WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 6, Issue 12, 917-926. Research Article ISSN 2277–7105

AN OPEN LABELLED CLINICAL STUDY TO ACCESS THE SAFETY AND EFFICACY OF *SHARBAT-E-EJAZ* A POLYHERBAL UNANI FORMULATION IN PATIENTS WITH DRY COUGH

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Article Received on
07 August 2017,
Revised on 28 August 2017,
Accepted on 18 Sept. 2017
DOI: 10.20959/wjpr201712-9709

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ABSTRACT

Objective: The study aimed to assess the safety and efficacy of a polyhedral Unani formulation in patients of Dry cough. **Background**: Cough is a natural reflex expulsive defence mechanism of the body, for clearing excessive secretions or inhaled irritants from the respiratory tract. Dry cough, a common presentation of respiratory diseases is the most common symptom for seeking medical care as it can adversely effects the quality of life. Since the drugs available in modern medicine produce varying adverse effects therefore traditional medicines including Unani medicine are now being seen with an eye of great interest and hope. Unani medicine claims to possess effective treatment for the management of dry cough and suggest an array of medicament for the purpose. Herein we have evaluated the efficacy and safety of *Sharbat-e-jaz*, one of the potential Unani formulations in patients with dry cough. **Methods:** An uncontrolled open labelled clinical study was conducted on 75 subjects with Dry cough of less than 3 weeks duration. The patients were clinically monitored for safety and efficacy through 2 weeks of treatment written informed consent was taken prior to the study and case sheets were maintained separately for each patient. Safety was assessed on pathological and biochemical parameters whereas efficacy was assessed on Cough Visual Analogue Scale (VAS). Statistical analysis was done by paired students test. **Results:** After two weeks of treatment the efficacy of the drug was significant ($p < 0.05$) in the pre and post treatment VAS scores. The test drug has shows an good anti-inflammatory

and anti-allergic effect, soothing the respiratory tract and relieving the symptoms. There was an significant reduction in VAS score after two weeks of treatment. There was no adverse effected reported or observed in the studied parameters. **Conclusion:** The polyherbal formulation was found effective in the management of Dry cough with no side effects reported.

KEYWORDS: Dry cough, *Sharbat-e-jaz*, Unani System of medicine, Respiratory diseases.

INTRODUCTION

Cough is an important defence mechanism in the respiratory system that is responsible for clearing excessive secretions, foreign material and infectious organisms from the airway[1]; Cough is an important defence mechanism in the respiratory system that is responsible for clearing excessive secretions, foreign material and infectious organisms from the airway.[3] It occurs due to the stimulation of chemoreceptor's in throat, respiratory passages and stretch receptors in lungs.[4] cough can be classified into productive (wet)cough and non productive (dry) cough. Airway[3,4] Dry cough is a common presentation of upper respiratory tract infections encountered in general practice[4], this type of cough is mostly caused by dry irritation, dust, smoke or due to oedema and mild secretion in resolving stage of illness.Asthma,rhinosinusitis and oesophageal reflux is the most common cause of this type of cough).[3,4]

Many Unani scholars have described this symptom as *Surfa* yaabis in their classical literatures (A'zam Khān, 2011, Majūsī, 2010, Jurjānī, 2010). In Arabic language *Surfa* means *Suāl* and in Hindi it is known as *Khansi* (Jurjānī, 2010). *Majūsī*, in his book *Kāmil al-Sanā'a* has mentioned about the *Surfa Yābis* in which phlegm is not coughed up. *Surfa Yābis* or dry cough can arbitrarily be defined as a non-productive cough with no expectoration.[5] Its predisposing factors can be both extrinsic (dust, smoke, fumes, cold air) and intrinsic (derangement of temperament).[5,6,7]

It may be benign and self limiting but sometimes it can be a warning sign of serious disease. The socioeconomic effects of cough are absenteeism from work, increased physician consultation cost, huge cost of prescription medication, and non-prescription medication.[8] More importantly, cough can be so profound that it may affect the patient's quality of life.[9,10]

A wide range of disease processes may present with dry cough and definitive treatment depends on identifying the cause and diagnosis. An increased sensitivity of the cough reflex can be observed in patients with dry cough.

Symptomatic relief must be considered when the cough interferes with the patient's daily activities. The currently available treatment is anti-tussive preparations which are available as a combination of antihistamines, decongestants and expectorants. The cough suppressants may produce nausea, vomiting, constipation, tolerance to antitussive, analgesic effects, and physical dependence.[11]

There is an increasing interest in the use of herbal medicine in health care for its claimed safety benefits. Herbal products are of interest to many patients and health care practitioners because much of World's population rely on herbal medicines as part of their primary health care system. Due to the increasing demand in herbal therapy, an effort has been made to search for a natural alternative possessing less adverse effects, hence the present study was planned to provide a safe and effective treatment for dry cough.

MATERIAL AND METHOD

120 patients attending the GOPD of RRIUM, Srinagar during July 2014 to July 2015 were screened for this open labelled quasi controlled clinical trial. Patients with a history of dry cough of less than 3 weeks duration in the age group of 18-60 years were included in the study. Patients suffering from Lower Respiratory Tract Infections including pneumonia, lung abscess, and acute bronchitis were excluded so were chronic obstructive airway disease (COAD) like bronchiectasis, pulmonary tuberculosis, pulmonary oedema, interstitial pulmonary fibrosis, tumours of larynx, bronchi, and lungs. Smokers and patients on Drug-induced Cough (e.g., ACE Inhibitors) were also excluded.

Approval from the institutional ethical committee was obtained prior to the study. Patients were registered for the study after taking their written informed consent. A unani pharmocopoeial formulation *Sharbat-e-jaz* was given to the patient orally in the dose of 20ml diluted in 40ml of luke warm water twice a day for 2 weeks. Clinically patients were assessed every week. The observations were recorded in a separate follow up sheet.

Efficacy Assessment

Cough severity was assessed and recorded using a cough visual analogue scale (VAS). The cough VAS is a vertically marked 10-points (0-9) linear scale which is responsive to changes in cough severity. (Birring et al, 2003).

Safety Assessment

Safety was assessed on Complete blood count (CBC), Liver Function Test (LFT) and Kidney Function Test (KFT) done at baseline and end of treatment. Any adverse event in clinical parameters during the course of treatment was documented.

Trial drug

The trial drug *Sharbat-e-jaz* is a pharmocopoeial Unani drug containing following ingredients, (NFUM part 1).

S. No.	Ingredients	Botanical / Chemical Name	Quantity
1.	Barg-e-Arusa	*Adhatoda vasica*	500 g
2.	Unnab	*Zyzifus sativa*	50 g
3.	Sapistan	*Cordia latifolia*	50 g
4.	Asl-us-Soos	*Glycyrrhiza glabra*	25 g
5.	Tukhm-e-Khatmi	*Althaea officinalis*	25 g
6.	Tukhm-e-Khubazi	*Malva sylvestris*	25 g
7.	Gul-e-Neelofar	*Nymphaea alba*	25 g
8.	Gul-e-Banafsha	*Viola odorata*	25 g
9.	Behidana	*Cydonia oblonga*	20 g
10.	Kateera	*Astragalus gummifer*	10 g
11.	Samag-e-Arabi	*Acacia arabica*	10 g
12.	Qand Safaid	*Saccharaum officinale*	1 kg
13.	Aab	*Oxidane (Water)*	Q.S.

Statistical Analysis

The results were analysed by using students paired test.

Adverse Events

None of the patients experienced any adverse reaction during or after the trial. There was no significant change in blood pathology or biochemistry of patients.

RESULTS AND DISCUSSION

A total of 120 patients were screened for the study, out of which 27 were excluded as they were not fulfilling the inclusion criteria.93 were registered for the study out of which 18 dropped out as they did not turn up for follow ups.75 patients completed the study.

Demographic Assessment

The characterization of seventy five subjects evaluated in the present study of different age group and gender are presented in Table 1.

Table 1: Characteristics of subjects (n=75).

Variable	Numbers
Age (Years)*	39.92 ± 12.32
Gender (Male: Female)	32: 43
Urban : Rural	45 : 30

* Values are expressed as Mean ± SD.

During the course of study it was observed that maximum number of cases (20) belonged to the age group of 41-50years.Various Studies have shown that all types of cough are common after age of 45years.

Among the total patients 43(51%) were females and 32(42%) were males. It has been observed that among the patients attending specialist cough clinic centre females exceeds male in number.[12,13] This is in compliance with our study wherein, dry cough is more common in females. The high incidence in females can be due to their having more sensitive cough receptors in females than males as is also shown by various studies[15-17], yet some studies have attributed this to modular effects of estrogens and progesterone on cough reflex.[18]

It was observed that urban population (60%) are more affected with cough than rural (40%). This can be probably due to excessive air pollution in urban environment than rural environment**.** Exposure to increasing particulate matter (PM10) is associated with increased respiratory symptoms such as cough, phlegm and sore throat.[19] Excessive exposure to nitrogen dioxide is also found to be a risk factor for cough as shown in some studies.[20]

Middle income group were the most affected (54%) especially housewives (49%) This could be due to the fact that. housewives are more exposed to house dust, gas fumes and coal heat etc.

Table 2: Vital parameters of subjects before and after treatment (n=75).

Parameter	Before treatment (Mean ± SD)	After treatment (Mean ± SD)
Body mass index (BMI)	25.10 ± 3.65	25.30 ± 3.91
Temperature (^{o}C)	98.47 ± 0.38	98.47 ± 0.31
Pulse (Beats per minute)	76.44 ± 3.93	76.28 ± 3.45
Blood Pressure (mmHg)	119 ± 10 / 79 ± 8	118 ± 9 / 77 ± 7.00
Respiratory rate (Breaths per minute)	15.80 ± 1.36	15.65 ± 1.51

The vital parameters including body mass index, temperature, pulse, blood pressure and respiratory rate were evaluated before and after treatment and are presented in Table 2. There was no statistically significant difference ($p > 0.05$) observed in the vital parameters before and after the treatment.

Efficacy Assessment

Table 3: Changes in Visual analogue scale values after treatment (n=75).

Parameter	Basel line	After
Visual analogue scale (VAS) values	8.66 ± 1.24	1.96 ± 1.78*

* Significant difference at $p < 0.05$ by paired *t*-test.

The patients studied shows a significant decrease in the frequency and severity of cough on VAS after 2weeks of treatment. Major improvement was shown in patients on every follow up after taking the test drug. The change in Visual analogue scale (VAS) values was found significant ($p < 0.05$) and is presented in Table 3.

The percentage efficacy with respect to VAS values were found to be 78.24 ± 20.56 %, whereas the changes in VAS were 6.53 ± 2.13 after treatment in the studied subjects. These actions could be due to the diverse pharmacological action of the ingredients of the test drug as shown by various studies.

The main ingredient Barg-e-Arusa (*Adhatoda vasica*) has been used traditionally in treatment of respiratory disorders. Both vasicine and vasicione the primary alkaloid of *Adhatoda* are well established as therapeutical respiratory agents[22] Extracts of *Adhatoda* leaves and roots are useful in treating cough and common cold due to its anti allergic activity.[24] Alkaloid vascinol.present in its leaves have also proven to have a soothing effect on respiratory diseases.[23,24]

The presence of phytochemical constiuents and pharmacological activities of Unnab (*Zyzifus sativa*) and Sapistan (*Cordia latifolia*) have proved to be very effective in cough management. The compound *ziziphin* has a soothing effect on throat. It is believed to modify immune response and reduces the allergic reaction.[25]

The fruit of *Cordia latifolia* have been proven to be beneficial in cough[26]) due to its anti inflammatory and anti allergic effects. Of the other ingredients of the trial drug Asl-us-Soos (*Glycyrrhiza glabra*,) is effective due to its constituent glycyrrhizin which reduces the inflammation of respiratory tract and treats spasmodic cough.

Tukhm-e-Khatmi (*Althaea officinalis*), Tukhm-e-Khubazi (*Malva sylvestris*), Gul-e-Neelofar (*Nymphaea alba*) and Gul-e-Banafsha (*Viola odorata*) have been useful in cough since ages due to its bronchodilator and cough suppressant activity.[27,28,29]

Safety Assessment

Table 4: Changes in laboratory parameters after treatment (n=75).

Parameter	Basel line	After
SGOT	24.95 ± 6.68	24.29 ± 6.11
SGPT	27.15 ± 10.31	24.45 ± 9.38
sCreatinine	0.80 ± 0.12	0.84 ± 0.17
Urea	28.04 ± 6.37	29.10 ± 9.74
Uric acid	4.70 ± 1.08	4.87 ± 1.38
S Bilrubin	0.80 ± 0.66	0.68 ± 0.18
ALP	71.19 ± 19.05	72.69 ± 19.52
Hb	11.11 ± 1.16	11.05 ± 1.19
White Blood Cell (WBC) count / mm^3	7580.66 ± 1494.08	7657.33 ± 1360.86
Erythrocyte sedimentation rate – Westergen method (mm in 1 hr)	15.61 ± 14.90	12.40 ± 10.74*

*Significant difference at $p < 0.05$ by paired *t*-test.

There was no statistically significant difference ($p > 0.05$) observed in laboratory parameters after the treatment It showed that the test drug have shown no adverse effect on liver and kidney.

Although a minor change in values of Erythrocyte sedimentation rate (ESR) was observed, however a statistically significant difference ($p < 0.05$) in ESR was observed after treatment (Table 4). This significant change in ESR may be due to the anti-inflammatory and anti allergic effect of most of the ingredients present in the test drug.

CONCLUSION

The study concluded that dry cough is more common in urban house wives with a mean age of 39.9years. The predisposing factors for this irritating symptom are various extrinsic allergens (house dust, gas fumes and coal heat, nitrogen dioxide and particulate matter) and intrinsic factors (more sensitive cough receptors and presence of oestrogen and progesterone). The test drug is a good cough suppressant with a potent anti inflammatory and anti allergen as was demonstrated by *Adhatoda*, *Ziziphin*, *Cordia latifolia* and glycyrrhizin. The drug's anti inflammatory property was demonstrated by significant change ($p < 0.05$) in ESR values. The drug is safe as no adverse event was reported nor any change was observed in the safety parameter.

The study had a short study period hence the patients could not be followed up to study the effect on recurrence of the problem. The study fell short in establishing the time period of its anti inflammatory effect. These shortfalls can be overcome by conducing post trial surveillance.

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