

Effects of combined Unani formulations in allergic rhinitis (Nazla Haar) with special reference to the eosinophils in nasal smear

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Abstract

Allergic rhinitis is an Immunoglobulin E mediated hypersensitivity disease of nasal mucosa characterized by sneezing, itching, watery nasal discharge and a sensation of nasal obstruction. The worldwide prevalence varies from 2% to 20%. The objective of the study was to evaluate the efficacy of Unani formulations in Allergic rhinitis along with the effect on nasal smear eosinophilia. A randomized single blinded placebo controlled study was conducted in the outpatient department of National Institute of Unani Hospital, Bangalore, India, over 40 patients. Test group was given decoction of *Behidana*, *Unnab* and *Sapistan* with *Sharbate Banafsha*, whereas, the placebo group was treated with caramel syrup. Both groups were received drugs in a dosage of 25 ml twice a day for 15 days. The efficacy of the study was observed in the Nasal Smear for Eosinophils (NSFE) on baseline and at the end of the treatment. The test drug was found to be effective with $P < 0.01$ in comparison with placebo. The study revealed that the test drug is effective in reducing the number of eosinophils in allergic rhinitis patients, without any adverse effects.

Introduction

Allergic rhinitis (AR), also known as nasal allergies [1] or hay fever [1, 2], is an IgE mediated hypersensitivity disease of nasal mucosa characterized by sneezing, itching, watery nasal discharge and a sensation of nasal obstruction [3]. This may also be associated with symptoms of itching in the eyes, palate and pharynx [4]. Common allergens are pollens of grasses, weed and trees, house-dust mites, animal dander mold [1, 5] and foods [1]. Exposure to an allergen triggers the release of histamine which causes the inflammatory reaction and onset of symptoms [1].

Every year nearly 80 million people experience 7 or more days of nasal or ocular symptoms [6]. It is one of the commonest allergic diseases affecting more than 50% of atopics in India [7]. Its worldwide prevalence rate varies from 2% to 20% and the maximum prevalence is observed in the second decade of life [8].

The association between eosinophils and allergic disease has been known for many years [7]. Usually there is no eosinophil in a normal healthy individual's nasal smear [9];

there is mounting evidence that eosinophils are implicated in pathophysiology of allergic respiratory diseases, the direct and easy access of airborne allergens and irritants to the airways stimulate mast cells to produce IgE and cytokines which serves as enhancing factors for eosinophilic infiltration in allergic diseases [2]. During natural exposure to allergen, eosinophils in nasal lavages increase 20 fold, followed closely by increasing nasal symptoms [10].

There is no single test as a gold standard for the diagnosis of AR, [11] but nasal smear for eosinophilia has been recommended as a useful tool for the diagnosis [12]. This is a simple, reproducible, easy to perform and economical as compared to other tests e.g. Skin prick test, radioallergosorbent test (RAST), Total IgE level and absolute eosinophils count [3].

In addition to the diagnosis of allergic rhinitis, nasal smear eosinophilia has been suggested for the diagnosis of a special type of non-allergic rhinitis, and patients can be identified who has many eosinophils in nasal secretions called eosinophilic non-allergic rhinitis [12].

Unani system of medicine considered *Nazla Haar* is a disease with multiple etiologies; accordingly it was treated with holistic approach by adopting the principle of contrary to the disease state. Based on the range of prescriptions comprises on single and compound formulations for the management of *Nazla Haar*, combined formulations from Bayaze Kabeer [13] consists of *Behdana* (*Cydonia oblonga*), *Unnab* (*Zizyphus jujube*), *Sapistan* (*Cordia dichotoma*) and *Banafsha* (*Viola odorata*) were selected to validate its safety and efficacy clinically.

The aim of this study was to evaluate the effect of Unani Formulations and its effect on nasal smear nasal eosinophilia.

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Materials and Methods

This was a randomized single blinded placebo controlled study conducted at Bangalore hospital, National Institute of Unani Medicine (NIUM), after the approval of the Institutional Ethical Committee (IEC) 2010/11, over a period of 9 months from March 2011 to December 2011. Forty patients randomly allocated to test (n=30) and placebo (n=10) groups between 12 to 50 years of age belongs to either sex, with typical history and clinical features of allergic rhinitis, who have agreed to follow the protocol, were included in the study after obtaining written informed consent. On the other hand, patients with atrophic rhinitis, sinusitis, deviated nasal septum, nasal polyps/ nasal growth/ adenoids, asthma, patients with systemic diseases like diabetes mellitus, cardiovascular, impaired renal and hepatic functions and who were on steroid therapy were excluded from the study.

Test group was treated with decoction of *Cydonia oblonga* (*Behdana*), *Zyziphus jujuba* (*Unnab*) and *Chordia dichotoma* (*Sapistan*) with syrup of *Viola odorata* (*Banafsha*) in the dosage of 25ml twice a day orally for 15 days, whereas, the placebo group was treated with caramel syrup, with the same quantity and duration. Nasal Smear for Eosinophils (NSFE) was observed as an objective parameter on baseline and at the end of the treatment, After 15 days of treatment, the pre and post treatment data were analyzed and subjected to comparison statistically to evaluate the efficacy and safety of the treatment. In order to determine adverse effect of test drug, safety parameters like haemogram, LFT and RFT were carried out.

Sample of nasal secretion was collected by a tightly wound cotton swab from the posterior part of the lower or middle turbinate, as described elsewhere [12]. Then the smear was spread out to a thin layer on a glass slides, stained by diluted Giemsa solution (1ml Giemsa stain was diluted by 9 ml of distilled water), and kept them for air dry. Then, the stained slides were observed under the electronic microscopy in different powers for eosinophils. For this single-blinded study, all the smears were coded and read by a single investigator.

Grading of nasal smear was done by using method of Shioda and Mishima [3]. 0: no cells, + : few cells or small clumps, ++ : moderate number or large clumps and +++ : larger clumps. After grading, the observation was correlated with the clinical findings.

Statistical analysis

Data were analyzed by using Paired and Kruskal- Wallis with Dunn's Multiple Comparison

Results and Observations

Total 40 patients were completed this trial. Among them, 22 had seasonal allergic rhinitis and the other 18 had persistent or perennial rhinitis.

A positive nasal smear for eosinophilia was identified in 26 patients (86.67%) in test group, out of which 18 were +, 5 were ++ and 3 were +++; and only 5 (50%) in controls, among them 3 were + and 2 were ++ (Table 1). The difference between the test and control groups was statistically significant ($p < 0.05$). Incidence of eosinophilia was found to increase in smears with increasing severity of sneezing and runny nose. It was significantly higher in patients with complaints of intermittent as compared to continuous nasal symptoms. There was no association between eosinophilia and age in either group, despite the fact that all 5 of the allergic rhinitis patients aged above 40 years old yielded positive results (Table 2).

Out of 30 patients, 26 in test and 5 out of 10 in placebo control groups were positive with nasal smear for eosinophils on baseline day of treatment. After the completion of the treatment i.e., the day 15th, in test group, 1 patient's NSFE was found still positive with reduction in number in comparison to baseline, and in control group all 5 patients' were remained same (Table 3). On statistical analysis by Kruskal-Wallis with Dunn's Multiple Comparison Pair tests, the test group exhibited highly significant ($p < 0.001$) effect on NSFE after the treatment in comparison of before treatment, whereas in placebo control group no significant change in NSFE was observed (Table-4 and Figures 1 & 2). In order to determine adverse effect of test drugs, safety parameters like haemogram, LFT and RFT were carried out, which were found within the normal.

Table 1- Distribution of patients according to Seasonal variation (n=40)

Grading of NSFE	Test group	Placebo group
0	4	5
+	18	3
++	5	2
+++	3	0
Total	30	10

Table 2: Age group and positive NSFE (n=40)

Age (years)	Test group (n=30)	Placebo group (n=10)
13 - 20	4	1
21 - 30	10	1
31 - 40	8	2
41 - 50	4	1
Total	26	5

Table 3- Overall Effect on the study Based on NSFE (n=40)

Groups	Sample Size	Before Treatment NSFE (+)	After Treatment NSFE (+)
Test Group	30	26	1*
Placebo Control Group	10	5	5
Total	40	31	6

* Significant reduction in numbers.

Table 4- Effects of drugs on Nasal Smear for Eosinophils (NSFE) (Mean± SEM and Median rating with range in brackets) (n=40)

Groups	Nasal Smear for Eosinophils	
	Before treatment	After treatment
Test Group	1.73±0.13 2 {0,2}	0.03±0.09* 0 {0,1}
Placebo Control Group	1.00±0.33 1 {0,2}	0.8±0.33 0 {0,2}

*P<0.001 extremely significant with respect to test before treatment

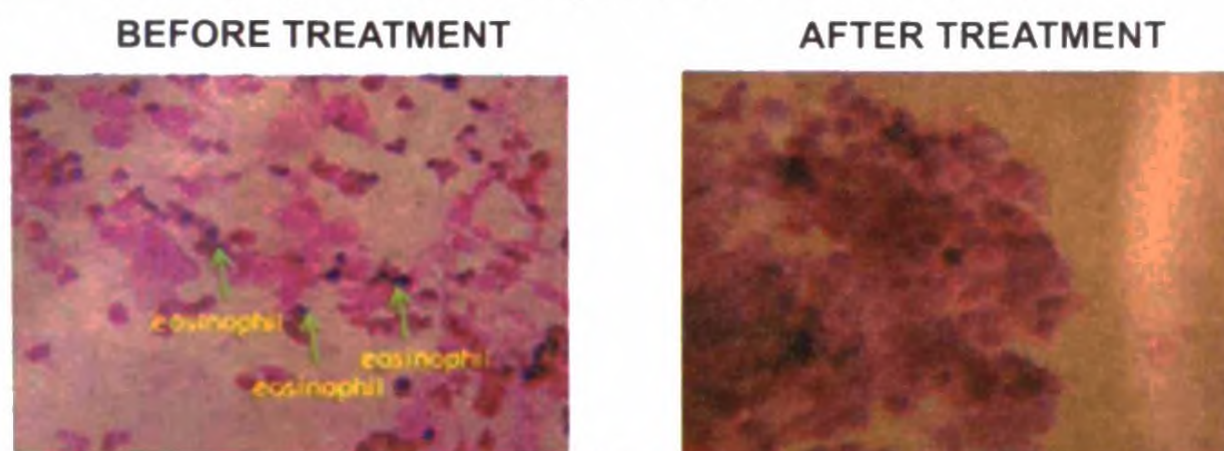


Fig: 1-Nasal smear with Giemsa stain (10 x) in test group

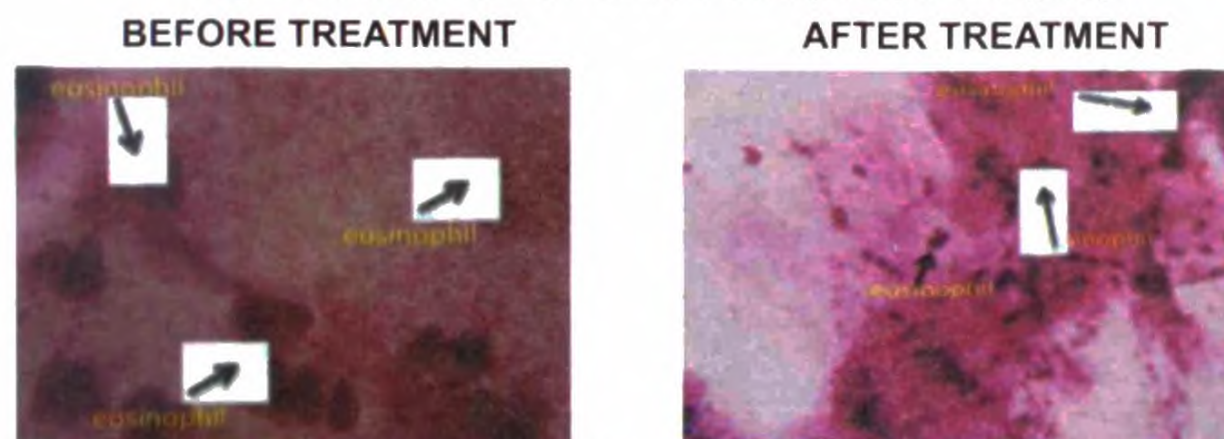


Fig: 2-Nasal smear with Giemsa stain (10 x) in placebo group

Discussion

In this study, it was established that the test drugs were effective in the treatment of allergic rhinitis by elimination or eradication of eosinophils in the nasal smear. The combined formulations consist of *Cydonia oblonga*, *Zizyphus jujube*, *Cordia dichotoma* and *Viola odorata* possess pharmacological properties of Dafe nazla (reduce post nasal drip), Dafe sual haar [14, 15], Mufarrih (exhilarant) [16], Mulattif (demulcent) [14, 15, 17], Muhallile varm (anti-inflammatory) [14, 15], Musaffie khoon (blood purifier) [17], Munaffise balgham (expectorant) [14- 16], Dafi' khushunate halq (improve sore throat) [16], Lazoojat (viscosity) [17] and Murattib wa munavvim (cooling and sedative) [16].

The overall response in the test group was significant than compared to the placebo group. The patients in both the groups did not report any adverse effects. In the present study, nasal smear for eosinophils was considered as the treatment outcome and it cannot be correlated with previous studies on treatment basis as such type of study was conducted for the first time.

The beneficial effects of test formulations are claimed that these drugs were used by the Unani scholars in varieties of respiratory diseases. A study has shown that *Cydonia oblonga* has an inhibitory effect on broad range of the late phase immune reactions of mast cells [18], *Zizyphus jujube* possesses anti allergic and anti-inflammatory properties [19, 20], *Cordia dichotoma* has analgesic, anti-inflammatory, expectorant and hepatoprotective properties [21, 22, 23], similarly the aqueous extract of *Viola odorata* has anti-inflammatory property equal to corticosteroids in the treatment of inflammatory conditions of the lung [24].

Conclusion

The test drugs were effective in reducing the number of eosinophils in allergic rhinitis with reduction in subjective symptoms along with no adverse effects, as the haematological tests of haemogram, renal and hepatic parameters were found within normal limits. The limitation of this study was small sample size. Therefore, large scale trials are required for further scientific validation of these remedies.

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