Indian J Otolaryngol Head Neck Surg
(October 2022) 74(Suppl 2):S1632–S1637; https://doi.org/10.1007/s12070-021-02686-7

ORIGINAL ARTICLE

Comparison of the Effects of Azelastine and Fluticasone Nasal Sprays in the Treatment of Allergic Rhinitis

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Received: 12 March 2021 / Accepted: 13 June 2021 / Published online: 2 August 2021

Abstract Allergic rhinitis is a highly prevalent, allergen-induced disease. Intranasal corticosteroids are currently the first-line therapy for these patients. It is uncertain whether intranasal antihistamines have comparable efficacy. This study compares effects of Azelastine and Fluticasone nasal spray in patients with allergic rhinitis. Prospective comparative study including 240 patients with allergic rhinitis was conducted with 120 each in fluticasone and azelastine group. Nasal sprays were given for period of three months along with an oral antihistamine. Follow up was done after three months. Pre and post treatment symptom assessment were done using Total nasal symptom score. The median TNSS in pre and post treatment of group A (fluticasone) is 10(4) and 1(3) which shows statistical significance with p value < 0.001. Median TNSS in pre and post treatment of group B (azelastine) is 9(4) and 1(2) which shows statistical significance with p value < 0.001. The median TNSS in pre and post treatment value between Group A and B shows no statistically significant difference between two groups with p value 0.56 and 0.06 respectively. Intranasal azelastine and fluticasone had comparable efficacy in symptom control in patients with allergic rhinitis. Azelastine due to its lesser side effects, can be safely used in children, patients with glaucoma and cataract. Azelastine may be considered as a safer replacement to fluticasone for long term use in patients with allergic rhinitis. A larger multicentric study with a bigger sample size may be required to confirm the efficacy and safety profile of azelastine nasal spray.

Keywords Allergic rhinitis · Fluticasone nasal spray · Azelastine nasal spray · Total nasal symptom score · Nasal congestion

Introduction

Allergic rhinitis is a symptomatic inflammatory disease affecting the nasal mucosa that is mediated by immunoglobin E (IgE). Although previously considered to be a condition that only affected the nasal passages, AR has now been observed as the presentation of systemic airway disease and is frequently comorbid in asthma patients [1]. It is known to have a significant impact on the quality of life. Intranasal corticosteroids (INSs) are recommended in current guidelines as first-line therapy for patients with moderate to severe Allergic Rhinitis, particularly when nasal congestion is the prominent symptom [1]. INSs inhibit the onset of the inflammatory response and reduce nasal mucosa permeability, the number of inflammatory cells and the release of mediators [2]. However few studies have shown that it may be appropriate to monitor growth while using in children because even in the absence of any effect on HPA axis, intranasal corticosteroids might result in a small but significant effect on their growth [3]. Intranasal steroids have been inconsistently shown to increase rate of cataract formation and discontinuation of intranasal steroids have shown a decrease in the intra ocular pressure, hence their use in patients with glaucoma is also questionable [4]. Practitioners should therefore be weary on the use of both intranasal and inhaled steroids, as the additive effect may take a toll on bone mineral density [3].

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Antihistaminic nasal sprays like Azelastine nasal spray is a fast-acting, efficacious and well-tolerated H1-receptor antagonist for the treatment of rhinitis [5]. In addition, it also has mast-cell stabilizing and anti-inflammatory properties, reducing the concentration of leukotrienes, kinins and platelet activating factor in vitro and in vivo, as well as inflammatory cell migration in rhinitis patients [5]. Well-controlled studies in patients with seasonal allergic rhinitis, perennial rhinitis or vasomotor rhinitis confirm that azelastine nasal spray has a rapid onset of action, and improves nasal symptoms associated with rhinitis such as nasal congestion and post-nasal drip [5]. Compared with intranasal corticosteroids, azelastine nasal spray has a faster onset of action and a better safety profile, showing comparable efficacy with fluticasone propionate [6]. Many studies have compared the effectiveness of intranasal steroids and antihistamine nasal spray in patients with allergic rhinitis for a shorter period of time, but this study aims at comparing these nasal sprays for a longer duration of three months and their subsequent follow up.

Materials and Methods

Participants

We included patients diagnosed with moderate to severe allergic rhinitis attending OPD between July 2018–2020 in the the department of Otorhinolaryngology Amrita Institute of Medical Sciences and research center, Kochi, Kerala.The inclusion criteria were patients with moderate to severe allergic rhinitis above the age of 4 years. The exclusion criteria included patients with proven nasal polyps, nasal mass and sinusitis. The study conforms to the Declaration of Helsinki and was reviewed and approved by the approved by Institutional Ethics committee of Amrita Institute of Medical Sciences, Kochi.

Data Collection

Patients were assessed by through history and clinical examination. Diagnosis of allergic rhinitis was made based on guidelines set by American Academy of Otolaryngology—Head and Neck Surgery Foundation (AAO-HNSF) [7] whereas severity of symptoms was assessed by the ARIA [8] guidelines. Symptoms like nasal congestion, runny nose, itchy nose, or sneezing which were consistent with allergic rhinitis whereas physical examination which was consistent with symptoms like clear rhinorrhoea, nasal congestion, pale discoloration of the nasal mucosa, and red and watery eyes were diagnosed to have allergic rhinitis. Participants/attendants were given a TNSS questionnaire [6] on their first visit which graded their allergic symptoms.

TNSS rates allergic symptoms like nasal congestion, rhinorrhoea, sneezing, itching and difficulty in sleeping. Each symptom had a maximum score of 3 and a minimum score of 0. Hence, the total TNSS score was 15 and the minimum score was 0.

After evaluation patients were divided into two groups-Group A and Group B based on OP visits to two different consultants. Consultant A prescribed Fluticasone nasal spray and these patients were categorized as Group A while consultant B prescribed Azelastine nasal spray and these patients were categorized as Group B. Both consultants prescribed Fluticasone nasal spray (50 mcg) and Azelastine nasal spray (0.1w/v) to be given as one puff twice daily in both nostrils for a period of three months along with an oral antihistamine (Desloratidine 5 mg) for one week.

Statistical Analysis

Statistical analysis was performed using IBM SPSS version 20.0 software. Categorical variables were expressed using frequency and percentage. Numerical variables were presented using mean and standard deviation/ Median (IQR). To test the statistical significance of the association of all categorical demographic and clinical parameters between two groups, Chi-square test was used. And to test the statistical significance of the comparison of continuous clinical parameters between two groups, Mann Whitney U test was used. To study the statistical significance of pre and post change of symptom scores, Wilcoxon's signed rank test was used. A p value of < 0.05 was considered to be statistically significant.

Results

Patient Characteristics

Study was conducted on 240 patients which was divided into 2 groups of 120 each. Group A was given Fluticasone nasal spray and group B was given Azelastine nasal spray. Out of 120 patients in group A (Fluticasone), 54(45%) were females,71(59%) were males. Out of 120 patients in group B (Azelastine) 49(40%) were females and 66(55%) were males (Table 1). Both groups had male gender predominance. Median age of patients in group A (fluticasone)was 32.5(23) and that in group B (azelastine) was 31.5(20.75). This showed no statistically significant difference with p value being 0.645 (Table 2). Out of 240 patients the lowest age was 4 and the highest age was79.

Table 1 Distribution of gender between groups

Gender	Groups		*p* value
	Fluticasone (Group A) (n = 120) n (%)	Azelastine (Group B) (n = 120) n (%)	
Female	54 (45%)	49 (40%)	0.51
Male	71 (59%)	66 (55%)	

Table 2 Association of age groups between two groups

Age	Groups		*p* value
	Azelastine (Group B) (n = 120) n (%)	Fluticasone (Group A) (n = 120) n (%)	
Below 18	14 (11.7%)	8 (6.7%)	0.18
18 and above	106 (88.3%)	112 (93.3%)	

Change in Parameters

The median TNSS in pretreatment of group A(fluticasone) is 10(4) and that of post treatment is 1(3) which shows statistical significance with p value < 0.001. Similarly, median TNSS in pretreatment of group B (azelastine) is 9(4) and that of post treatment is 1(2) which shows statistical significance with p value < 0.001. The median total nasal symptom score in pretreatment and post treatment value between Group A and B shows no statistically significant difference with p value being 0.56 and 0.06 respectively (Table 3). The median (IQR) nasal congestion score in pre-treatment of group A (fluticasone) is 3(1) and that of post treatment is 0(1) which shows statistical significance with p value < 0.001. Similarly, median nasal congestion score in pre-treatment of group B (azelastine) is 3(1) and that of post treatment is 0(1) which shows statistical significance with p value < 0.001. The median nasal congestion score in pre-treatment and post treatment value between Group A and B shows no statistically significant difference with p value being 0.31 and 0.14 respectively (Table 4).

Discussion

Total of 240 patients were divided into 2 groups of 120 each. In our study we had a male preponderance with 59% males in group A (fluticasone) and 55% in group B (azelastine) In a study conducted by Carr W et al. had 66% females in the fluticasone group and 63% in the azelastine group. Mean age was 38 in fluticasone group and 39 in azelastine group [6]. In our study mean age was 34. Gender and age of both groups were comparable.

Patients can present with a range of symptoms in allergic rhinitis. Despite the increasing number of medications and delivery systems on the market, including the expanding availability of over the-counter products, AR continues to substantially impact patients' quality of life [9]. Patients continue to report bothersome symptoms, including nasal congestion, headache, postnasal drip, episodes of sneezing, runny nose, on a daily or near-daily basis during peak nasal allergy exacerbations, sometimes regardless of treatmen [9]. In our study the three most common and severe symptoms in allergic rhinitis was found to be nasal congestion followed by sneezing and rhinorrhoea. Out of 120 people in Group A (Fluticasone) around 90 (75%) had severe nasal congestion while in group B (Azelastine) 84 (70%) had severe nasal congestion. Out of 120 people in Group A (Fluticasone) around 83 (69%) had severe sneezing while in group B (Azelastine) 80 (66%) had severe nasal sneezing. While in Group A (Fluticasone) around 71 (59%) had severe rhinorrhoea while in group B (Azelastine) 64 (53%) had severe rhinorrhea.

According to a study done by Berger W Et Al [9], the percentage of patients who completely or nearly completely eliminated nasal symptoms after 2 weeks of

Table 3 Pre and post treatment comparison of TNSS

	n	Azelastine		Fluticasone		*p* value
		Median	IQR	Median	IQR	
Pre-treatment	120	9.00	4.00	10.00	4.00	0.56
Post treatment	120	1.00	2.00	1.00	3.00	0.06
p value		< 0.001		< 0.001		

Table 4 Distribution of nasal congestion score

Nasal congestion	Groups	
	Azelastine (Group B) (n = 120) n (%)	Fluticasone (Group A) (n = 120) n (%)
0	4 (3.3)	0
1	0	0
2	32 (26.7)	30 (25)
3	84 (70)	90 (75)

treatment 9.3% and 7.1% for fluticasone propionate and azelastine respectively. In our study, out of 120 patients in group A (fluticasone), 36 patients (30%) had complete relief of symptoms by the end of 3 months. Out of 120 patients in group B (azelastine), 44 (36%) had complete relief of symptoms by the end of 3 months with no significant statistical difference between both groups.

In the study conducted by Carr W et al., both nasal sprays were given for a period of two weeks and patients were followed up after two weeks and this was not combined with any oral antihistamine. Patients who used azelastine hydrochloride experienced comparable nasal and ocular symptom relief as those treated with fluticasone propionate. Intranasal AZE and FP treatment resulted in similar reductions from baseline in the TNSS. There was no significant difference between AZE and FP on any day during the 14 day treatment period for the overall rhinitis symptom complex score. In our study, the median TNSS in pretreatment of group A(fluticasone) was 10(4) and that of post treatment was 1(3) which showed statistical significance with p value < 0.001. Similarly, median TNSS in pretreatment of group B (azelastine) was 9(4) and that of post treatment was 1(2) which showed statistical significance with p value < 0.001. In this study oral antihistamines were given only for the initial one-week duration. These results show reasonable long-term relief of symptoms with nasal sprays alone without oral antihistamines after three months durationThe median total nasal symptom score in pretreatment and post treatment value between Group A and B shows no statistically significant difference with p value being 0.56 and 0.06 respectively.

Looking at individual symptoms, the median nasal congestion score in pre-treatment of group A (fluticasone) was 3(1) and that of post treatment was 0(1) which showed statistical significance with p value < 0.001. Similarly, median nasal congestion score in pre-treatment of group B (azelastine) was 3(1) and that of post treatment was 0(1) which showed statistical significance with p value < 0.001. Similarly, the median rhinorrhoea score in pre-treatment of group A (fluticasone) was 3(1) and that of post treatment was 0(1) which showed statistical significance with p value < 0.001. Similarly, median rhinorrhoea score in pre-treatment of group B (azelastine) was 3(1) and that of post treatment was 0(0) which showed statistical significance with p value < 0.001. The median sneezing score in pre-treatment of group A (fluticasone) was 3(1) and that of post treatment was 0(1) which showed statistical significance with p value < 0.001. Similarly, median sneezing score in pre-treatment of group B(azelastine) was 3(1) and that of post treatment was 0(1) which showed statistical significance with p value < 0.001. Patients had improvement in itching even without simultaneous use of oral antihistamines after 3 months. In our study it was difficult to get patients to continuously use nasal sprays beyond three months as most of them stopped these when they were symptomatically better and started using them on demand. Hence even though it was not a part of our study long term follow up was difficult.

In the study by Carr W et al., a direct comparison of AZE and FP revealed a comparable overall change from baseline for nasal congestion, nasal itch and sneezing. In our study also similar results were established. The median change from base line for nasal congestion score was 2(1) for group A and was 2(1) for group B which did not show any statistically significant difference. The median change from base line for rhinorrhoea score was 2(1) for group A and was 2(1) for group B which did not show any statistically significant difference. The median change from base line for itching score was 1(2) for group A and was 1(2) for group B which did not show any statistically significant difference. The median change from base line for sneezing score was 2(1) for group A and was 2(1) for group B which did not show any statistically significant difference. The median change from base line for sleep disturbance score was 0(1) for group A and was 0(1.75) for group B which did not show any statistically significant difference.

In a study done by Weiler et al. [10], groups received azelastine nasal spray 1 puff twice daily, 2 puffs once daily, 2 puffs twice daily, chlorpheniramine and placebo. It was found that the subjects who received 2 sprays of azelastine twice daily had the most improvement and were comparable to chlorpheniramine group suggesting azelastine nasal spray had a quick onset of action and can be used an on-demand nasal spray [10]. Study was suggestive of the fact that azelastine was still active as long as 24 h after administration. In our study azelastine nasal spray was given as one puff twice daily and this was found to be adequate for symptom control.

In another study by Shah S MD et al., which compares the efficacy and safety of 0.15% and 0.10% of azelastine nasal spray, the onset of action with azelastine 0.15% was within 30 min [11]. Bitter taste was the most common adverse effect with both 0.15% and 0.10% azelastine spray (8.4% and 9.4% patients effectively. Somnolence was reported by 1.7% of patients using 0.15% and 0.6% using 0.10% sprays. Both these nasal sprays at 2 sprays/nostril daily significantly improved nasal symptoms associated with allergic rhinitis and were well tolerated. In our study sedation was not reported by patients using either of the nasal sprays.

In a study by Berger et al., the most commonly reported adverse event was epistaxis and/or the subjective report of nasal irritation (e.g., mucosal crusting, redness, burning), which occurred with all treatments, and, for epistaxis, with no statistically significant between-treatment differences in the percentage of patients reporting: INAH, 1.7–10%; INCS, 0.4–4%. Dysgeusia is an adverse effect associated with the INAH (azelastine). Higher doses of azelastine are associated with an increased incidence of dysgeusia. In our study around 50% patients who used azelastine nasal sprays complained of dysgeusia as a common side effect. Another common side effect which was encountered by most patients using nasal sprays was local nasal irritation while using these spray medications. None of the patients using either of the nasal sprays had symptoms suggestive of increased intraocular pressure, HPA axis suppression or osteoporosis. Several studies done have stated that patients treated with Combination nasal spray (Azelastine + fluticasone) experienced significantly greater relief from their nasal symptoms than patients treated with either azelastine or fluticasone propionate alone.

Conclusions

Intranasal azelastine and intranasal fluticasone nasal sprays had comparable effects in terms of symptom control in patients with moderate to severe allergic rhinitis. Dysgeusia which was tolerable was seen in fifty percent of the patients using azelastine nasal spray. Patients on fluticasone nasal spray did not have any persistent side effects during three months of study. Patient compliance for both azelastine and fluticasone nasal sprays were comparable. Azelastine nasal spray being a non-steroidal antihistaminic nasal spray may be safely used in children and in patients with glaucoma and cataract with equal efficacy as fluticasone nasal spray. Intranasal Azelastine may be considered as a safer replacement or as an alternative to fluticasone for long term use in patients with allergic rhinitis. A larger multicentric study with a bigger sample size may be required to confirm the efficacy and safety profile of azelastine nasal spray.

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