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Original Article

Evaluating Clinical Efficacy and Safety of A Unani Formulation in the Management of *Nazla-i-Muzmin* (Chronic Rhinosinusitis)

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ABSTRACT

Nazla-i-muzmin (Chronic rhinosinusitis) is one of the commonest diseases prevalent all around the world. In India one in eight Indian suffers from this ailment. The current medical management and surgical intervention do not provide complete cure as a result there is a need to search a better alternative drug. The main objective of this study was to evaluate the safety and efficacy of a Unani formulation in the management of chronic rhinosinusitis. This study was designed as a randomised, controlled, parallel group and open label clinical study. It was carried out in 60 participants (30 participants in each group) of chronic rhinosinusitis aged between 18-65 years of either sex. The participants were enrolled based on the symptoms rhinorrhoea, sneezing, facial pain, nasal blockage, post nasal drip and thick nasal discharge. The participants of the test group was treated with a Unani formulation (9 gm) whereas Levocetrizine (10mg) was given to the participants of the control group once at night. In this study the average age of the participants was 30.36 (±10.20) years and 32.63 (±10.97) years in the control and test groups respectively with an average chronicity of 31.26 (± 43.46) months in the control group and 23.86 ± 39.4 months in the test group. The Unani formulation was found effective in reducing rhinorrhoea, sneezing, facial pain, nasal obstruction, post nasal discharge and thick nasal discharge. The snot score at post treatment comparing to the baseline was reduced to 2.1 and 2.0 in the test and control groups respectively. The Unani formulation improved the symptoms of chronic rhinosinusitis in the test group due to the possible action of the ingredients having, deobstruent, anti-inflammatory, concoctive, analgesic, expectorants and antimicrobial activities. It was concluded that the outcome of the study showed the successful management of chronic rhino-sinusitis. The formulation was well tolerated and showed no adverse effect.

Keywords deobstruent, *nazla-i-muzmin*, rhino-sinusitis, sneezing, Unani formulation

INTRODUCTION

Nazla-i-muzmin (chronic rhinosinusitis) refers to the inflammation of the mucosal lining of nose and paranasal sinuses lasting for more than 12 weeks. The term sinusitis is replaced by rhinosinusitis because sinusitis often preceded by rhinitis and rarely occurs without concurrent nasal airway inflammation (Benninger, 2003). The repeated attacks of acute sinusitis lead to chronic sinusitis or acute sinusitis may lead to chronic sinus disease (Schlossberg, 1987). The bacteria or fungi are commonly associated with this disease. Clinically, it is very difficult to cure most cases in the stage when ciliary activity is impaired due to thickening and damage of the mucous membrane (Braunwald and Fauci, 2001). This condition may headway until the sinus is filled with polypi and pus which is allowed at frequent intervals into the nose. The discharge is frequently foul. Pain and tenderness may disappear as the condition is settled into chronic stage (Hall and Colman, 1981). Chronic sinusitis is a major health care issue that affects a large group of population. The prevalence of sinusitis in Southern countries like India 134,198,900 out of 1,065,070,607 populations (U.S census bureau, 2004). Roughly 12% of Americans beneath the age of 45 years report side effect of incessant sinusitis. (Adams and Marano, 1995) Around 40 million Americans are influenced by sinusitis consistently, with 33 million instances of interminable sinusitis revealed every year to the U.S communities for infection control and prevention (Hodgson and Cohen, 1999). When sinusitis is viewed as together with usually related comorbid conditions, for example, un-favourably susceptible rhinitis, asthma and constant bronchitis, worsening of these sicknesses influences in excess of 90 million individuals about one of three Americans (Mihail, 2009).

The current medical management includes the use of decongestants, antihistaminics and antibiotics but they do not cure all the patients. The surgical intervention e.g antral puncture and drainage is also recommended as a therapeutic approach which fails to provide permanent cure to all patients. The Unani medicines have been used to treat chronic rhino-sinusitis since ages. They have been found safe and effective in its management. But there is a lack of documentary evidence to prove its efficacy in terms of clinical study. Keeping in view the given circumstances, this study was designed to evaluate the safety and efficacy of the classical Unani formulation containing the

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ingredients *Shoniz (Nigella sativa), Zaranbad (Curcuma zedoaria), Bisbasa (Myristica fragrans), Asal (honey).* (Anonymous, YNM). The outcome of this study could be utilized to generate documentary evidence of effectiveness of the Unani formulation in clinical practice.

MATERIALS AND METHODS

This study was carried out with 60 participants (30 participants in each group) diagnosed with chronic rhinosinusitis at outdoor patient department of National Research Institute of Unani Medicine for skin disorders (NRIUM-SD) Hyderabad during 1st July 2019 and 30th July 2020. The protocol of the study was approved by the institutional ethics committee (38-18/2018-19/CRIUM/Tech/IEC-10/12) and registered in Clinical Trials Registry-India(CTRI) under registration no. CTRI/2019/04/018668 before enrolment of the first participants. This study was designed as a randomized, controlled, parallel group and open label clinical study. The participants aged between 18 years to 65 years of either sex were included in this study based on the symptoms such as rhinorrhoea, sneezing, facial pain, nasal discharge, and nasal blockage. The participants having comorbid conditions such as diabetes mellitus, hypertension, pregnancy, immunosuppressed participants, ischaemic heart disease and hepato-renal dysfunction were not included in this study.

Sample Size Estimation

Sample size for this study was empirically fixed to be 75 participants including 25% dropout so that the completed sample size was 60 participants (n=30 in each group). Out of 120 participants screened for the study, 45 participants did not fulfil the inclusion and exclusion criteria. 75 participants were enrolled and randomized into the test and control groups as per scheme of block randomization developed a priori. Of them, 7 participants in the test group and 8 participants in the control group did not complete the duration of the protocol therapy due to noncompliance of the therapy, lost to follow-up, concurrent illness and migration of the participants.

Intervention

The participants of the test group were treated with the classical Unani formulation having *Shoniz (Nigella sativa), Zaranbad (Curcuma zedoaria), Bisbasa (Myristica fragrans), Asal (honey)* in semisolid dosage form at a dose of 9 gm thrice daily for 21 days. Moreover, allopathic drug levocetrizine hydrochloride was given orally in a dose of 10 mg at bed time for 21 days to the participants of the control group (Phillip Auckland 1311, New Zealand).

Method of preparation of the drugs

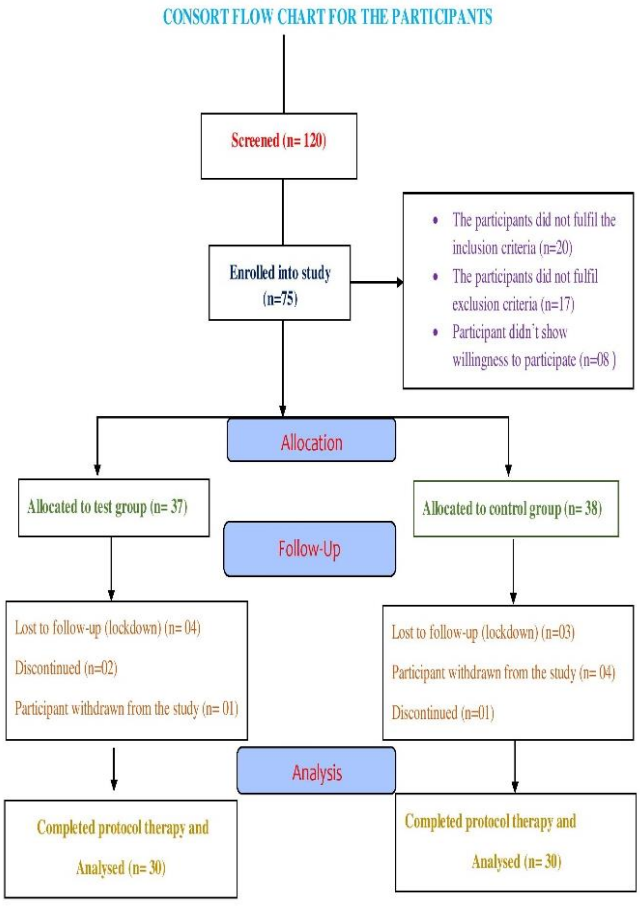
The classical Unani formulation was prepared in the GMP certified pharmacy of the institute. All the 4 ingredients of the Unani formulation were purchased from the open market at Hyderabad and identified by the botanist of SMPU of the institute. It was prepared as per instructions given in the classical book *"Ikseer-i-Azam"* Volume II. The impurities and superfluous materials were removed from the raw single drugs and then powdered them. The crude powder were mixed with honey and the formulation was prepared in semisolid dosage form. The prepared formulation was stored in an opaque plastic container.

Assessment of efficacy and safety of the drugs

The efficacy of the drugs was assessed in terms of post treatment reduction in SNOT (Sino-nasal outcome test) Score. The Systemic safety was assessed on the basis of hemogram (haemoglobin %, total leucocyte count, differential leucocyte count, erythrocyte sedimentation rate), absolute eosinophil count, biochemical (serum bilirubin, serum glutamic-oxaloacetic transaminase, serum glutamic-pyruvic transaminase, serum alkaline phosphatase, serum creatinine, blood urea nitrogen and fasting blood sugar), complete urine examination (routine and microscopic) and X-ray paranasal sinus (water's view).

Statistical analysis of the data

The data were analyzed as per protocol. The continuous variables were measured in Means and standard deviation. The categorical variables were measured in frequency and ranges. The charts and tables were prepared in MS excel (2016). The Paired t-test was used to determine the statistical significance of the difference in SNOT score at post treatment. $\alpha \leq 0.05$ was considered to determine statistical significance.



OBSERVATIONS AND RESULTS

Table 1. Baseline characteristics of the participants

Baseline characteristics	Study Groups	
	Test Group (n= 30)	Control Group (n= 30)
SEX		
Male, n, (%)	11 (36.6)	11 (36.6)
Female, n, %	19 (63.3)	19 (63.3)
Average Age (± S.D) years	32.63 ± 10.97	30.36 ± 10.20
18-27 years, n, (%)	11 (36.6)	13 (43.3)
28-37 years, n, (%)	10 (33.3)	12 (40)
38-47 years, n, (%)	6 (20)	3 (10)
48-57 years, n, (%)	1 (3.3)	2 (6.6)
58-67 years, n, (%)	2 (6.6)	0
Average Chronicity (months) Mean (± S.D)	23.86 (± 43.46)	31.26 (± 39.01)

The demographic characteristics at baseline of the participants is shown in Table 1. The baseline characteristics were comparable in both groups. In this study we enrolled 30 participants (63.3% female and 36.6% male) in each group. The average age (± SD) was 30.36 (± 10.20) years and 32.63 (± 10.97) years in the control and test group respectively. The maximum number of the participants was present in 18-27 years age group i.e., 13 participants (43%) in the control group versus 11 participants (36.6%) in the test group. Average chronicity of rhinosinusitis was 31.26 (± 39.01) months in the control group and 23.86 (± 43.46) months in the test group at the baseline. The haematological and biochemical parameters were remained within the normal limits at baseline as well as post treatment.

Table 2. Distribution of the participants according to their symptoms

S.No.	Symptoms	Test group (n=30) n, (%)	Control group (n=30) n, (%)
1	Rhinorrhoea	27 (90%)	29 (96.7%)
2	Sneezing	29 (96.7%)	29 (96.7%)
3	Facial pain	21 (70%)	23 (76.7%)
4	Loss of sense of smell	27 (90%)	28 (93.3%)
5	Cough	26 (86.7%)	20 (66.7%)
6	Post Nasal Discharge	29 (96.7%)	27 (90%)
7	Thick Nasal Discharge	29 (96.7%)	26 (86.7%)
8	Ear Pain	17 (56.7%)	14 (46.7%)
9	Dizziness	21 (70%)	16 (53.3%)
10	Nasal Blockage	27 (90%)	29 (96.7%)

Table 2 shows the presence of the symptoms of chronic rhinosinusitis at baseline in the test and control groups. The sneezing was present in 29 participants (96.7%) in each test and control groups. Facial pain was found in 21 participants (70%) in the test group versus 23 participants (76.7%) in the control group. In the control group, 28 participants (93.3%) had loss of sense of smell whereas it was present in 21 participants (90%) in the test group. In the control group 26 participants (86.7%) reported cough in comparison to 20 participants (66.7%) in the test group. The post nasal drip, thick nasal discharge, ear pain, nasal blockage and dizziness were reported in 29 participants (96%), 29 participants (96%), 17 participants (56.7%), 27 participants (90%) and 21 participants (70%) in the test group.

Table 3. Snot score at baseline and post treatment

S.N	Symptoms	Test group		Control Group	
		Baseline Mean (± S.D)	Post treatment Mean (± S.D)	Baseline Mean (± S.D)	Post treatment Mean (± S.D)
1.	Rhinorrhoea	3.03 (±1.1)	0.86 (±1.3)	2.8 (±1.06)	0.9 (±0.78)
2.	Sneezing	3.03 (±1.12)	0.87 (±1.07)	3.13 (± 0.9)	1.17 (±0.79)
3.	Facial Pain	1.8 (±1.42)	0	1.93 (±1.3)	0.03 (±0.18)
4.	Loss of sense of smell	2.3 (± 1.23)	0.4 (±0.93)	2.34 (±1.15)	0.2 (± 0.48)
5.	Cough	1.87 (± 0.96)	0.43 (±0.6)	1.6(±1.33))	0.56 (±0.97)
6.	Post Nasal Discharge	2.2 (±1.0)	0.1 (±0.40)	2.3 (± 1.08)	0.2 (± 0.55)
7.	Thick nasal Discharge	2.16 (±0.84)	0.16 (±0.)	2.1 (±1.16)	0.06 (±0.24)
8.	Ear Pain	1.23 (±1.1)	0.06 (±0.12)	1 (±1.12)	0.1 (±0.38)
9.	Dizziness	1.67 (±1.2)	0.17 (±0.3)	1.2 (±1.3)	0
10.	Nasal blockage	2.9 (±1.5)	0.7 (±0.86)	3.06 (±1.04)	0.43 (± 0.62)

Improvement in the symptoms in terms of snot score has been summarised in Table 3. In the test group, the difference in snot score at post treatment comparing to the baseline of the symptoms rhinorrhoea, sneezing, facial pain, loss of sense of smell, cough, post nasal drip, thick nasal discharge, ear pain, nasal blockage and dizziness had been found clinically and statistically significant. On comparing inter-group, the difference in snot score at post treatment of the symptoms

rhinorrhoea, sneezing, facial pain, loss of sense of smell, cough post nasal drip, thick nasal discharge, ear pain, nasal blockage and dizziness was not statistically significant.

DISCUSSION

Our study focused on clinical evaluation of efficacy and safety of a Unani formulation in management of chronic rhinosinusitis. It was observed that the majority of participants were female (63.3%) in each group corresponding to the study done by Seys SF (Seys and De Bont, 2020). The mean age of the participants was 32.63 (±10.97) years in the test group and 30.36 (±10.20) years in the control group. A previous study also showed the similar mean age of the participants (Dar and Lone, 2013). The majority of the participants were in the age group of 18-27 years. The similar findings was reported in an another study (Chaturvedi and Grewal, 2020). In this study family history of chronic rhinosinusitis was present in 36.7% participants and 30% participants in the test and control groups respectively. Our findings corresponds to the previously reported study (Chaturvedi and Grewal, 2020). It was observed that chronic rhinosinusitis was prevalent in 23.3% *damvi (sanguine)* participants followed by 43.4% participants *balghami (phlegmatic)*, 23.3% participants *safravi (bilious)* and 10% participants *sawdawi (melancholic)* in the test group. On the contrary, the control group had 50% participants *balghami* followed by 10% participants *safravi*, 33.3% participants *damvi* and 6.7% participants *saudawi* temperaments. This observation correspond to the observation given by Unani physician who observed that chronic rhinosinusitis was a *balghami* disease. (Anonymous, YNM)

The efficacy of the formulation was assessed in terms of reduction in Snot score at post treatment comparing to baseline in each group. This study demonstrated that the difference in mean Snot score in test group and control group were 2.1 and 2.0 comparing with baseline. The difference in mean Snot score was statistically significant in both the groups. The result of this study revealed that Unani formulation was comparatively more effective clinically than that of control drug. The magnitude of reduction in Snot score was comparatively higher in the test group. The Unani formulation had shown encouraging results in terms of reduction in Snot score after treatment of 21 days.

The Unani formulation had been found effective in alleviating signs and symptoms of chronic rhinosinusitis in this study. Its possible mechanism of action may be explained in terms of pharmacological properties of the ingredients of the Unani formulation. The Unani formulation used as a test drug in this study contained four ingredients (i.e, Nigella sativa, Curcuma zedoaria, Myristica fragrans and Honey*). Shoniz (Nigella sativa)* is a known anti-inflammatory (Anonymous, 2007), concoctive (Munshi, 2007) expectorant (Kabīruddīn, YNM) deobstruent (Shamshuddin, 2008) and analgesic (Anonymous, 2007) medicine. It may help in reducing inflammation of nasal mucosa and expulsion of accumulated secretions. It also possess anti-bacterial (Ahmad and Ghafoor, 2004) and anti-fungal (Bita and Rosu, 2012) properties. Moreover, *Zaranbad (Curcuma zedoaria)* is another ingredient of the Unani formulation and used as deobstruent (Baitar, 1999) and expectorant (Hakeem, 2002). It may facilitate excretion of accumulated secretions from the paranasal sinuses. *Bisbasa (Myristica fragrans)* possess anti-inflammatory activity. A study revealed that the methanol extract of *Myristica fragrans* (1.5g/kg), ether fraction (0.9g/kg) and n-hexane fraction (0.5g/kg) had anti-inflammatory activity similar to that of indomethacin (10mg/kg). The phytochemical myristicin was responsible for the anti-inflammatory activity (Ozaki and Soedigdo, 1989). Honey is a potent laxative and deobstruent. (Hakeem, 2002) It may help in excretion of viscid phlegm accumulated in paranasal sinuses. Its antibacterial properties controlled the growth of microorganisms in the sinuses as a result facial heaviness, nasal obstruction, nasal irritation and postnasal drip may got improved.

The Unani formulation was found safe and tolerable. All biochemical and haematological parameters remained within normal limits when compared from the baseline value with that of post treatment. There are certain limitations in this study. The sample size was small. The duration of protocol therapy was very short. The time period and financial funding were very limited. Although the study was designed to minimize the biases and effect of confounder (if any), the outcome of the study could have biases due to not implementation of blinding in the study due to differences in physical features of the test and control drugs. It may be suggested that another rigorous clinical study may be conducted to further establish its effectiveness and safety in larger population.

CONCLUSION

The outcome of this study suggests that this Unani classical formulation may be recommended for the management of chronic rhinosinusitis. Although this formulation had been used as a therapeutics for chronic rhinosinusitis since a long time, the outcome of this study validates its effectiveness in the treatment of chronic rhinosinusitis. Nowadays there is an emerging demand regarding scientific evidence of effectiveness of the pharmacopoeial and classical Unani formulations. The outcome of this study could be utilized to carry out another study with large sample size to establish the effectiveness of this Unani formulation in the management of chronic rhinosinusitis.

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CONFLICT OF INTEREST

Authors declared that there was no conflict of interest.

REFERENCES

Bita A, Rosu A, Calina D, *et al*. An alternative treatment for Candida infections with Nigella sativa extracts, *European Journal of Hospital Pharmacy: Science and Practice,* 2012;19:162.

Adams PF, Marano MA. Current estimates from the national health interview survey, 1994. Vital and health statistics. Series 10, Data from the National Health Survey, 1995;193 (1):1-260.

Anonymous. U.S census bureau, International data base. USA; 2004.

Anonymous. Ikseer Azam, YNM; 515.

Anonymous. Standardization of Single Drug of Unani medicine, (New Delhi, India: CCRUM), pp.196-200, 1992.

Anonymous. The Unani Pharmacopoeia of India: Ministry of Health & family Welfare, Dept. of AYUSH, New Delhi, 2007;1(1): 42-3

Benninger SM. Adult chronic rhinosinusitis: Definitions, Diagnosis, Epidemiology, and Pathophysiology, Otolaryngology-Head and Neck Surgery, 2003;129 (3): S1-S32.

Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL. Harrison's principles of internal medicine, McGraw Hill, 2001.

Chaturvedi A, Grewal DS. A Cross-Sectional Study on Demographic and Clinical Profile of Chronic Rhinosinusitis (CRS) Patients in a Tertiary Care Hospital. *Galore International Journal of Health Sciences and Research*, 2020; 5 (1):17-9.

Dar AK, Lone AH. Demographic Study of Sinusitis in Patients Visiting Govt: Unani Hospital Srinagar and Ayush Centres in Kashmir, Medical Journal of Islamic World Academy of Sciences, 2013; 109 (893):1-4

Ghulam Nabi Munshi. *Makhzanul Mufradat wa Murakkabat.* (New Delhi, India; CCRUM), pp.100, 2007

Hair PI, Scott LJ. Levocetirizine: a review of its use in the management of allergic rhinitis and skin allergies, *Drugs*, 2006; 66(7):973-96. doi: 10.2165/00003495-200666070-00017.

Hakeem M. Bustanul Mufradat. (New Delhi, India: Idara Kitabul Shifa), 2002, pp. 267, 268, 384, 385, 432, 433, 476, 477

Hall IS, Colman HB. Disease of Nose Throat and Ear. 2nd ed. (Edinburgh, UK: Longman Group Ltd), pp. 61-8, 223-8, 1981

Hodgson TA, Cohen AJ. Medical expenditures for major diseases, 1995, *Health Care Financing Review,* 1999; 21(2):119

Ibn Baitar. Al-Jamiul Mufradatul Advia. wa al-Aghziya, (Urdu translation CCRUM). III volume, (New Delhi, India: Ministry of Health and Family Welfare, Govt. of India.), pp.271-275, 1999

Ibn Baitar. Al-Jamiul Mufradatul Advia. wa al-Aghziya. (Urdu translation CCRUM), (New Delhi, India: Ministry of Health and Family Welfare, Govt. of India.), pp.248-249, 186, 187, 330, 331, 1999

Kabīruddīn HM. Makhzan al-Mufradāt. (New Delhi, India: Ejaz Publishing House), pp.460-1, YNM

Mihail F. Herbal, traditional and alternative remedies, In Common Cold, pp. 309-347, 2009

Ozaki Y, Soedigdo S, Wattimena YR and Suganda AG. Anti-inflammatory effect of mace, aril of Myristica fragrans Houtt. and its active principles, *Jpn J Pharmacol*, 1989; 49(2): 155-63.

Ray NF, Baraniuk JN, Thamer M, Rinehart CS, Gergen PJ, Kaliner M, Josephs S, Pung YH. Healthcare expenditures for sinusitis in 1996: contributions of asthma, rhinitis, and other airway disorders, *Journal of Allergy and Clinical Immunology*, 1999; 103 (3):408-14.

Schlossberg D. Infections of the Head and Neck. (New York, USA; Springer). pp. 81-87, 1987

Seys SF, *et al.* Real-life assessment of chronic rhinosinusitis patients using mobile technology: The my Sinusitis Coach project by EUFOREA, *Allergy*, 2020; 75(11):2867-78.

Shamshuddin IQ. Tibb-i-Nabvi. (Al Darul Salfia Mumbai), pp. 553-6, 2008

Tembhurne, SV, Feroz, S, More, BH, & Sakarkar, DM. A review on therapeutic potential of Nigella sativa (kalonji) seeds, *Journal of Medicinal Plants Research*, 2014; 8(3), 167-177.