** at the baseline. After 12 weeks of drug administration the IgE levels were found elevated in 26.67% ($n = 8$) of subjects (Vide Table 4). The mean average of serum IgE at baseline and end of the study was found to be 490.13 (+ 221.4) IU/mL and 231.19 (+121.54) IU/mL respectively ($p < 0.001$).

Serum IgE was found elevated in 63.33 % ($n = 19$) of subjects in **Group 3** at the baseline. After 12 weeks of drug administration the IgE levels were found elevated in 30% ($n = 9$) of subjects (Vide Table 5). The mean average of serum IgE at baseline and end of the study was found to be 435.55 (+ 270.48) IU/mL and 224.76 (+159.88) IU/mL respectively ($p < 0.001$).

The mean reduction of IgE in all the three groups is statistically as well as clinically significant when comparison made between the values at baseline and at end of the study ($p < 0.001$ in each group). However, there was no significant difference between the groups in percentage of relief ($p > 0.05$) showing that all the three interventional drugs have similar or comparable effect Vide: Chart 3).

Effect of trial drugs on AEC

The AEC was found elevated in 73.33 % ($n = 22$) of subjects in **Group 1** at the baseline. After 12 weeks of drug administration, the AEC was found elevated in 36.67 % ($n = 11$) of subjects (Vide Table 6). The mean average of AEC at baseline and end of the study was found to be 647.10 (+ 176) /Cmm and 341.00 (+100) /Cmm respectively ($p < 0.001$).

The AEC was found elevated in 63.33 % ($n = 19$) of subjects in **Group 2** at the baseline. After 12 weeks of drug administration, the AEC was found elevated in 30 % ($n = 9$) of subjects (Vide Table 7). The mean average of AEC at baseline and end of the study was found to be 621.30 (+ 173) /Cmm and 390.80 (+186) /Cmm respectively ($p < 0.001$).

The AEC was found elevated in 73.33 % ($n = 22$) of subjects in **Group 3** at the baseline. After 12 weeks of drug administration, the AEC was found elevated in 30 % ($n = 9$) of subjects (Vide Table 8). The mean average of AEC at baseline and end of the study was found to be 624.40 (+ 161) /Cmm and 366.80 (+198) /Cmm respectively ($p < 0.001$).

The mean reduction of AEC in all the three groups is statistically as well as clinically significant when comparison made between the values at baseline and at end of the study ($p < 0.001$ in each group). However, there was no significant

difference between the groups in percentage of relief ($p > 0.05$) showing that all the three interventional drugs have similar or comparable effect Vide: Chart 4).

Severity of Asthmatic Attack

Out of 30 enrolled subjects in **Group 1**, 20% ($n = 6$) had history of severe asthmatic attacks, 60% ($n = 18$) reported moderate attacks and rest 20% ($n = 6$) reported presence of mild asthmatic attacks at baseline. After administration of Puskaramula for twelve weeks it was observed that in 86.67% ($n = 26$) subjects the severity was mild and in rest 13.33% ($n = 4$) severity was moderate. No subject reported severe asthmatic attack. The details are given in table 9.

Out of 30 enrolled subjects in **Group 2**, 23.33% ($n = 7$) had history of severe asthmatic attacks, 63.33% ($n = 19$) reported moderate attacks and rest 13.33% ($n = 4$) reported presence of mild asthmatic attacks at baseline. After administration of Kustha for twelve weeks it was observed that in 86.67% ($n = 25$) subjects the severity was mild and in rest 13.33% ($n = 4$) severity was moderate. No subject reported severe asthmatic attack. The details are given in table 10.

Out of 30 enrolled subjects in **Group 3**, 26.67% ($n = 8$) had history of severe asthmatic attacks, 53.33% ($n = 16$) reported moderate attacks and rest 20% ($n = 6$) reported presence of mild asthmatic attacks at baseline. After administration of Erandamula for twelve weeks it was observed that in 86.67% ($n = 26$) subjects the severity was mild and in rest 13.33% ($n = 4$) severity was moderate. No subject reported severe asthmatic attack. The details are given in table 11.

The percentage of relief from severity of asthmatic attack in all the three groups is statistically as well as clinically significant when comparison is made between baseline and end of the study ($p < 0.001$ in each group). However, the difference between the groups in percentage of relief is non significant ($p > 0.05$) showing that all the three interventional drugs have similar effect or comparable effect.

Effect of the trial drug on Spirometric parameters

Spirometry was performed for all the subjects recruited into the trial both at the baseline and at the end of the study (i.e., after 12 weeks) using 12 parameter MicroLabs spirometer. It is observed that the FEV₁ in **group 1, 2 and 3** is respectively 2.44 ± 0.54 ; 2.27 ± 0.38 and 2.32 ± 0.27 at the baseline. The same at the end of the study is 2.43 ± 0.53 ; 2.20 ± 0.40 and 2.29 ± 0.28 in **group 1, 2 and 3** respectively.

The PEF reading in **group 1, 2 and 3** is respectively 6.54 ± 1.38 ; 6.18 ± 1.26 and 6.28 ± 1.26 at the baseline. The same at the end of the study is 6.67 ± 1.33 ; 6.26 ± 1.32 and 6.25 ± 1.27 in **group 1, 2 and 3** respectively.

FVC in **group 1, 2 and 3** are respectively 3.53 ± 1.01 ; 3.56 ± 1.31 and 3.52 ± 1.30 at the baseline. The same at the end of the study is 3.24 ± 0.77 ; 2.92 ± 0.55 and 2.98 ± 0.53 in **group 1, 2 and 3** respectively (Vide : Table No. 12).

The % reduction of FEV₁ and PEF in the trial subjects is comparable in each group. But the variation between the groups is statistically not significant ($p > 0.05$).

Use of Inhaler

It was observed that 60% subjects ($n=18$) in Group 1 were using inhalers/oral medication at baseline. At the end of study this percentage came down to 23.33% ($n=7$) (Vide: Table 13).

It was observed that 66.67% subjects ($n = 20$) in Group 2 were using inhalers/oral medication at baseline. At the end of

study this percentage came down to 20% ($n = 6$) (Vide: Table 14).

It was observed that 70% subjects ($n=21$) in Group 3 were using inhalers/oral medication at baseline. At the end of study this percentage came down to 16.67% ($n=5$) (Vide Table 15).

RESULTS

Evaluation of the observations on the basis of the obtained results indicate that there is clinical as well as statistical significance ($p < 0.001$) in the improvement observed in symptoms i.e. dyspnoea, wheezing and cough during the study in each group. The relief percentage is comparable between three groups i.e., statistically non-significant ($p > 0.05$).

There is statistically highly significant change observed in reduction of VAS scores of dyspnoea ($p < 0.001$) in each group, thereby inferring that dyspnoea in Bronchial Asthma can be controlled to a great extent by administering all the three interventional drugs. Their therapeutic benefit is comparable.

The IgE reducing effect of Puskaramula, Kustha and Erandamula churna are found to be comparable ($p < 0.05$). Serum IgE was found elevated in 53.33 % ($n = 16$) of subjects in **Group 1** at the baseline. After 12 weeks of drug administration the IgE levels were found elevated in 33.33% ($n = 10$) of subjects. The mean average of serum IgE at baseline and end of the study was found to be 553.23 (+ 215.51) IU/mL and 279.11 (+188.97) IU/mL respectively ($p < 0.05$). Serum IgE was found elevated in 73.33 % ($n = 22$) of subjects in **Group 2** at the baseline. After 12 weeks of drug administration the IgE levels were found elevated in 26.67% ($n = 8$) of subjects. The mean average of serum IgE at baseline and end of the study was found to be 490.13 (+ 221.4) IU/mL and 231.19 (+121.54) IU/mL respectively ($p < 0.05$). Serum IgE was found elevated in 63.33 % ($n = 19$) of subjects in **Group 3** at the baseline. After 12 weeks of drug administration the IgE levels were found elevated in 30% ($n = 9$) of subjects. The mean average of serum IgE at baseline and end of the study was found to be 435.55 (+ 270.48) IU/mL and 224.76 (+159.88) IU/mL respectively ($p > 0.05$). The AEC was elevated in 73.33 % ($n = 22$), 63.33 % ($n = 19$) & 73.33 % ($n = 22$) of subjects in **Group 1, 2 & 3** respectively at the baseline. After 12 weeks of drug administration, the AEC was elevated only in 36.67 % ($n = 11$), 30 % ($n = 9$) & 30 % ($n = 9$) of subjects. The mean average of AEC at baseline was found to be 647.10 (+ 176) /Cmm, 621.30 (+ 173) /Cmm & 624.40 (+ 161) /Cmm respectively in **Group 1, 2 & 3** respectively. The same is found to be 341.00 (+100) /Cmm, 390.80 (+186) & 366.80 (+198) /Cmm respectively at the end of the study in **Group 1, 2 & 3**.

The mean reduction of AEC in all the three groups is statistically as well as clinically significant when comparison made between the values at baseline and at end of the study ($p < 0.001$ in each group). However, there was no significant difference between the groups in percentage of relief ($p > 0.05$) showing that the interventional drugs have comparable effect

The daily dose of consumption of oral bronchodilators as well as other inhalers has come down significantly i.e., about 60% subjects ($n=18$) in Group 1 who were using inhalers/oral medication at baseline have come down to 23.33% ($n=7$) at the end of the study; about 66.67% subjects ($n = 20$) in Group 2 who were using inhalers/oral medication at baseline have come down to 20% ($n = 6$); and about 70% subjects ($n=21$)

in Group 3 who were using inhalers/oral medication at baseline have come down to 16.67% (n=5).

There is a significant reduction in the severity of Asthma attacks after the use of trial medicines in all the three groups. Out of 30 enrolled subjects in **Group 1**, 20% (n = 6), 60% (n = 18) and 20% (n = 6) reported presence of severe, moderate and mild asthmatic attacks respectively at baseline. After administration of Puskaramula for twelve weeks in 86.67% (n = 26) subjects the severity was mild and in rest 13.33% (n = 4) severity was moderate while, no subject reported with severe attack. Out of 30 enrolled subjects in **Group 2**, 23.33% (n = 7), 63.33% (n = 19) and 13.33% (n = 4) reported presence of severe, moderate and mild asthmatic attacks respectively at baseline. After administration of Kustha for twelve weeks in 86.67% (n = 25) subjects the severity was mild and in rest 13.33% (n = 4) severity was moderate while no subject reported with severe asthmatic attack. Out of 30 enrolled subjects in **Group 3**, 26.67% (n = 8), 53.33% (n = 16) and 20% (n = 6) reported presence of severe, moderate and mild asthmatic attacks respectively at baseline. After administration of Erandamula for twelve weeks in 86.67% (n = 26) subjects the severity was mild and in rest 13.33% (n = 4) severity was moderate while no subject reported with severe attack.

All the trial drugs were found to be safe. No adverse drug reactions/ side effects of what so ever nature were observed in any of the subjects during the course of trial.

Therefore, it can be concluded on the basis of above findings that all the three trial drugs were equally effective in reducing the signs and symptoms of chronic bronchial asthma and has the capacity to reduce the dosage of oral medication as well as inhalers to a great extent (> 60%). The relief percentage within the groups is statistically highly significant ($p < 0.001$) while the same between the groups is non-significant ($p > 0.05$). Therefore it is concluded that all the three trial drugs are equally potential in reducing the symptoms of asthma.

Safety Profile

No significant change was observed in haemogram, Liver function tests (L.F.T.) and Renal function tests (R.F.T.) of any subject, carried out at baseline and after the treatment with trial drug ($p > 0.05$).

Adverse Drug Reactions (ADRs)

None of the subjects have reported with any major ADRs except nausea and vomiting in less than 1% of the subjects. Even these subjects attributed the symptoms to the bitter taste of Puskaramula and Kustha.

Drop outs & Early Withdrawal

There were two drop outs in group 1 and three each in group 2 and 3. But, these were noted to be due to personal reasons, not treatment related. None of the subjects withdrawn from study due to any adverse drug reaction or adverse event during the course of treatment with trial drug.

DISCUSSION

In the present study it is attempted to understand the rationality behind the concept of substitutes as mentioned in the ayurvedic texts. The study reveals statistically highly significant change in reduction of VAS scores of dyspnoea, cough and wheezing ($p < 0.001$) in group 1 & 2, confirming such observation made by earlier observers on Puskaramula and Kustha. The results in the group 3 are also comparable to group 1 & 2 indicating the anti-asthmatic effect of

Erandamula for the first time. This effect is attributed to the unidentified tri-terpinoids present in the root of *R. communis*. All the three trial herbs have exhibited comparable results on IgE reduction ($p < 0.05$). The mean reduction of AEC in all the three groups is statistically as well as clinically significant when comparison made between the values at baseline and at end of the study ($p < 0.001$ in each group). However, there was no significant difference between the groups in percentage of relief ($p > 0.05$) showing that all the three interventional drugs have comparable effect.

The daily dose of consumption of oral bronchodilators as well as other inhalers has come down significantly in all the groups indicating that the trial drugs have comparable effects owing to the tri-terpenoids commonly present in all the three herbs. Similar studies on other substitutes will provide substantial information on the Abhavapratidhi dravyas on the scientific basis.

CONCLUSION

The trial herbs (Pushkarmula / PM, Kushta / KS and Erandamula / EM) in the form of powder administered at the dose of 2 g twice daily with honey to the subjects suffering from Tamakaswasa / Bronchial Asthma showed comparable efficacy both statistically as well as clinically ($p > 0.05$) justifying the substitute status.

Kustha (*Sausurea lappa*) root exhibited morphological, chemical and therapeutic similarity as a substitute for Puskaramula (*Inula racemosa*) whereas Erandamula (*Ricinus communis*) exhibited only therapeutic similarity as a substitute for Puskaramula.

The study proves the value of the fundamental concepts of Ayurveda. For example, doshapratyanika cikitsa stands proven in this context of Erandamula as the substitute to Puskaramula while, vyadhipratyanika cikitsa is the case with Kustha as the substitute to Puskaramula.

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