Clinical Efficacy and Safety of “Vasavaleha” in the Management of Stable Chronic Bronchitis: A Prospective Open Label Multicenter Study

ABSTRACT

Introduction: Chronic bronchitis is one of the common clinical problems seen in middle–older age group and occurs as a result of inflammation and swelling of the lining of the airways, leading to narrowing and obstruction generally resulting in persistent cough, associated with wheezing, chest pain, and shortness of breath. Chronic bronchitis can be symptomatically compared with Kasa Roga in Ayurveda.

Aims and objectives: To evaluate the efficacy and safety of Vasavaleha in patients suffering from stable chronic bronchitis (CB).

Materials and methods: A prospective, open label multicenter study was carried out at three peripheral units under intramural clinical research program from 2012 to 2013. One hundred and twenty six patients satisfying the selection criteria were enrolled at the Outpatient Department of the centers and were administered Vasavaleha (10 gm) twice daily after food with water for 12 weeks. Follow-up was done finally after 2 weeks without medication. Laboratory parameters were assessed at baseline, 42nd day, and at the end of the treatment period of 12 weeks (i.e., 84th day). Paired sample t-test was used to compare mean change from baseline to the 84th day. A p-value of <0.05 was considered significant.

Results: At the end of 12 weeks, statistically significant improvement was observed in clinical symptoms of CB and also in peak expiratory flow rates (PEFR), forced expiratory volume (FEV1), and St. George Respiratory Questionnaire (SRGQ) Score (p < 0.001). The treatment was found to be safe and effective in the patients of CB as all the safety parameters were within the normal range. No adverse drug reaction or adverse event was reported during the trial period.

Conclusion: Vasavaleha in the above prescribed dose is found to be effective and safe in the management of stable CB.

Keywords: Kasa roga, St. George Respiratory Questionnaire, Stable chronic bronchitis, Vasavaleha.


Source of support: Nil
Conflict of interest: None

INTRODUCTION

Chronic bronchitis is one of the most distressing diseases and is quite common in all the socioeconomic strata and is more common in middle-aged males than in females. Approximately 20% of adult males and 5% of adult women are affected. Chronic bronchitis is defined as chronic cough and sputum production for at least 3 months a year for two consecutive years. The hypersecretion of mucus is a result of hypertrophy of submucosal glands and increased numbers of goblet cells in the epithelium. Mucociliary clearance is delayed due to excess mucus production and loss of ciliated cells, and this leads to a history of productive cough. The other identifying symptoms are chronic cough with expectoration, dyspnea, chest pain, wheezing, sore throat, and nasal congestion. If not treated it could lead to major outcomes, such as reduced lung function, impaired health status, reduced exercise capacity, frequent exacerbations, and possibly increased mortality.

Cough with sputum is more noticeable in the morning because of pooling of nocturnal secretions in the supine position which are then mobilized with morning activities. Chronic upper respiratory disease of both allergic and infectious nature may be a commonly associated or precipitating factor. The most frequent fatal consequence is acute exacerbation with respiratory failure in 50% cases.
with 10 years history of CB. Such acute exacerbations are often precipitated by bacterial infection.

Chronic bronchitis can be symptomatically correlated with Kasa in Ayurveda. Kasa is a Vata-kaphaj vyadhī that occurs when obstructed Vyan Vayu travels upward in Pratiloma Gati and vitiates Udana Vayu propelling the air upward and out of the body. It has its physical origin in the Purishavaha Srotas (large intestine) where accumulation and aggravation of the Dosha takes place. At the initial stage of onset, it is said to be Sadhya (Curable) but in chronic and especially in old age it becomes Yapya (Manageable/controllable).

The contemporary treatment of bronchitis is only symptomatic, which includes bronchodilators, expectorants, steroids and artificial supply of oxygen, while in chronic conditions strengthening of the respiratory muscles, supplemental oxygen, hydration, and nutritional support are required. Several indigenous drugs have been successfully tested and used as conservative therapy in CB. The goal of CB treatment has shifted from symptom relief to disease control and it also ensures the patient’s wellbeing. Herbal preparations have been cited as the third most popular complementary treatment modality. The medicine Vasavaleha is used since ages for various types of Kasa treatment but no validation study is completed till date, hence this study is carried out to evaluate the efficacy and safety of this compound formulation with clinical validation in the management of CB.

OBJECTIVES
To evaluate the efficacy and safety of Vasavaleha in patients suffering from stable CB.

MATERIALS AND METHODS

Study Design
The study was conducted as an interventional open label multicenter trial executed at three peripheral centers of the Central Council for Research in Ayurvedic Sciences, Ministry of AYUSH. The study was approved by respective Institutional Ethics Committee of all the three participating centers and was done in accordance with World Health Organization—Good Clinical Practices Guidelines. The clinical trial has also been registered in Clinical Trial Registry of India (CTRI/2014/06/004704).

Study Participants
A total of 126 participants were enrolled in the trial, 42 from each of the three centers, viz., Regional Ayurveda Research Institute for Mother and Child Health, Nagpur; Regional Ayurveda Research Institute for Skin Disorders, Vijayawada, and Regional Ayurveda Research Institute for Endocrine Disorders, Jaipur. Patients were screened in accordance with the inclusion and exclusion criteria mentioned in the protocol. A total of 126 patients fulfilling the screening criteria were recruited in the study after obtaining the written informed consent.

Inclusion Criteria
Patients of either sex aged between 16 and 70 years, with history of uncomplicated chronic bronchitis and who were willing to participate in the study for 14 weeks.

Exclusion Criteria
Patients suffering from acute bronchitis, patients having PEFR < 50% of the predicted value, presence of other pulmonary diseases like emphysema, cor pulmonale, cyanosis, pneumonia, asthma, cystic fibrosis, tuberculosis, lung cancer, etc., patients with uncontrolled diabetes mellitus (blood sugar fasting > 250 mg/dL), patients with poorly controlled hypertension [mean sitting blood pressure (BP) ≥160/100 mm Hg], patients on prolonged (>6 weeks) medication with corticosteroids, bronchodilators, mast cell stabilizers, antidepressants, anticholinergics, etc., or any other drugs that may have an influence on the outcome of the study. Patients suffering from major systemic illness necessitating long-term drug treatment (rheumatoid arthritis, tuberculosis, psycho-neuro-endocrinal disorders, etc.), patients who have a past history of atrial fibrillation, acute coronary syndrome, myocardial infarction, stroke, or severe arrhythmia in the last 6 months, symptomatic patients with clinical evidence of heart failure were excluded from the trial.

Patients with concurrent serious hepatic disorder (defined as aspartate aminotransferase and/or alanine aminotransferase, total bilirubin, alkaline phosphatase >3 times upper normal limit) or renal disorders (defined as serum creatinine >1.2 mg/dL), alcoholics, and/or drug abusers, patients with history of hypersensitivity to the trial drug or any of its ingredients, patients who have completed participation in any other clinical trial during the past 6 months, pregnant or lactating women, and any other condition which the investigator thinks may jeopardize the study were also excluded from the study.

Study Interventions
The study medications including vasavaleha in the dose of 10 gm twice daily were given with water for a period of 12 weeks. The formulation was procured from IMPCL, a government pharmacy as per pharmacopoeia
standards, which was good manufacturing practice certified and it was standardized following the standards laid in Ayurvedic Pharmacopoeia of India. Patients were also guided regarding pathya–apathya and during their follow-up visits they were asked in details for their diet patterns.

**Study Procedure**

On the enrolment day at baseline (Visit 1), patient’s demographic profile, family history, medical history, particularly related to PEFR, FEV1 in first second and SGRQ score. Subsequent visits were planned at an interval of 2 weeks [14th day (Visit 2), 28th day (Visit 3), 42nd day (Visit 4), 56th day (Visit 5), 70th day (Visit 6), and 84th day (Visit 7)]. Patients were assessed and given study medications at each subsequent visit till 84th day. There was also a without medication follow-up after 2 weeks of 84th day visit. Details of clinical assessment and study schedule are given in Flow Chart 1.

At the study site, data of all the patients were recorded in predesigned case report forms (CRFs) and was also entered in electronic formats (e-formats) designed in MS-Excel with many data validation checks to ensure correct data entry. The e-formats and Xerox of the CRFs along with the laboratory investigations reports of the patients were sent by the participating centers to the Council’s headquarters on weekly basis for the purpose of clinical trial monitoring.

Out of the total 126 patients enrolled in the study, three dropped out during the course of the study. Imputation was applied on those three patients. Hence, data of a total 126 patients was used for statistical analysis. Flow Chart 2 shows the outflow of the patients in the study.

**Outcomes**

The primary outcome measures were change in the clinical symptoms of CB. The secondary outcome measures were change in SGRQ scores and any acute exacerbations of bronchitis occurring during the trial period.

**Statistical Analysis**

Clinical symptoms, subjective parameters, and laboratory parameters were subjected to univariate and multivariate analysis using Statistical Packages for the Social Sciences 15.0 version with appropriate statistical methods.

**RESULTS**

Data of 126 patients (67 males and 59 females) were used for statistical analysis, out of which maximum patients 37 (29.4%) were in the age group of 34 to 42 years; 86 (68.3%) patients were of pitta-kaphaja sharirik prakriti. Among total patients, 94 were married (74.6%). Number of literate patients who were able to read and write was 114 (90.5%). Socioeconomic condition was good (above poverty line) in 90 (71.4%) patients. Maximum number of patients 95 (75.4%) were having desk work. Maximum numbers of...
patients were residing in urban area 107 (84.9%). Vital parameters of the patients recorded at baseline of the patients are shown in Table 1. Mean systolic blood pressure was 121.29 and mean diastolic blood pressure was 77.48.

Significant effect of *vasavaleha* was seen on the common complaints faced by patients suffering from CB. The complaint of productive cough was observed in 126 patients at baseline and was found only in 93 patients at the end of treatment. Complaint of dyspnea reduced in 39.7% patients and wheezing was reduced in 21.4% patients. Likewise, complaint of chest pain, sore throat, and nasal congestion got reduced in 37.2, 64.3 and 57.2% patients respectively. The effect of the trial medication *Vasavaleha* on the complaints faced by patients of CB is shown in Table 2.

Table 1: Distribution of patients according to physical parameters

<table>
<thead>
<tr>
<th>Physical parameters (n = 126)</th>
<th>Height (inches)</th>
<th>Weight (kg)</th>
<th>Respiratory rate (per minute)</th>
<th>Pulse rate (per minute)</th>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>64.112 (4.36)</td>
<td>63.25 (24.22)</td>
<td>19.42 (1.631)</td>
<td>76.35 (4.78)</td>
<td>121.29 (10.82)</td>
<td>77.48 (9.299)</td>
</tr>
<tr>
<td>Values are expressed as mean (standard deviation)</td>
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</tr>
</tbody>
</table>

Table 2: Effect of treatment on chief complaints

<table>
<thead>
<tr>
<th>Chief complaints</th>
<th>Baseline (n = 126)</th>
<th>84th day</th>
<th>Follow-up at the end of 14th week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Productive cough</td>
<td>126 (100%)</td>
<td>93 (73.8%)</td>
<td>69 (70.6%)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>77 (61.1%)</td>
<td>27 (21.4%)</td>
<td>26 (20.8%)</td>
</tr>
<tr>
<td>Wheezing</td>
<td>28 (22.2%)</td>
<td>10 (0.8%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>58 (46.0%)</td>
<td>11 (8.8%)</td>
<td>10 (7.9%)</td>
</tr>
<tr>
<td>Sore throat</td>
<td>108 (85.7%)</td>
<td>27 (21.4%)</td>
<td>29 (23.0%)</td>
</tr>
<tr>
<td>Nasal congestion</td>
<td>85 (67.5%)</td>
<td>13 (10.3%)</td>
<td>11 (8.7%)</td>
</tr>
<tr>
<td>Values are expressed as n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Graph 1: Effect of the treatment on PEFR (L/min)

Graph 2: Effect of the treatment on FEV1 (L/min)
Clinical Efficacy and Safety of "Vasavaleha"

Table 3: Effect of treatment on outcome parameters

<table>
<thead>
<tr>
<th>Parameters (n = 126)</th>
<th>Baseline</th>
<th>84th day</th>
<th>Follow-up at the end of 14th week</th>
<th>t-value</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEFR (L/min)</td>
<td>351.69 (89.04)</td>
<td>419.25 (100.109)</td>
<td>417.37 (96.908)</td>
<td>14.930</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FEV1 (L/min)</td>
<td>1.84 (0.634)</td>
<td>2.00 (0.555)</td>
<td>2.05 (0.589)</td>
<td>4.106</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>St. George’s Respiratory Questionnaire</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Domain—symptoms</td>
<td>52.31 (21.376)</td>
<td>38.72 (28.516)</td>
<td>38.15 (28.327)</td>
<td>9.747</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Domain—activity</td>
<td>24.42 (18.725)</td>
<td>12.62 (4.616)</td>
<td>12.25 (4.342)</td>
<td>8.302</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Domain—impacts</td>
<td>28.40 (15.227)</td>
<td>10.32 (5.942)</td>
<td>9.97 (5.706)</td>
<td>17.017</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total score</td>
<td>31.16 (16.671)</td>
<td>15.66 (8.279)</td>
<td>15.37 (7.827)</td>
<td>17.916</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are expressed as mean (standard deviation); *Compared using paired t-test at baseline and 84th day; *p-value of <0.05 has been considered as significant.

Graph 3: Effect of treatment on safety parameters [blood urea, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT)]

Graph 4: Effect of treatment on safety parameters (serum uric acid and serum creatinine)

Graph 5: Effect of treatment on safety parameters (serum alkaline phosphatase)

day. Table 3 shows the results of the analysis of those parameters.

The study shows significant effect on the outcome parameters as the PEFR value increased from 351.69 (at the baseline) to the 417.37 (at the 84th day). Likewise, value of FEV1 was increased from 1.84 on the baseline to 2.05 at the 84th day. Also, significant results were found in all the domains of SGRQ, and total value decreased from 31.16 at the baseline to the 15.66 on 84th day.

Safety Profile

The effect of this treatment on various safety parameters, such as liver function tests and renal function tests, was assessed at baseline and at 84th day visit. The values were within limits during the entire trial period (Graphs 3 to 5). Table 4 shows the effect of the drugs on the safety parameters. No adverse reaction or adverse event was observed during the entire trial period.

DISCUSSION AND CONCLUSION

In CB, there is inflammation and swelling of the lining of the airways, leading to narrowing and obstruction generally resulting in daily cough. The inflammation stimulates production of mucus, which can cause further blockage of the airways. Chronic bronchitis can be symptomatically compared with kasa roga. Kasa originates by Pratiloma gati of Apana vayu due to sroto-avarodha which manifests through Pranavaha Srotas. Hence, the drugs which are having...
vata kapha hara properties with anulomana properties can remove the srotovardhadha leading to adhoga of apana vayu, thus relieving Kasa. The drug Vasavaleha contains Vasa (Justicia adhatoda), Pippali (Piper longum), Sarpi (butter), Sharkara (sugar candy), and Madhu (honey). Majority of these drugs are having kaphavatahara and vatanulomana properties. Vasa is a well-known expectorant,9 Pippali is Vata-kaphaghna, bronchodilator, immuno-stimulator and antiinflammatory,10 Sarpi is vatanulomana, Vata-kaphaghna, Sharkara is anulomaka, honey is yogvahi.11 Hence, the synergistic effect of these ingredients might help in relieving the subjective and objective parameters of Kasa (CB).

Based on this multicenter clinical trial, it is inferred that Vasavaleha has good efficacy in the management of CB. This drug has shown significant improvement in all the clinical parameters, lung function tests, viz., PEFR, FEV1, and also SGRQ score. This drug can be safely used for the management of CB. This type of validation study on commonly used Ayurvedic formulations will be helpful in designing national health policies and globalization of the traditional system.

REFERENCES

हिंदी सारांश

जीर्ण कास में वासवालेह की आनुवृत्त प्रभावकारीता का मूल्यांकन — एक प्रयासित बहुकंडीय अन्वलोकनात्मक अध्ययन

'निलिन्द सूर्यस्वरी, 'शरि एम. एल. मीरा, 'कृषि. बाबू, 'बबीता यादव, 'खेता चौधरी, 'उदय आर. एस. नंबूरी, 'अनु भदनागर, 'वाराणसी सुमोस, 'श्रृंगि खुडूनी, 'भरतन एस. शर्मा

शून्यक: जीर्ण कास, प्रीड़वस्था एवं बुद्धिवस्था में होने वाली एक प्रमुख व्याधि है। इस व्याधि में प्लास्ट परिसर में लक्षण आता है जिसके कारण प्लास्ट परिसर के अंतर्गत बहुकंडीय अन्वलोकनात्मक अध्ययन करने के लिए संस्था निर्देशित करता है। जीर्ण कास में बुद्धिवस्था होने के लिए रोगियों में व्याधि की प्रभावकारीता एवं इसके सुरक्षित पाये जाने हेतु कोशिश करना।

साबन एवं विषय: यह एक बहुकंडीय ऑपन लेवल अध्ययन है, जो कि केंद्रीय आयुर्वेद अनुसंधान परिषद के 3 केंद्रों (नागपुर, विजयवाड़ा एवं जयपुर) पर चलता प्रक्रिया के अनुसार बहिरोंग विभाग के 126 रोगियों में किया गया। 10 प्राम के मात्र में वासवालेह व्यवस्थित रोगियों को डिन में 2 वार तक समय उपलब्ध कराए। उसके बाद भी रोगियों को बिना जीर्ण किया दिए 2 सवारी तक निश्चित किया गया। नैदानिक प्रयोगशाला में रोगी के रस की जांच, पहले डिन व 42 वें डिन एवं 86 वें डिन की गई। इस जीर्ण के दौरान महापूर्ण परिणाम प्राप्त हुए।

परिणाम: 84 वें डिन के समय होने पर जीर्ण कास के प्रकाश में सावधानी एवं नैदानिक तौर पर सुधार पाया गया, अतः यह लद्दलस जीर्ण कास में प्रभावकारी एवं सुरक्षित सिद्ध हुई है।

निष्कर्ष: जीर्ण कास में वासवालेह प्रभावकारी एवं सुरक्षित जीविका में सिद्ध हुई है।