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Clinical efficacy of Unani herbal formulation in *Zeeq-Un-Nafas Shoabi* (Bronchial asthma)

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Abstract
Asthma and chronic obstructive pulmonary disease (COPD) are among the top ten most common diseases worldwide causing significant social and economic burden on the patient, family and health system. Despite the availability of safe and effective respiratory medication, problems such as under diagnosis, medication, adherence issue and poor understanding of asthma and COPD have led to the condition being poorly managed worldwide.
The term *Zeeq-Un-Nafas Shoabi* (Bronchial Asthma) is clinically used for those conditions where longstanding irritation in mucous membrane of bronchioles results in cough and excessive production of sputum. Although *Zeeq-Un-Nafas Shoabi (*bronchial asthma*)* has not been described as such in Unani literature but the features mentioned under the headings of *sual barid*, *sual ratab* and *sual nazli muzmin* in various books correspond with the signs and symptoms of *Zeeq-Un-Nafas Shoabi* (Bronchial Asthma). Among all the treatment modalities, polyherbal combinations are said to be well-accepted, safe and effective in asthma. The reason for the therapeutic efficacy of herbal combinations in asthma is due to multiple blocking and homeostasis of very complex and interdependent cellular and mediator networks supporting and involved in the inflammatory process of asthma, whereas modern synthetic drug therapy aimed at blocking one mediator alone would be unlikely to have any significant effect on the disease process. None of the available treatments are found to be effective to provide a complete cure of this disease.

Keywords: asthma, *Zeeq-Un-Nafas Shoabi*, dyspnoea, forced expiratory volume, spirometer

Introduction
Bronchial asthma is a chronic inflammatory disorder of the airway and the most common distressing disease affecting 3-5% of the total population [1]. In 1998, the national asthma campaign estimated the prevalence of diagnosed asthma cases in India to be 3.4 million [7]. In the field of allergic respiratory diseases, several indigenous drugs have been successfully tested and used as conservative therapy in asthma. Unani, the great indigenous system of medicine is a complete healthcare system and deals with the preventive and curative aspect of many diseases. Pulmonary disease (COPD) and Asthma is a common cause of morbidity and mortality worldwide. It is of major concern for society as the progressive disease causes increasing disability for the patients and a burden for society. It is the fourth leading cause of death worldwide and is estimated to be the third leading cause of death by 2020. Asthma affects 2.05% of adult population with an estimated national burden of 18 million. Medical management as offered by modern system of medicine, consisting of the use of antibiotics, bronchodilators, antiallergics and steroid therapy is only able to provide temporary relief. Besides, the group of drugs mentioned above entails elements of side effects. Chronicity of the disease also limits the use of drugs over a long period of time [8]. Considering this unconvincing scenario regarding the use of drugs and side effects thereof, researchers are pursuing the golden formula of turning to nature and the traditional pathies. Unani medicine axiomatically comes to the fore as the *Zeeq-Un-Nafas Shoabi* (bronchial asthma) has successfully been treated since ancient time without considerably obnoxious side effects on the body [5, 6]. The principle underlying the management of *Zeeq-Un-Nafas Shoabi* (bronchial asthma) is to remove the causative material (*Asbab maddi*). Thus for treating *Zeeq-un-nafas Shoabi*, we need to concoct the morbid matter by using *munzije balgham* drugs and finally eliminate them by using *mukhrij balgham*/ *munaffise balgham* drugs. From a pool of efficacious drugs for this disease, a pharmacopeia (‘*Quarabadin-e-Azam*’) compound formulation comprising drugs namely Kalongi (*Nigella sativa*), Darchini (*Cinamum zeylanicum* and, Honey, has been taken for the trial purpose. These drugs have already been tried with good results in the treatment of *Warme shooab muzmin* by ancient Hakims and are extant in their manuscripts and have been described to be *Munzije Balgham*, *Mulattif*, *Munaffis balgham*, *Muhallil* and *Mufatteh*, which forms a rationale for a working hypothesis that is put

forward to test a pharmacopeial compound formulation comprising the above mentioned drugs, may be beneficial in people suffering from *Zeeq-un-nafas Shoabi*. The study was designed as a randomized, single blind, and standard controlled clinical study with fixed subjective and objective parameters [12, 13].

Materials and Methods

Patients

The study involved a total of 40 patients of either sex of bronchial asthma aged between 14-65 years. The study was carried out in the P.G. department of Jamia Tibbiya Hospital, Deoband (U.P) from July 2017 to February 2018.

Inclusion criteria

Patients above the age of 14 years and below the age of 65 years were included, irrespective of their sex, on the basis of clinical signs and symptoms. Bronchial asthma with a history for at least one year, non-smokers and absence of long-term remissions of asthma (lasting more than one month) are included in the study.

Exclusion criteria

Patients with bronchial asthma with accompanying diagnosis of heart disease, Tuberculosis, Lung carcinoma arterial hypertension and patients with chronic asthmatic bronchitis along with bronchiectasis were excluded from the study. Patients who had long-term history of smoking, abnormal baseline haematology, blood chemistry or urinalysis, and lactating mothers and pregnant ladies, patients on other therapies (allopathic, homeopathic or other drugs) along with our trial drug and not willing for this herbal treatment were excluded. Written informed consent was obtained from each patient and the institutional ethical committee approved clinical protocol.

Study design and duration

The study was designed as a randomized, single blind, and standard controlled clinical study over 40 cases of bronchial asthma. The study was a preliminary attempt to know the efficacy of this Unani formulation. The 40 patients were randomly allocated by using lottery method into two groups comprising 20 patients in each of test (Group A) and control (Group B) groups respectively. The treatment period in both Test and Control groups was 45 days.

Trial drug

The contents of Unani formulation along with their doses are given below [12, 13, 14].

- Kalongi (*Nigella sativa*) 10gm
- Darchini (*Cinamum zeylanicum*) 10gm
- Shehad (Pure Honey) 20gm

Authenticated drugs were provided by the pharmacy of Jamia Tibbiya, Deoband. Before preparing the formulation, all the ingredients were properly identified by an expert to ascertain their originality. The drugs were cleaned by weeding out unwanted material and then pounded to find a coarse powder. The pounded drugs were supplied to the patients in transparent polypacks as per recommended dosage to be consumed over a week after making a decoction of it. The contents of one polypack contained 140 gms of test drug. This test drug formulation was given to Group B (test group) patients. 20 gms of test formulation in semi-solid form twice daily (10 gm) in morning, before breakfast and 10 grams at bed time. Ambroxol, in the dosage of 75 mg per day in tablet form was administered in 20 patients of Group A (Control Group).

Assessment

45 days study was divided into four visits of follow up which were made at an interval of 15 days. At every visit, the patients were asked about the improvement or worsening in their symptoms and subjected to examination to assess clinical findings. Concomitant treatment was not allowed during the protocol period. The patients, who were taking any other medicine as a treatment of *Zeeq-Un-Nafas Shoabi* (bronchial asthma), were advised to observe abstinence for a week from consuming any other drug before commencing treatment with the test or control drug. The assessment of the efficacy in the test and control groups was based on Subjective parameters such as cough with sputum, wheezing and breathlessness. While assessment of objective parameters included laboratory investigations, radiology (X Ray chest PA view) and spirometry measurements of the patients suffering from *Zeeq-Un-Nafas Shoabi* (bronchial asthma) As these parameters differ in severity from patient to patient, an arbitrary grading of subjective parameters was improvised for appropriate assessment and statistical evaluation of various signs and symptoms to evaluate the efficacy of the Test drugs. Before starting treatment, each sign and symptom were recorded in the case report form according to their grades at the maiden visit and any worsening or improvement in any of the parameters was noted down at every visit of follow up till the end of the treatment.

After 45 days of the treatment, the pre and post treatment values of different parameters (subjective and objective) were analysed grade wisely and subjected to comparison and statistical analysis to evaluate the efficacy of the treatment.

Criteria for overall assessment of results [13-16]

I. Subjective parameters.

Cough; Grades of cough (According to diurnal variations)

Grade 0	None	O hour
Grade 1	Mild	½- 1hr
Grade 2	Moderate	1-2 hrs
Grade 3	Severe	2-3 hrs

2. Sputum.

Grades of sputum production (according to the quantity produced in 24 hours)

Grade 0	None	0 ml
Grade 1	Mild	Up to 50 ml
Grade 2	Moderate	51-100 ml
Grade 3	Severe	>100ml

Dyspnoea on exertion; Grades of dyspnoea on exertion

Grade 1	Not troubled by breathlessness except on strenuous exercise
Grade 2	Short of breath when hurrying or walking up a slight hill
Grade 3	Walks slower than a contemporary on level ground because of breathlessness, or has to stop for breath when walking at own pace
Grade 4	Stops for breath after walking about 100m or after a few minutes on level ground
Grade 5	Too breathless to leave the house, or breathless when dressing or undressing

Wheezing; Grades of Wheezing

Grade 0	None	No wheezing at expiration, no wheezing at inspiration and no wheezing in specific location
Grade 1	Mild	Wheezing at end expiration, at part of inspiration, and segmental (2 of 4 lung fields) in location.
Grade 2	Moderate	Wheezing at one-half expiration, during full inspiration, and diffuse (>3 of 4 lung fields) in location#
Grade 3	Severe	Wheezing during three-quarters of expiration,
Grade 4	Very severe	Wheezing during all of expiration.

5. Crepitations (crackles)

Grades of Crepitations (crackles)

Grade 0	None	No Creptitations
Grade 1	Mild	Crepitations at bases
Grade 2	Moderate	Crepitations up to basal one-half
Grade 3	Severe	Crepitations up to full basal region

II. Objective parameters;

Pulmonary function test (by spirometry)

Grade 0	Normal	$FEV_1/FVC > 0.70$; $FEV_1 \geq 80\%$ predicted
Grade 1	Mild	$FEV_1/FVC < 0.70$; $FEV_1 \geq 80\%$ predicted
Grade 2	Moderate	$FEV_1/FVC < 0.70$; $50\% \leq FEV_1 < 80\%$ predicted
Grade 3	Severe	$FEV_1/FVC < 0.70$; $30\% \leq FEV_1 < 50\%$ predicted
Grade 4	Very severe	$FEV_1/FVC < 0.70$; $FEV_1 < 30\%$ predicted *or* $FEV_1 < 50\%$ predicted plus chronic respiratory failure

Radiological changes (X Ray chest P A View)

Grade 0	Normal	Normal
Grade 1	Mild	Prominent bronchovascular markings up to lateral border of lung Field
Grade 2	Moderate	Markedly prominent bronchovascular markings up to lateral border of lung field
Grade 3	Severe	Findings of cor-pulmonale

Observation and Results

The present clinical trial was conducted to evaluate the efficacy of a test formulation in the management of *Zeeq-Un-Nafas Shoabi*. 40 patients of *Zeeq-Un-Nafas Shoabi* (bronchial asthma) were selected and randomly assigned, each comprising 20 patients to the test and the control groups.

Table 1: Cough-assessment in two groups of patients at different time studied

Cough	0th Day	15th Day	30th Day	45th Day	% difference
Test Group (n=20)					
No Symptom	0(0%)	3(15%)	7(35%)	11(55%)	55.0%
Mild	3(15%)	4(20%)	5(25%)	4(20%)	5.0%
Moderate	7(35%)	8(40%)	6(30%)	4(20%)	-15.0%
Severe	10(50%)	5(25%)	2(10%)	1(5%)	-45.0%
Control Group (n=20)					
No Symptom	0(0%)	1(5%)	3(15%)	6(30%)	30.0%
Mild	4(20%)	5(25%)	4(20%)	5(25%)	5.0%
Moderate	5(25%)	6(30%)	8(40%)	6(30%)	5.0%
Severe	11(55%)	8(40%)	5(25%)	3(15%)	-40.0%
P value	0.834	0.587	0.340	0.222	-

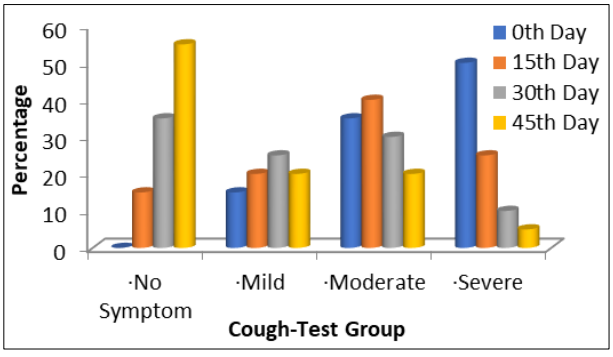

Fig 1

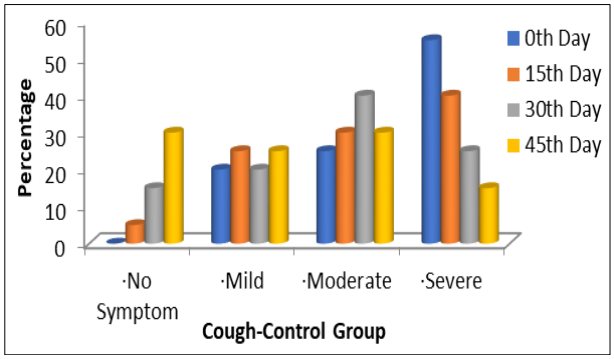

Fig 2

Table 2: Breathlessness- assessment in two groups of patients at different time studied

Breathlessness	0th Day	15th Day	30th Day	45th Day	% difference
Test Group (n=20)					
No Breathlessness	0(0%)	2(10%)	9(45%)	15(75%)	75.0%
Mild	4(20%)	7(35%)	10(50%)	4(20%)	0.0%
Moderate	6(30%)	10(50%)	1(5%)	1(5%)	-25.0%
Severe	10(50%)	1(5%)	0(0%)	0(0%)	-50.0%
Control Group (n=20)					
No Breathlessness	0(0%)	0(0%)	0(0%)	0(0%)	0.0%
Mild	4(20%)	5(25%)	7(35%)	7(35%)	15.0%
Moderate	4(20%)	8(40%)	9(45%)	11(55%)	35.0%
Severe	12(60%)	7(35%)	4(20%)	2(10%)	-50.0%
P value	0.910	0.075+	0.004**	<0.001**	-

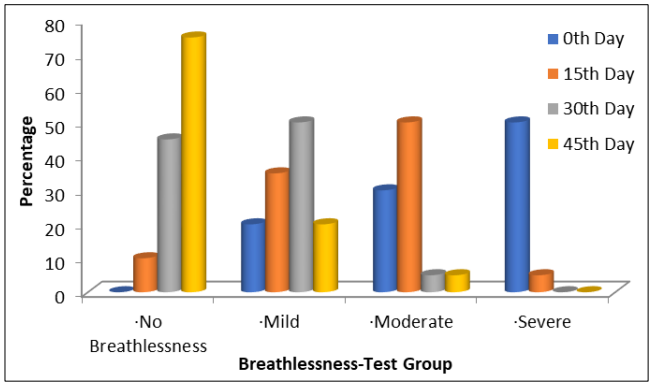

Fig 3

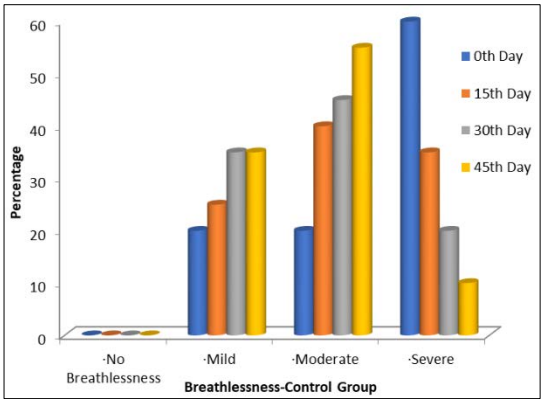

Fig 4

Table 3: Wheeze- assessment in two groups of patients at different time studied

Wheeze	0th Day	15th Day	30th Day	45th Day	% difference
Test Group (n=20)					
No Wheeze	0(0%)	0(0%)	5(25%)	12(60%)	60.0%
Mild	4(20%)	12(60%)	14(70%)	7(35%)	15.0%
Moderate	9(45%)	6(30%)	1(5%)	1(5%)	-40.0%
Severe	7(35%)	2(10%)	0(0%)	0(0%)	-35.0%
Control Group (n=20)					
No Wheeze	0(0%)	0(0%)	1(5%)	2(10%)	10.0%
Mild	4(20%)	6(30%)	6(30%)	6(30%)	10.0%
Moderate	3(15%)	8(40%)	11(55%)	10(50%)	35.0%
Severe	13(65%)	6(30%)	2(10%)	2(10%)	-55.0%
P value	0.104	0.134	<0.001**	<0.001**	-

Chi-Square/Fisher Exact Test

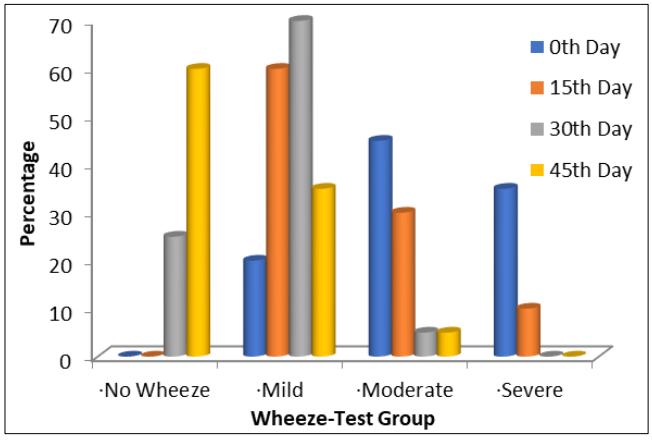

Fig 5

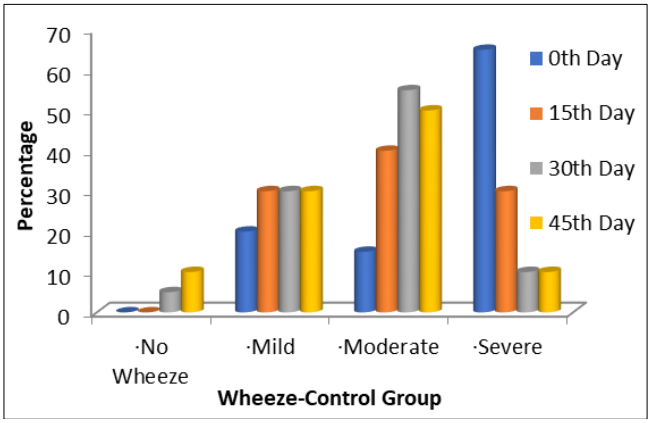

Fig 6

Table 4: Crepitations- assessment in two groups of patients at different time studied

Crepitations	0th Day	15th Day	30th Day	45th Day	% difference
Test Group (n=20)					
No Crepitations	4(20%)	8(40%)	12(60%)	14(70%)	50.0%
Mild	8(40%)	7(35%)	6(30%)	5(25%)	-15.0%
Moderate	6(30%)	5(25%)	2(10%)	1(5%)	-25.0%
Severe	2(10%)	0(0%)	0(0%)	0(0%)	-10.0%
Control Group (n=20)					
No Crepitations	3(15%)	5(25%)	6(30%)	12(60%)	45.0%
Mild	4(20%)	10(50%)	12(60%)	8(40%)	20.0%
Moderate	13(65%)	5(25%)	2(10%)	0(0%)	-65.0%
Severe	0(0%)	0(0%)	0(0%)	0(0%)	0.0%
P value	0.102	0.523	0.165	0.501	-

Chi-Square/Fisher Exact Test

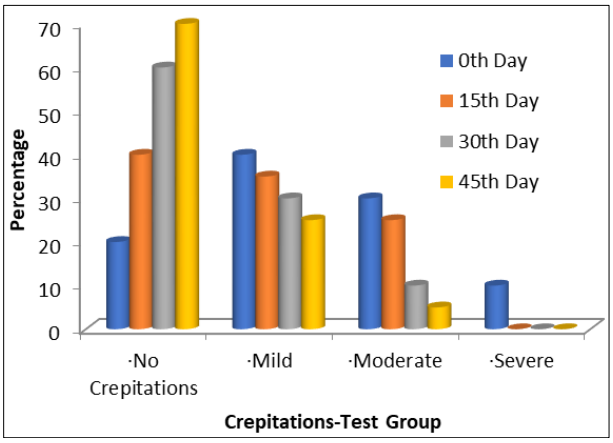

Fig 7

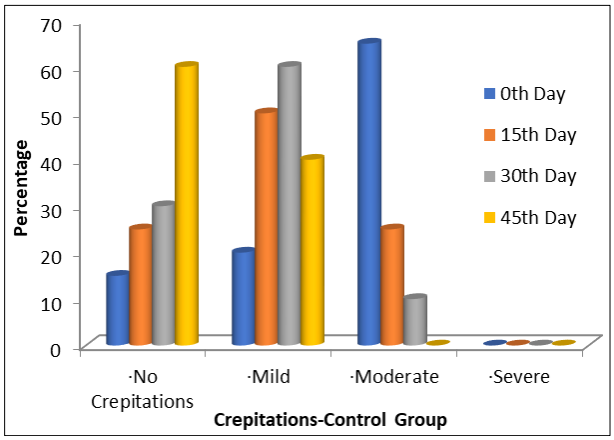

Fig 8

Table 5: 0th Day- Comparison of clinical variables in two groups of patients at 0th day of assessment

variables at 0th Day	Test Group	Control Group	Total	P value
Hemoglobin (g/dl)	12.51±2.02	12.09±2.39	12.30±2.20	0.557
TLC	9090.00±2700.08	9635.00±2602.48	9362.50±2632.02	0.520
Neutrophil	61.95±6.72	88.30±112.86	75.13±80.03	0.304
Lymphocytes	35.70±6.42	34.95±6.19	35.33±6.24	0.709
Eosinophils	1.70±0.92	1.4±1.10	1.55±1.01	0.355
Basophils	0.25±0.44	0.35±0.49	0.30±0.46	0.503
Monocytes	0.40±0.75	0.20±0.41	0.30±0.61	0.304

Student t test (Two tailed, independent)

Table 6: Comparison of clinical variables in two groups of patients at 45th days of assessment

variables at 45th Day	Test Group	Control Group	Total	P value
Hemoglobin (g/dl)	12.64±1.85	12.03±2.24	12.33±2.05	0.353
TLC	8660.00±2683.95	13590.00±20434.82	11125.00±14600.65	0.291
Neutrophil	60.35±5.99	62.95±5.38	61.65±5.77	0.157
Lymphocytes	38.70±5.95	36.20±5.71	37.45±5.89	0.183
Eosinophils	0.70±0.80	0.55±0.76	0.63±0.77	0.547
Basophils	0.05±0.22	0.25±0.55	0.15±0.43	0.140
Monocytes	0.05±0.22	0.05±0.22	0.05±0.22	1.000

Student t test (Two tailed, independent)

Table 7: CXR- assessment in two groups of patients at different time studied

CXR	Test Group (n=20)	Control Group (n=20)	Total (n=40)
0th Day	13(65%)	13(65%)	26(65%)
45th Day	13(65%)	13(65%)	26(65%)

Table 8: 0th Day- Comparison of Spirometry variables in two groups of patients at 0th day of assessment

Spirometry variables at 0th Day	Test Group	Control Group	Total	P value
FEV1% PRED	72.15±6.69	71.66±8.82	71.91±7.73	0.846
FEV1/FVC%	70.31±6.09	72.72±9.22	71.51±7.81	0.335
PEF	4.06±0.58	4.90±0.91	4.48±0.86	0.001**

Student t test (Two tailed, independent)

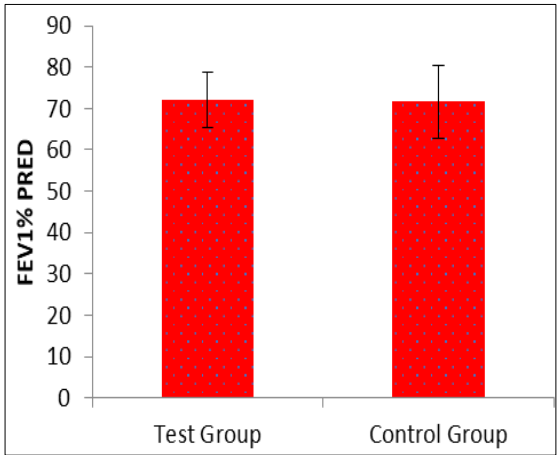

Fig 9

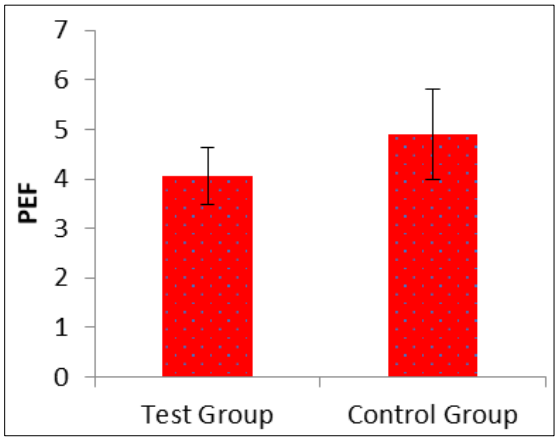

Fig 10

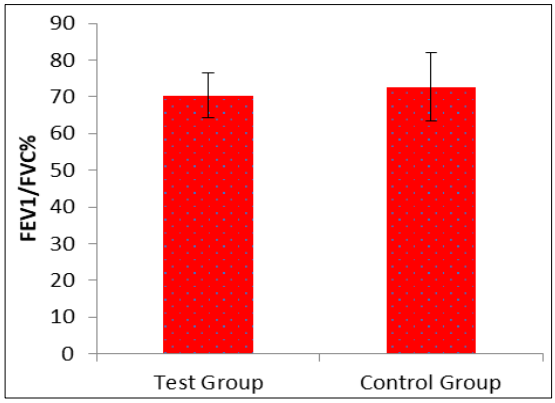

Fig 10

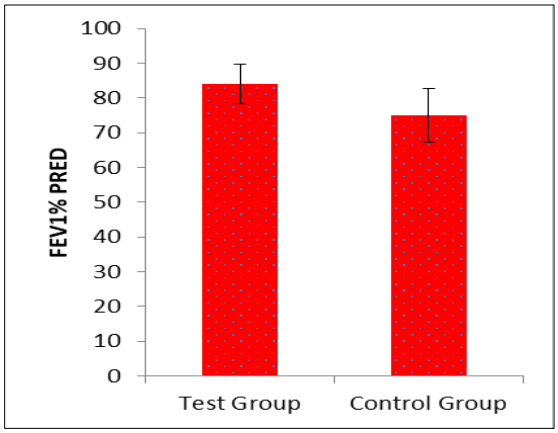

Fig 11

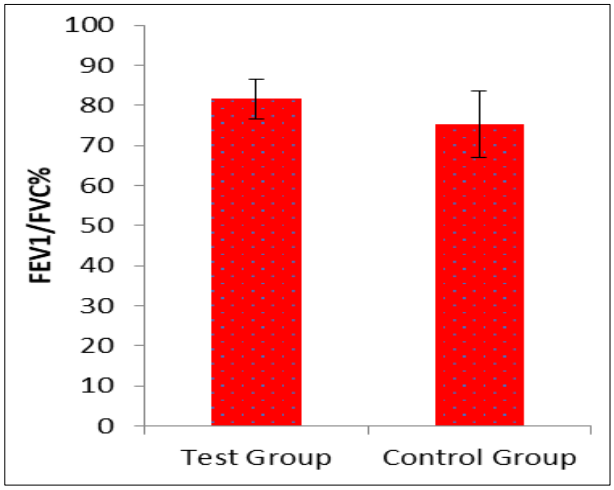

Fig 12

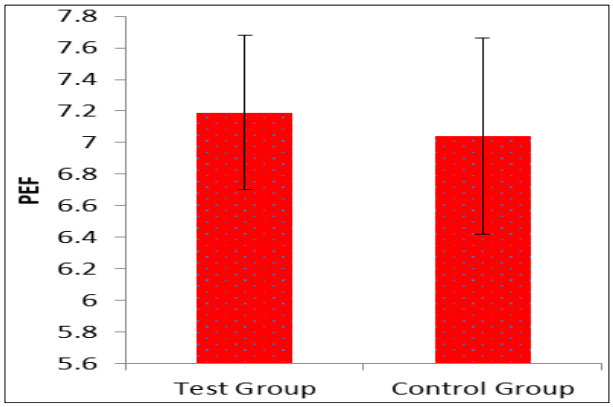

Fig 13

Table 9: 45th Day-Comparison of Spirometry variables in two groups of patients at 45th day of assessment

45th Day	Test Group	Control Group	Total	P value
FEV1% PRED	83.92±5.66	75.10±7.72	79.51±8.04	<0.001**
FEV1/FVC%	81.59±4.94	75.27±8.30	78.43±7.46	0.006**
PEF	7.19±0.49	7.04±0.62	7.12±0.55	0.415

Student t test (Two tailed, independent)

Table 10: Difference of Spirometry variables (45th day and 0th day) in two groups of patients studied

Difference	Test Group	Control Group	Total	P value
FEV1	11.77±6.95	3.43±2.96	7.60±6.75	<0.001**
FEV1/FVC	11.28±4.93	2.56±3.89	6.92±6.22	<0.001**
PEF	3.13±0.67	2.14±0.82	2.64±0.89	<0.001**

Student t test (Two tailed, independent)

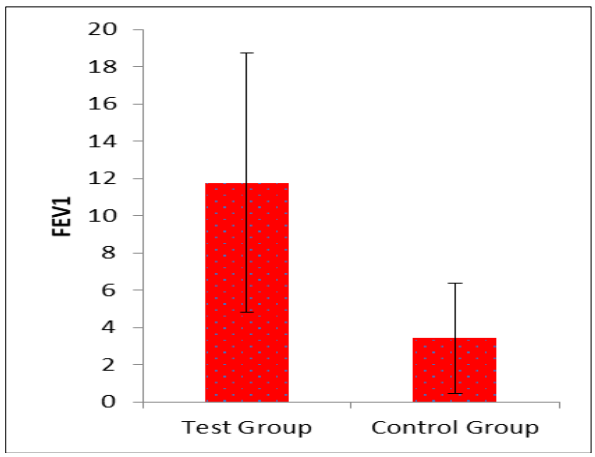

Fig 14

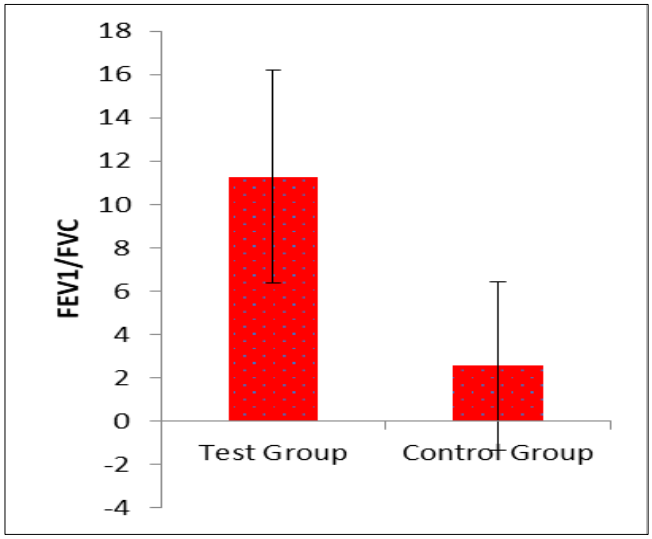

Fig 15

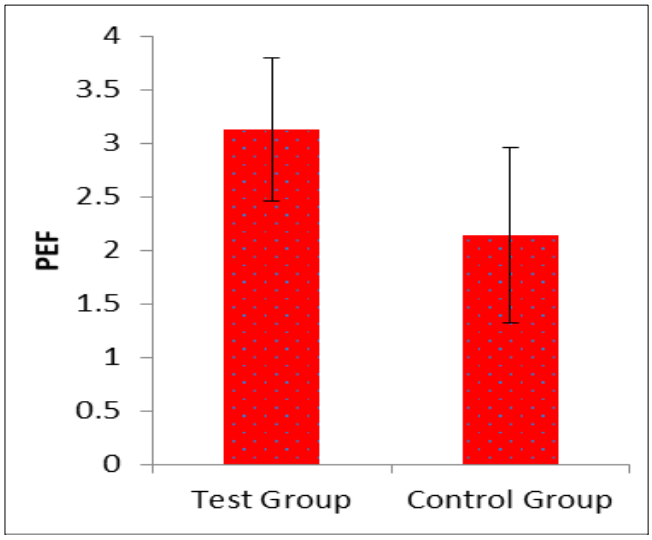

Fig 16

Statistical Methods

Student 't' test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Leven`s test for homogeneity of variance has been performed to assess the homogeneity of variance.

Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. Fisher exact test used when cell samples are very small.

Significant figures

+ Suggestive significance (P value: 0.05<P<0.10), * Moderately significant (P value: 0.01<P ≤ 0.05), ** Strongly significant (P value: P≤0.01).

Statistical software

The Statistical software namely SPSS 18.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Discussion

Cough was assessed and graded as severe, moderate, mild and absent and was coded as 3 (severe), 2 (moderate), I (mild) and 0 (no symptom), respectively. When the median scores of Cough in both Groups, A and B, were compared statistically using chi-square/Fisher Exact Test, it was found that the difference between the median scores of Test group at 45th day compared with baseline was highly significant. Intergroup comparison on 45th day was also very significant (P<0.834). Intergroup comparison on 45th day was also highly significant (p<0.222). (Table no.1). The severity of breathlessness was assessed and graded as per "MRC dyspnoea scale". The median scores of breathlessness in both Groups, A and B, were compared statistically using chi-square/Fisher Exact Test and it was found that the difference between the median scores of Test group at 45th day compared with baseline was highly significant (P<0.001). Intergroup comparison after 45 days was also very significant (p<0.910). (Table no.2). Wheezes were assessed and graded as very severe, severe, moderate, mild and absent and was coded as 4, 3, 2, 1 and 0 respectively. The results suggest that only test drug reduce wheezes when compared against that of control group. (Tab. no. 3). The present study observed that Ambroxol as well as test formulation are equally ineffective in supressing crepitations. (Tab.no.4) [17, 18].

When the median scores of chest X- Ray findings in both Groups, A and B, were compared statistically using Chi-Square/Fisherman Exact test for intergroups and for intragroups, there was no significant difference between the median scores of intergroups comparison at 45th day. (Tab.no.5) The significant improvement in test groups suggests that the test formulation is definitely superior to control drug in reverting the pathological findings of *Zeeq-Un-Nafas Shoabi (bronchial asthma).*to normal, Reversal of abnormal chest X- Ray findings to near normal is a strong indicaton of reduction in inflammatory pathological process.

The severity of FEV1 % predicted was assessed and graded as per "GOLD scale". The Mean ± SEM score for FEV1 % predicted in group A (control group) was 54.434 ± 6.115 on baseline and 62.018 ± 6.588 on 45th day, whereas in group B (Test group) the Mean ± SEM score of FEV1 % predicted was 49.434 ± 3.644 on 0 day and 70.248 ± 3.619 on 45th day [19, 20, 21].

When Mean ± SEM scores of predicted % of FEV_1 in both Groups, A and B, were compared statistically using student's 't' test, it was found that the difference between the Mean ± SEM score of Test group at 45th day compared with baseline was very significant (P<0.01). But there was no significant difference in intergroups comaprison (p>0.05). (Tab.no.8 & 9) [22, 23].

PEF in both Groups, A and B, were compared and it was found that the difference between the Mean ± SEM score of Test group (Group B) at 45th day compared with baseline was significant (P< m0.03). But there was no significant difference in inter groups comparison (p>0.05). (Tab.no.10). The spirometric measures of FEV_1 predicted %, FEV_1/FVC % and PEF are objective parameters that assess the extent of bronchial obstruction and conversely, available space for air transaction in the lungs. *Zeeq-Un-Nafas Shoabi* (bronchial asthma) affects bronchial space for air due to inflammation, narrowing, air trapping during expiration and excessive sputum. Present study evaluates the efficacy of test formulation for the enhancement of available free space for air transaction in *Zeeq-Un-Nafas Shoabi (bronchial asthma).*patients [24, 25].

Conclusion

The overall effect of the Unani test drug formulation (Kalongi (*Nigella sativa*) 10gm, Darchini (*Cinamum zeylanicum*) 10gm

& Shehad (Pure Honey) 20gm was found quite encouraging in the treatment of *Zeeq-Un-Nafas Shoabi* (bronchial asthma). Significant improvement was observed in cough, breathlessness, rhonchi and values of predicted FEV_1%, FEV_1/FVC and PEF in test group in comparison to standard control group. It is evident from the above described observations that the test drug is found significantly effective in improving almost all subjective and objective parameters in comparison to the 'Ambroxol'. The ingredients of the test formulation are economic, affordable to a common man, easily available, consistent with better compliance and palatability and devoid of any side effects. With all these qualities, the test drug can be proclaimed as a safe and effective medicine in the treatment of *Zeeq-Un-Nafas Shoabi* (bronchial asthma).

References

1. Masoli M, Fabian D, Holt S, Beasley R. Global Initiative for Asthma (GINA) Program The global burden of asthma: executive summary of the GINA dissemination committee report. Allergy. 2004;59:469-478.
2. Amraze Riya. New Delhi: CCRUM. 1995, 129-141.
3. Ibne Sina. AL-Qanoon-Fil-Tib. N. Delhi: Urdu translated by Kantoori G H, Idara Kitabul Shifa. 2007;59(88):163-247.
4. Jurjani I. Tarjumae Zakhirae Khuwarzam Shahi. Lucknow: Matabe Nami, Munshi Naval Kishore; YNM. 11, 264-71.
5. Tabri AAM. *Molaejat Buqratiyah*. N. Delhi. Urdu Transalated by CCRUM. 1997;11:468-469.
6. Majoosi AA. Kamil ul Sanaah. Lucknow: Urdu translation by Kantoori GH. Munshi Naval Kishore. 1889;1:490-91.
7. Eder W, Ege MJ, Von Mutius E. The asthma epidemic. N Engl J Med. 2006;355:2226-2235.
8. Anandan C, Nurmatov U, Van Schayck OCP, Sheikh A. Is the prevalence of asthma declining? Systemic review of epidemiological studies. Allergy. 2010;65:152-167.
9. Boskabady MH, Mohsenpoor N, Takaloo L. Antiasthmatic effect of *Nigella sativa* in airways of asthmatic patients. Phytomedicine. 2010;17(10):707-713.
10. Bell SG. The therapeutic use of honey. Neonatal Netw. 2007;26:247-51.
11. Jayaprakasha GK, Rao LJ. Chemistry, biogenesis, and biological activities of cinnamomum zeylanicum. Crit Rev Food Sci Nutr. 2011;51:547-562.
12. Hippocratic journal of Unani medicine. CCRUM. 2008;3(2):15-19.
13. Khan Azam. Quarabadine-Azam; New Delhi, Ejaz Publication House. 1994, 538.
14. Hakeem AM. Bustan ul mufradat. New Delhi: Idara Kitab ul shifa. 2002;165:266-267, 321, 518, 556.
15. Najmul Ghani. Khazain ul Advia. New Delhi: Idara Kitabul Shifa; YNM. 682-684, 1061, 1062.
16. Pride NB. Stockkley RA. Chronic obstructive pulmonary disease. Oxford text book of medicine. 3rd ed. 1996;2:766-78.
17. Mannino DM, Homa DM, Akinbami LJ, Ford ES, Redd SC. Chronic obstructive pulmonary disease surveillance—United States, 1971-2000. MMWR Surveill Summ. 2002;51(6):1-16.
18. Di Stefano A, Maestrelli P, Roggeri A, Turato G, Calabro S, Potena A. Severity of airflow limitation is associated with severity of airflow inflammation in smokers. Am J Respir Crit Care Med. 1998;158:1277-1285.
19. Spector SL, Nicklas RA. Practice parameters for the diagnosis and treatment of asthma. J Allergy Clin Immunol. 1995;96:729-31.
20. Matsuba K, Wright JL, Wiggs BR, Pare PD, Hogg JC. The changes in airways structure associated with reduced forced expiratory volume in one second. Eur Respir J. 1989;2:834-839.
21. Lamb D, McLean A, Gillooly M, Warren PM, Gould GA, MacNee W. Relation between distal airspace size, bronchiolar attachments, and lung function. Thorax. 1993;48:1012-1017.
22. O'Donnell DE, Revill SM, Webb KA. Dynamic hyperinflation and exercise intolerance in chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2001;164:770-777.
23. Rodriguez-Roisin R, MacNee W. Pathophysiology of chronic obstructive pulmonary disease. Eur Respir Mono. 1998;3:107-126.
24. Razi AMBZ. Kitab-ul-Mansoori. Urdu translation by CCRUM. New Delhi. 1991, 350-351.
25. Jeelani G. Makhzane Hikmat. Aijaz publishing house. New Delhi. 1994;11:379-381.