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Research Article

CT EVALUATION FOR THE EFFICACY OF A UNANI FORMULATION WITH *INKEBAB* IN THE TREATMENT OF ILTEHAB TAJAWEEFE ANAF MUZMIN

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ABSTRACT

Objective: To establish the efficacy of the oral Unani formulations with inhalation of *Kalonji* in comparison with the standard control in *Iltehab Tajaweefe Anaf Muzmin* (Chronic Rhinosinusitis [CRS]) based on the computed tomography (CT) paranasal sinuses (PNS) findings. To provide safe, effective, and economical treatment for Iltehab Tajaweefe Anaf Muzmin.

Methods: In this randomized, single-blind, standard-controlled study of 45 patients with CRS, the patients were allocated to two groups. In Group A, patients received Unani oral formulation: *Katan* (*Linum usitatissimum*), *Filfil siyah* (*Piper nigrum*), and *Asl-e-Khalis* in a 6 g BD dose with steam inhalation of *Kalonji* (*Nigella sativa*) BD and Tab Alaspan 1OD with Karvol Plus inhalation BD in Group B. Statistical data was analyzed using a paired-t test by comparing the total sinus score (TSS) of CT PNS calculated based on the Lund Mackay staging system before and after treatment.

Results: The result is statistically significant in Group A in comparison to the non-significant effect in Group B ($p<0.05$). After treatment, there was a 30% complete resolution of the TSS in CT PNS imaging in group A, in comparison to the 0% complete resolution of the TSS in group B. No adverse effects were reported during the study.

Conclusion: The oral Unani formulation with inhalation of *Kalonji* is safe and has a statistically significant effect on TSS (CTPNS) in patients with CRS in Group A. A multicentric trial of the test drug on a larger sample size for a longer duration is required to establish the efficacy of the *Inkebab* of *Kalonji* with oral Unani formulation on patients with CRS.

Keywords: Chronic rhinosinusitis, Unani formulation, *Katan*, *Kalonji*, Inhalation, Computed tomography paranasal sinuses.

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INTRODUCTION

Rhinosinusitis is a chronic inflammation of the nasal sinuses and mucosa that causes physical symptoms and has a significant impact on quality of life with functional and emotional impairment.

Chronic rhinosinusitis (CRS) is a very common disease that adversely affects the health of the population all over the world [1].

In the US, as per an earlier estimate by the American Academy of Otolaryngology, more than 37 million Americans have at least one episode of CRS in a year, which lasts for more than 8–12 weeks. It can significantly affect the worker's productivity and school performance on an individual level. There was a loss of a total of 21.2 household days per year on sinus care needs per day, with a yearly efficiency expenditure of $10,077.07 on a patient [2].

The national Institute of Allergy and Infectious Disease, India, has estimated that about 134 million Indians suffer from CRS [3].

Standard medical therapy for CRS includes both a broad-spectrum antibiotic and a topical intranasal steroid to address the strong inflammatory component of this disease. Local decongestants and mucolytic agents such as nasal drops and antihistamines are also recommended as adjunctive therapy as per the needs of the patient. In a few patients, the cavities are so blocked that surgery is advised [4]. However, revision surgeries were required in 20% of cases [5].

The potential side effects of the above-mentioned regimen with long-term usage, like drug resistance, allergic reactions, altered normal flora of the intestine, etc., are also of concern. Seemingly, all these and many other reasons are forcing patients to opt for alternative therapies in traditional medicine, including the Unani System of Medicine [6].

Unani physicians are treating the patients with CRS successfully with a compound formulation composed of *Katan* (*Linum usitatissimum* Linn.), *Filfil siyah* (*Piper nigrum* Linn.), and *Asl-e-Khalis* (Honey) with *Inkebab* (Medicated Steam Inhalation) of *Kalonji* (*Nigella sativa* Linn.) [7].

The present study was undertaken to evaluate the efficacy of the Unani compound formulation in the treatment of CRS patients based on computed tomography (CT) findings.

METHODS

Patients

The present randomized, single-blind, standard-controlled clinical trial was conducted in the Department of Moalejat, Faculty of Unani Medicine, Majeedia Hospital, and HAH Hospital, Jamia Hamdard, New Delhi, during July 2014–June 2015. The CRS patients were recruited based on the CRS definition: "Chronic sinusitis is defined as a condition of more than 12 weeks duration with two or more major symptoms or at least one major and two or more minor symptoms." [8] Ethical clearance was taken from the Jamia Hamdard Institutional Ethics Committee (No. 03/14, dated February 27th, 2014).

The patients were selected based on the inclusion criteria and were randomly allocated to the two groups with the block randomization method. The medical staff and patients were blind to the way of randomization. Guidelines for conducting clinical trials, i.e., Good

Clinical Practices and the Helsinki Declaration 2013, were followed strictly during the clinical trial.

Inclusion criteria

CRS patients between 18 and 70 years of age of both sexes have impaired quality of life, calculated by the rhinosinusitis disability index, and are willing to participate in the study. The patients using any other investigational agent in the last 30 days and constant or irregular use of inhaled, oral, IM, IV, and/or potent steroids, diabetes mellitus, chronic renal failure, liver failure, and pregnancy were excluded from the study [9]. Patients failed to pursue the protocol, any undesirable reaction or adverse event occured, and drug defaulters were taken as withdrawn cases.

Test drug

Composition of oral compound formulation

1. *Katan* (*L. usitatissimum* Linn.) 10.0 g/day.
2. *Filfil siyah* (*P. nigrum* Linn.) 2.0 g/day.
3. *Asl-e-Khalis* (Honey) 10.0 g/day
   Kalonji (*N. sativa* Linn.) 100 mg/kg for steam inhalation.

Control drug

Composition of Tablet Alaspan AM

- Loratadine 05 mg
- Ambroxol 60 mg

Capsule Karvol Plus for inhalation (Indoco Remedies Ltd.).

Dose and administration

1. Group A (test drug group): The patients were instructed to take oral medication of 6.0 g BD after the meal. Patients were instructed to pound, then boil *Kalonji* in water and inhale its steam after covering the head and face with a towel for 10 min BD [10,11].
2. Group B (control group): The patients were directed to get Tab Alaspan AM and 1Tab OD. The patients were directed to place Capsule Karvol Plus contents in boiling water and inhale its steam after covering the head and face with a towel for 10 min BD.

Study procedure

The detailed history and examination of the patients were recorded in the CRF after obtaining informed consent and were screened in the following manner:

Complete blood count with erythrocyte sedimentation rate, blood sugar fasting and pp, immunoglobulin E (0–10=low, 10–100=normal, 100≥ elevated), absolute eosinophil count, liver function test, kidney function test, X-ray chest postero-anterior view, CT scan paranasal sinuses (PNS), nasal swab culture, sensitivity test and cytology, electrocardiogram, and urine R/M [12]. The patients were given 1-week medication and directed to follow the patient's follow-up schedule (Table 1).

CT assessment

The findings of CT PNS were recorded as mucosal thickening >5 mm, polypoid changes, and opacification of one or more sinuses. The CT response to the treatment was assessed on the following parameters after calculating the total sinus score (TSS) calculated on the basis of the Lund Mackay staging system and comparing the TSS before and after treatment.

1. Resolution: Complete clearing of TSS
2. Improvement: Reduction in TSS
3. No change: No change in TSS
4. Worsened: Worsening in TSS [13].

Laboratory and CT scan PNS assessments were made before day zero and after the completion of protocol therapy on day 42.

RESULTS

Out of forty-five patients, 5 were excluded due to various reasons, and 40 patients completed the study, 20 in each group.

Demographic data

In group A, the average age of the patients was 29.7 years with a range of 18–52 years, and the male to female ratio was 10:10. In group B, the average age of the patients was 32.8 years, ranging between 18 and 50 years; the male to female ratio was 11:09.

Analysis of age data showed no statistically significant difference between the groups at the start of treatment, thus justifying the randomization in both groups (Table 2).

Effect of treatment on TSS of CT PNS findings

Resolution

The percentage of complete resolution of TSS was 30% in group A in comparison to 0% in group B (Table 3 and Figs. 1-3).

Improvement

The percentage of improvement in TSS was 45% in group A, in comparison to 0% in group B.

Unchanged

The percentage of unchanged TSS was 15% in group A, in comparison to 95% in group B.

Worsened

The percentage of worsened TSS was 10% in Group A in comparison to 05% in Group B (Tables 3-5).

Nontaxable transaction certificate (NCCT) PNS images of a 27-year-old male patient. A before-treatment scan dated January 20, 2015 shows extensive peripheral mucosal thickening in bilateral maxillary sinuses, as indicated by the arrows in Fig. 1a. After treatment, NCCT PNS dated March 11th, 2015 shows near-total resolution of the mucosal thickening, as indicated by the arrows in Fig. 1b.

NCCT PNS images of a 47-year-old female patient. A beforetreatment scan dated January 27th, 2015 shows extensive peripheral mucosal thickening in bilateral maxillary and ethmoid sinuses, as indicated by

Table 1: Patient's follow-up schedule

Visits	Ist	2nd	3rd	4th	5th
Days	0	7th	14th	28th	42th

Table 2: Age data of patients in group A and B

Group A	Group B	p-value
Mean±SD	Mean±SD	0.171604
29.7±9.89	32.85±10.752	NS at P<0.05

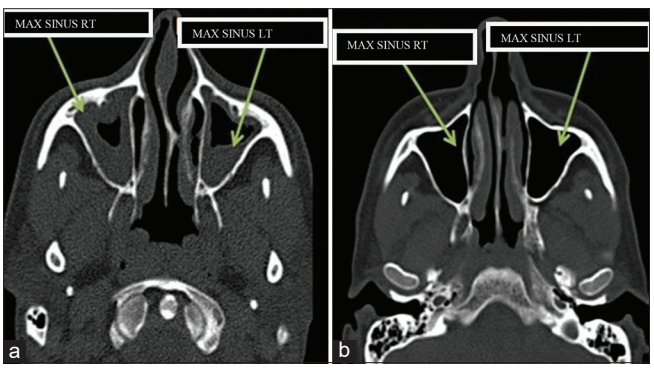

Fig. 1: (a and b) Effect of UNANI formulation on nontaxable transaction certificate of chronic rhinosinusitis patient in group-A

Table 3: Effect of treatment on TSS (CT PNS findings) in group A

S. No.	Grades	BT	%	AT							
				1	%	2	%	3	%	4	%
1.	Mucosal Thickening	15	75	5	25	6	30	2	10	2	10
2.	Polypoidal changes	03	15	1	05	1	05	1	05	0	00
3.	Opacification	02	10	0	00	2	10	0	00	0	00
	Total	20	100	6	30	9	45	3	15	2	10

BT: Before treatment, AT: After treatment, 1: Resolution, 2: Improvement, 3: Unchanged, 4: Worsened. CT: Computed tomography, PNS: Paranasal sinuses, TSS: Total sinus score

Table 4: Effect of treatment on TSS (CT PNS findings) in group B

S. No.	Grades	BT	%	AT							
				1	%	2	%	3	%	4	%
1.	Mucosal thickening	08	40	0	00	0	00	7	35	1	05
2.	Polypoidal changes	07	35	0	00	0	00	7	35	0	00
3.	Opacification	05	25	0	00	0	00	5	25	0	00
	Total	20	100	0	00	0	00	19	95	1	05

BT: Before treatment, AT: After treatment, 1: Resolution, 2: Improvement, 3: Unchanged, 4: Worsened. CT: Computed tomography, PNS: Paranasal sinuses, TSS: Total sinus score

Table 5: Effect of treatment on total sinus score of CT PNS in CRS patients (group A and B)

S. No.	Parameters	Group A (%)	Group B (%)
1.	Resolution	06 (30)	00 (0)
x2.	Improvement	09 (45)	00 (0)
3.	Unchanged	03 (15)	19 (95)
4.	Worsened	02 (10)	01 (05)

CRS: Chronic rhinosinusitis. CT: Computed tomography, PNS: Paranasal sinuses, TSS: Total sinus score

Table 6: Paired-t test analysis to show effect of treatment on TSS in group A and B

Groups	LM TSS AT/BT (SD±Mean)	p-value	Significance
A	2.9±2.75	0.00044	The result is significant at $P<0.05$
B	1.0198±2.75	0.66626	The result is not significant at $P<0.05$

LM: Lund Mackay staging system, BT: Before treatment, AT: After treatment. TSS: Total sinus score

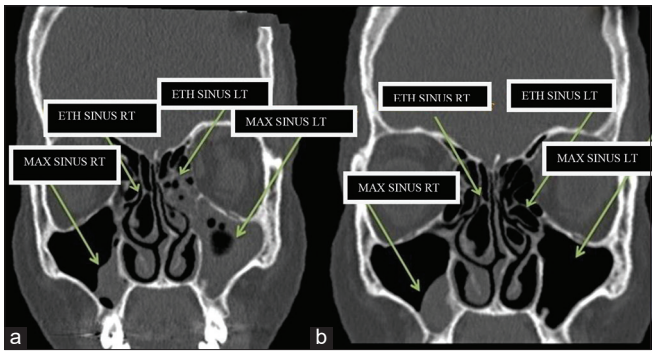

Fig. 2: (a and b) Effect of UNANI formulation on nontaxable transaction certificate of chronic rhinosinusitis patient in group-A

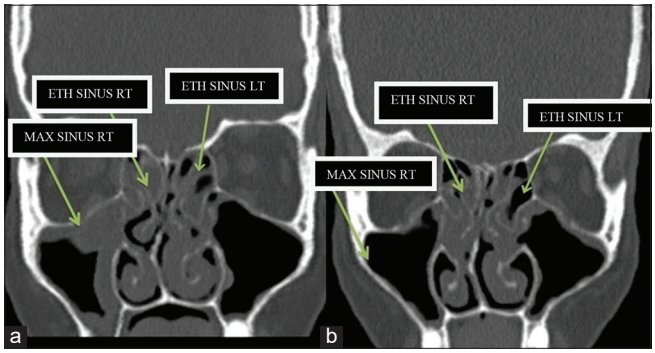

Fig. 3: (a and b) Effect of UNANI formulation on nontaxable transaction certificate of chronic rhinosinusitis patient in group-A

the arrows in Fig. 2a. After treatment, NCCT PNS dated March 05th, 2015 shows near-total resolution of mucosal thickening, as indicated by the arrows in Fig. 2b.

NCCT PNS images of an 18-year-old female patient. A before-treatment scan dated January 27th, 2015 shows extensive peripheral mucosal thickening in the left maxillary and bilateral ethmoid sinuses, as indicated by the arrows in Fig. 3a. After treatment, the NCCT PNS dated March 05th, 2015 shows near-total resolution of mucosal thickening in the left maxillary sinus, as indicated by arrows. Mucosal thickening in bilateral ethmoid sinuses persists (Fig. 3b).

Statistical analysis

On the statistical analysis of the data using a paired-t test by comparing the TSS of CT PNS before and after treatment, the result is statistically significant in group A and statistically non-significant in group B at $p<0.05$ (Table 6).

DISCUSSION

The Unani System of Medicine is one of the ancient systems of medicine in the world and is still in practice. It is based on the theory of four temperaments, i.e., hot, cold, wet, and dry. The cause of the diseases is an imbalance of the four humors of the body, i.e., blood, phlegm, yellow bile, and black bile besides other factors. In USM, CRS has been mentioned as *Iltehab Tajaweef-e-Anaf Muzmin/Nazla Muzmin,* a phlegmatic disease of cold temperament, and it is treated with hot temperament drugs [14].

In this study, we evaluated the efficacy and safety of the test drug with medicated steam inhalation of *Kalonji* on the basis of CT PNS findings. In a clinical study, it was found that after inhalation of hot steam at

42°C, there was an increased microcirculatory perfusion of the nasal mucosa. Up to the inhalation of steam 100 times, it leads to an effective increase in the microcirculation of the nasal mucosa [15]. CT PNS is the gold standard of investigation for the diagnosis of CRS. It is also a tool to evaluate the efficacy of functional endoscopic sinus surgery and other treatments in CRS patients [16].

The test drug with steam inhalation of *Kalonji* has a statistically significant effect on TSS in CT PNS, and there was complete resolution of TSS in 30% of patients after treatment with the test formulation.

This effect may be attributed to the anti-inflammatory effects of the *Katan* (*L. usitatissimum*), *Filfil siyah* [17,18], *Asl-e-Khalis* [19], and *Kalonji* [20-23]. The constituents of *L. usitatissimum,* like fatty acids, have anti-inflammatory action by affecting interleukin-6 and 13, cytokines, and tumor necrosis factor-α. The anti-histaminic and antibacterial effects of *Kalonji* contributed to the resolution of chronic inflammation [21-23]. *Filfil siyah* (*P. nigrum*) enhanced the bioavailability of *Katan* for a longer period [24].

In USM classical literature, *Katan*, *Filfil siyah*, *Asl-e-Khalis*, and *Kalonji* have been described as having *Mohallile Auram* (anti-inflammatory) and *Mullaiyene warm* (resolvent) effects [25-28].

In a randomized, single-blind, comparative clinical study of the same formulation, it was concluded that after 42 days of treatment, it has a statistically highly significant effect on major and minor symptoms of CRS in the test drug group ($p<0.0001$) in comparison to the significant effect in the control group ($p<0.01$) [29].

These findings approve the age-old claims of the Unani Physicians regarding the efficacy of this formulation in *Iltehab Tajaweefe Anaf Muzmin/Nazla Muzmin* (CRS).

CONCLUSION

Based on the above results, it may be concluded that the Unani formulation with *Inkebab* (medicated inhalation) of *Kalonji* (*N. sativa*) is a promising regime with a significant effect on TSS in CT PNS, with a higher percentage of complete resolution of the TSS in CT PNS of *Iltehab Tajaweefe Anaf Muzmin* (CRS) patients.

The test formulation, along with *Inkebab,* is considerably safe and well-tolerated, as no adverse effects were reported during the study period.

The trial period of 6 weeks of the study is short, and the sample size is also small.

A multicentric trial of the test drug on a larger sample size for a longer duration may be undertaken to establish the efficacy of the formulation based on a CT PNS scan.

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AUTHOR'S CONTRIBUTION

Zehra Zaidi has contributed to the planning, collection of data, analysis of research, and writing of research articles. Abhinav Jain analyzed the CT PNS data and finalized the CT scan for inclusion in the article. Asim Ali Khan edited the write-up of the research article.

CONFLICT OF INTERESTS

Nil.

FUNDING

Nil.

ETHICAL APPROVAL

This study was approved by the Jamia Hamdard Institutional Ethics Committee.

STATEMENT OF INFORMED CONSENT

Informed consent from patients was obtained.

REGISTRATION OF CLINICAL TRIAL

Clinical Trial Registry India, Registration No. CTRI 2018/04/013353.

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