

Original Research Article

Comparative study of fluticasone propionate combined with azelastine versus fluticasone propionate alone as nasal spray in allergic rhinitis

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ABSTRACT

Background: Allergic rhinitis (AR) is a symptomatic disorder of the nose induced after allergen exposure due to an IgE-mediated inflammation of membranes lining the nose. Allergic rhinitis is subdivided into intermittent (IAR) or persistent (PER) disease and the severity into mild or moderate/severe. The most widely used and effective medications to treat allergic rhinitis are oral or topical antihistamines and topical nasal steroids.

Methods: This prospective case series study included 80 patients of PER divided randomly in to 2 groups of 40 each with group 1 receiving fluticasone propionate and azelastine and group 2 receiving fluticasone propionate alone. Individual symptom scores and total symptom score (TSS) were recorded before treatment and after 4 weeks of treatment.

Results: The difference in mean TSS before and after 4 weeks study period were statistically significant in both groups ($p < 0.01$ in both). Group 1 had TSS of 1.525 ± 1.06 and group 2 had TSS of 3.275 ± 1.75 after 4 weeks of treatment and the difference between them was statistically significant ($p < 0.01$).

Conclusions: In allergic rhinitis, both fluticasone propionate + azelastine nasal spray and fluticasone propionate nasal spray are effective in relieving symptoms. But, fluticasone propionate and azelastine has significant reduction of symptoms when compared with fluticasone propionate alone.

Keywords: Allergic rhinitis, Fluticasone propionate, Azelastine, Total symptom score

INTRODUCTION

Allergic rhinitis (AR) is a symptomatic disorder of the nose induced after allergen exposure due to an IgE-mediated inflammation of membranes lining the nose. It is clinically defined as a symptomatic condition with four major symptoms as anterior or posterior rhinorrhoea, sneezing, nasal itching and nasal congestion.¹ In addition, non-nasal symptoms such as itching of the throat and/or palate, and conjunctival symptoms can occur in individuals with AR with exposure to their relevant allergen(s).² Allergic rhinitis symptoms result in sleep disturbance, fatigue, depressed mood and cognitive

function compromise that impairs quality of life and productivity.³

AR is a common disease, affecting between 0.8 and 39.7% of the world population.⁴ The prevalence of AR, its associated factors and burden on the society is largely unknown in India. One Indian study showed the prevalence to be more than 10% in the general population; however, among asthmatic subjects, the prevalence rises to almost 80%.⁵

Allergic rhinitis is subdivided into intermittent (IAR) or persistent (PER) disease and the severity into mild or

moderate/severe.⁴ The history and symptoms are crucial in diagnosis. The timing of symptoms will often lead to diagnosing the allergy.⁵ The score for AR (SFAR) be used as a simple valid instrument to diagnose and monitor treatment of allergic rhinitis, as it has a positive correlation with standard diagnostic laboratory tests.⁶ A SFAR value ≥ 7 allowed satisfactory discrimination between the outpatients with AR from those without (annexure 1).⁷

Clinical practice guidelines for the management of AR recommend clear goals, including the prevention of allergy, reduction in allergen exposure, and effective pharmacological treatment.⁸ The most widely used and effective medications to treat allergic rhinitis are oral or topical antihistamines and topical nasal steroids. These medications aim to achieve improved symptom control and are not a cure for allergy. They generally need to be taken for as long as there is allergen exposure causing symptoms.⁴ Fluticasone propionate is a topically active corticosteroid with low systemic bioavailability due to massive first pass metabolism in liver. It acts on many of the cell types and inflammatory mediators participating in allergic inflammation. Corticosteroids act by reduction in antigen presenting Langerhans cells and inhibiting the migration of basophils and mast cells to the nasal epithelium and their release of mediators. Azelastine nasal spray is a topically administered second generation antihistamine and selectively antagonizes the H1-receptor. It has one of the fastest onsets of action (15 min with nasal spray) among the currently available rhinitis medications. The effect of azelastine lasts at least 12 hours, thus allowing for a once or twice daily dosing regimen. It exhibits a very fast and long-acting effect based on a triple mode of action, with anti-inflammatory and mast cell stabilizing properties in addition to its anti-allergic effects.⁹ No sedative effects have been but the occurrence of a short-lasting perversion of taste has been described for azelastine.¹⁰

Objectives of the study are to clinically evaluate the effectiveness of topical treatment with fluticasone propionate and antihistaminic azelastine in patients with persistent allergic rhinitis, to clinically evaluate the effectiveness of topical treatment with fluticasone propionate alone in patients with persistent allergic rhinitis and to compare the effectiveness of topical treatment with fluticasone propionate alone and fluticasone propionate with antihistaminic azelastine in patients with persistent allergic rhinitis.

METHODS

Sample size

Sample size calculation was done using open epi software version 2. At 95% confidence interval and 80% power of study sample size was calculated according to the study conducted by Havle et al, in which mean (standard deviation) symptom score of nasal obstruction of 2

groups of allergic rhinitis patients after treatment was 0.4 (0.6) and 0.1 (0.3).¹¹

Inclusion criteria

Inclusion criteria included age of patients >15 years, SFAR score ≥ 7 , persistent allergic rhinitis symptoms based on history and informed consent for study and willingness to follow up.

Exclusion criteria

Upper or lower respiratory tract infection with in last 2 weeks of entry visit patients were excluded.

Patients with symptoms due to structural abnormalities such as grossly deviated nasal septum, nasal polyps, tumours, previous surgical operations involving the nose and paranasal sinuses and patients requiring surgical management.

Use of systemic/oral corticosteroids within 30 days of the entry visit, women in pregnancy and lactation. Diabetes, regardless of its control status. Hypersensitivity to antihistamines or corticosteroids.

Study design

This prospective study was carried out in outpatient department of otorhinolaryngology and head and neck surgery in S. Nijalingappa medical college and HSK hospital and research centre, Bagalkot from June 2019 to May 2020. In the initial visit, comprehensive medical and allergy histories were obtained, clinical examination done.

All symptomatic cases in the study were divided into group I and group II alternately on first come first serve basis with selection and allocation ratio 1:1 and thus, conforming simple random selection. Out of 80 patients, 40 were treated with fluticasone propionate (50 mcg) and azelastine (140 mcg) and 40 patients were treated with fluticasone propionate (50 mcg). All participants of both groups were assessed before and after the treatment on 4-point symptom scale (0 to 3) for symptoms like sneezing, nasal block, nasal discharge and nasal itching. In each case, the subjective assessment of symptoms was done to increase the creditability of the symptom scale. The symptoms were assessed as per US department of health and human services, FDA allergic rhinitis criteria (Table 1). The symptom scores were recorded in follow up after 4 weeks. Effectiveness of treatment was assessed by relief of symptoms during follow-up using 4-point symptom evaluation scale.

Statistical methods

Data entered in Microsoft excel sheet and data analysis was done using statistical software SPSS version 21. Chi square test, paired and unpaired t tests are used for

statistical analysis. P<0.05 was considered statistically significant.

Table 1: Symptom evaluation scale, US department of health and human services FDA, allergic rhinitis.

Evaluation scale	Symptoms	Description of symptoms
0	Absent	No symptoms
1	Mild	Symptoms present but not troublesome
2	Moderate	Symptoms frequently troublesome but not disturbing daily activity or sleep
3	Severe	Symptoms disturbing daily activity or sleep

RESULTS

A total of 80 patients presenting with persistent allergic rhinitis included in this study based on eligibility criteria were grouped into two groups and were started on either fluticasone propionate (50 mcg) and azelastine (140 mcg) or fluticasone propionate (50 mcg) alone and using symptom evaluation scale, individual symptom score of each group was noted before and after treatment.

The mean age group of group 1 and group 2 were 29.77 and 29.55 years respectively. Hence, 21-30 years is the commonest age group of presentation of allergic rhinitis in this study (Table 2). There was no difference among the two group in age distribution (difference was statistically insignificant, p=0.92). There were 19 males and 21 females in group 1 as compared to 13 males and 27 females in group 2 in the study with no significant difference in sex distribution (p=0.08) (Table 3). The difference between mean SFAR between group was statistically insignificant (p=0.46).

The mean total symptom score and mean individual symptom score between two groups prior to study were comparable indicating similar severity of symptoms among all cases at initiation of the study (Table 4 and 5). The differences in mean TSS before and after 4 weeks study period was statistically significant in both groups (p<0.01 in both) (Table 4). Hence, both fluticasone propionate with azelastine and fluticasone propionate alone are individually effective in treatment of allergic rhinitis. Both drugs were also effective in reducing individual symptom score in both groups.

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Group 1 had TSS of 1.525±1.06 and group 2 had TSS of 3.275±1.75 after 4 weeks of treatment and the difference between them was statistically significant (p<0.01) (Table 4). The difference in reduction of nasal obstruction, nasal discharge and nasal itching was significant between 2 groups after treatment but the difference was insignificant with reduction of sneezing (Table 6). Hence, though both drugs are effective in symptom reduction of allergic rhinitis, the symptom reduction was significant in group 1 receiving fluticasone propionate and azelastine. No patients experienced drug reactions in this study.

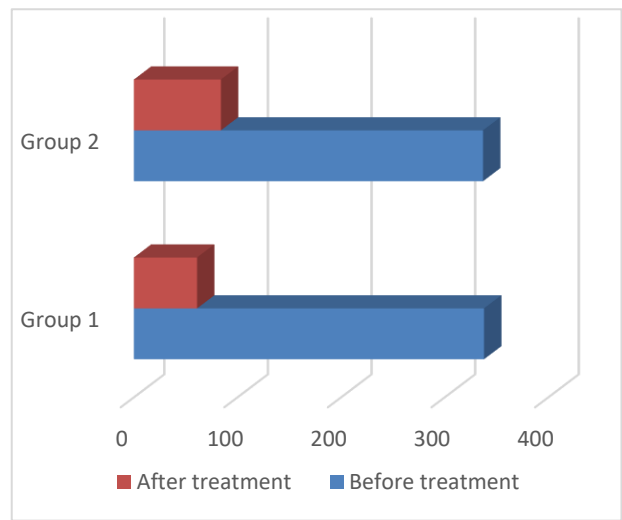


Figure 1: TSS analysis before and after treatment.

Table 2: Distribution of patients according to age.

Age (year)	Group 1		Group 2	
	No. of patients	%	No. of patients	%
<20	11	27.50	9	22.5
21-30	12	30	16	40
31-40	9	22.5	10	25
41-50	6	15	5	12.5
51-60	2	5	0	0
Mean±SD	29.77±11.53		29.55±9.21	
P value	0.92			

Table 3: Distribution of patients according to gender.

Gender	Group 1		Group 2	
	No. of patients	%	No. of patients	%
Male	19	47.5	13	32.5
Female	21	52.5	27	67.5
Total	40	100	40	100
Chi square test	p=0.08			

Table 4: Total symptom score.

Groups	Before treatment (Mean±SD)	After treatment (Mean±SD)	P (paired t test)
Group 1	8.45±1.06	1.525±1.06	<0.0001
Group 2	8.42±1.12	3.275±1.75	<0.0001
P value (unpaired t test)	0.92	<0.0001	

Table 5: Baseline individual symptom score before treatment of each symptom in group 1 and group 2.

Symptom	Group 1 (n=40) Mean±SD	Group 2 (n=40) Mean±SD	P (unpaired t test)
Sneezing	2.6±0.5	2.5±0.5	0.53
Nasal obstruction	2.1±0.7	2.2±0.8	0.57
Nasal discharge	2.2±0.5	2.2±0.8	0.86
Nasal itching	1.6±0.6	1.6±0.7	0.86

Table 6: Baseline individual symptom score after treatment of each symptom in group 1 and group.

Symptom	Group 1 (n=40) Mean±SD	Group 2 (n=40) Mean±SD	P (unpaired t test)
Sneezing	0.5±0.5	0.7±0.8	0.19
Nasal obstruction	0.7±0.5	1±0.7	0.025
Nasal discharge	0.2±0.4	0.9±0.6	<0.001
Nasal itching	0.02±0.2	0.7±0.8	<0.001

DISCUSSION

Allergic rhinitis is a chronic upper airway disease of increasing prevalence and remains an important healthcare problem. The condition can have a major detrimental impact on quality of life and social productivity. Clinical practice guidelines for management of AR recommend clear goals, including the prevention of allergy, reduction in allergen exposure and effective pharmacological treatment. The use of corticosteroids and antihistamines in AR has been discussed since long time.

Most of the cases of allergic rhinitis were in the age group of 21-30 years in this study. This is comparable to study by Bhadouriya et al, in which most cases were in age group of 21-30 years with mean age of 31.5 years and the study of Negus and Hagy.^{12,13}

There were 21 females in group 1 as compared to 27 females in group 2 in the study. The gender distribution

difference was not significant. This is comparable to study by Dalvi and Havle et al.^{11,14} The presentation and clinical course of AR does not differ per se between males and females.

In almost all cases four main symptoms were present before therapy: sneezing, nasal obstruction, nasal discharge and nasal itching. In this study, fluticasone propionate alone group was also effective in reducing symptoms of AR. This is in accordance with study by Havle and Dykewicz et al.^{11,15} Which say that patients treated with fluticasone nasal spray were greatly relieved of symptoms AR. The difference in reduced TSS between group 1 and group 2 was statistically significant indicating fluticasone propionate and azelastine nasal spray is more effective in reducing symptoms of AR than fluticasone propionate alone. This result is comparable to the study by Ratner et al that observed a drop in baseline in the TSS (*p<0.001) of fluticasone propionate with azelastine hydrochloride nasal spray.¹⁶ The fluticasone propionate with azelastine group also had significantly greater reduction in individual symptom of nasal obstruction, nasal discharge and nasal itching. The study done by Dalvi et al showed significant reduction in both sneezing and nasal obstruction with nasal spray of fluticasone propionate combined with azelastine compared to fluticasone propionate alone.¹⁴ The topical azelastine relieves symptoms of AR rapidly and effectively according to study by Bhadouriya et al.¹² The topical effect of various corticosteroids and antihistamines in allergic rhinitis, however, needs to be studied further.

CONCLUSION

In allergic rhinitis, both fluticasone propionate with azelastine nasal spray and fluticasone propionate nasal spray are effective in relieving symptoms. But, fluticasone propionate with azelastine has significant reduction of symptoms when compared with fluticasone propionate alone. Both were comparable in reduction of sneezing but fluticasone propionate with azelastine nasal spray was significantly superior than fluticasone propionate nasal spray in relief of nasal obstruction, nasal discharge and nasal itching. The limitations of our study are the sample size is small due to less time of study and a clear-cut clinical efficacy evaluation cannot be made in the present study as no control group was available.

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REFERENCES

1. Varshney J, Varshney H. Allergic Rhinitis: a Overview Indian J Otolaryngol Head Neck Surg. 2015;67(2):143-9.
2. Ellis AK, Soliman M, Steacy L, Boulay ME, Boulet LP, Keith PK et al. The allergic rhinitis-clinical investigator collaborative (AR-CIC): nasal allergen challenge protocol optimization for studying AR pathophysiology and evaluating novel therapies. *Allergy Asthma Clin Immunol.* 2015;11:16.
3. Meltzer EO. Quality of life in adults and children with allergic rhinitis. *J Allergy Clin Immunol.* 2001;108(1):S45-53.
4. Gardiner Q. Allergic rhinitis. In: Watkinson JC, Clarke RW, Clark LJ, Mehanna HM, Donne AJ, McGarry GW, et al editors. *Scott-brown's otorhinolaryngology head and neck surgery.* 8th ed. Vol 1. Florida: CRC press; 2018: 999-1010.
5. Gaur SN, Gupta K, Rajpal S, Singh AB, Rohtagi A. Prevalence of bronchial asthma and allergic rhinitis among urban and rural adult population of Delhi. *Indian J Allergy Asthma Immunol.* 2006;20:90-7.
6. Ologe FE, Adebola SO, Dunmade AD, Adeniji KA, Oyejola BA. Symptom Score for Allergic Rhinitis. *Otolaryngol Head and Neck Surg.* 2013;148(4):557-63.
7. Annesi-Maesano I, Didier A, Klossek M, Chanal I, Moreau D, Bousquet J. The score for allergic rhinitis (SFAR): a simple and valid assessment method in population studies. *Allergy.* 2002;57:107-14.
8. Brozek JL, Bousquet J, Baena-Cagnani CE, Bonini S, Canonica GW, Casale TB et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 revision. *J Allergy Clin Immunol.* 2010;126:466-76.
9. Horak F. Effectiveness of twice daily azelastine nasal spray in patients with seasonal allergic rhinitis. *Therap Clin Risk Management.* 2008;4(5):1009-22.
10. Nielsen LP, Dahl R. Comparison of intranasal corticosteroids and antihistamines in allergic rhinitis: a review of randomized, controlled trials. *Am J Respir Med.* 2003;2(1):55-65.
11. Havle A, Jain V, Ahmed MF, Shedge S, Dokania V, Bagwe V, et al. Olopatadine Hydrochloride and Fluticasone Propionate in Topical Treatment of Allergic Rhinitis: A Single Blind Randomised Study. *J clin diagn res.* 2016;10(12):MC04-07.
12. Bhadouriya SKS, Srivastava M, Saxena R, Srivastava A. Comparative clinical evaluation of effect of topical verses systemic anti -allergic drug in allergic rhinitis: a prospective study. *Int J Otorhinolaryngol Head Neck Surg.* 2018;4:141-7.
13. Hagy GW, Saltipane GA. Risk factors for developing asthma and allergic rhinitis. *J Allergy Clin Immunol.* 1976;58:330-6.
14. Dalvi R, Havle AD. Comparitive analysis of treatment of allergic rhinitis utilising azelastine and fluticasone. *Int j res pharma sci.* 2020;11(3):4636-43.
15. Dykewicz MS, Kaiser HB, Nathan RA, Goode-Sellers S, Cook CK, Witham LA et al. Fluticasone propionate aqueous nasal spray improves nasal symptoms of seasonal allergic rhinitis when used as needed (prn). *Ann Allergy, Asthma Immunol.* 2003;91(1):44-8.
16. Ratner PH, Hampel F, Bavel JV, Amar NJ, Daftary P, Wheeler W et al. Combination therapy with azelastine hydrochloride nasal spray and fluticasone propionate nasal spray in the treatment of patients with seasonal allergic rhinitis. *Ann Allergy, Asthma Immunol.* 2008;100(1):74-81.

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ANNEXURE 1

Standardized questionnaire for SFAR assessment

1. In the past 12 months, have you had a problem apart from cold or flu with (please tick appropriate cases(s): (1 score for each symptom)?
Sneezing No Yes
Runny nose No Yes
Blocked nose No Yes
If YES (at least one nose problem):
2. In the past 12 months, has this nose problem been accompanied by itchy-watery eyes? (2)
No Yes
3. In which of the past 12 months (or in which season) did this nose problem occur? (1 for perennial and 1 for pollen season)
Jan Feb Mar Apr May June
July Aug Sept Oct Nov Dec
(or alternatively)
Winter Spring Summer Autumn
4. What trigger factors provoke or increase your nose problem? (Pollens, house dust mites, dust-2, Epithelia of cats, dogs-1)
House dust House dust mites
Pollens Animal (cat, dogs...)
Others (please specify)
5. Do you think to be allergic? (2)
No Yes
6. Have you already been tested for allergy (SPT, IgE)? (2)
No Yes
If YES: 6a What was the result?
Positive Negative
7. Has a doctor already diagnosed that you suffer/suffered from asthma, eczema or allergic rhinitis? (1)
No Yes
8. Is any member of your family suffering from asthma, eczema or allergic rhinitis? (2)
No Yes
If YES: Who and what disease? (please tick appropriate cases(s)):
Father Asthma Eczema Allergic rhinitis
Mother Asthma Eczema Allergic rhinitis
Siblings Asthma Eczema Allergic rhinitis