



**COMPARATIVE STUDY OF EFFICACY AND SAFETY BETWEEN FLUTICASONE  
FUROATE AND AZELASTINE NASAL SPRAY IN ALLERGIC RHINITIS**

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**ABSTRACT**

**Aims of the study:** Allergic rhinitis (AR) is a common inflammatory disease condition of upper respiratory tract. Currently, most commonly used drugs for treatment of AR are: anti-histaminics, corticosteroids etc. Fluticasone Furoate nasal spray has been studied extensively in allergic disease. Azelastine has also shown efficacy in controlling AR. This pilot study compares the efficacy and safety of Fluticasone Furoate versus Azelastine nasal spray in treatment of AR. **Materials and methods:** 26 patients with AR are randomly assigned into 2 parallel groups in this prospective open label study. Group A containing 13 patients are treated with Azelastine nasal spray 140 microgram twice daily administered as one spray in each nostril. Group B containing 13 patients are treated with Fluticasone Furoate nasal spray 110 microgram once daily administered as 2 sprays in each nostril. Follow up visits done at 7 days and 14 days. The efficacy was assessed by the change in nasal and ocular symptom scores as their subtotals (Total Nasal Symptom Score and Total Ocular Symptom Score) and grand total (Total Symptom Score). **Results:** 10 patients in azelastine group and 12 patients in fluticasone group have completed the study. Baseline parameters were comparable. Both azelastine and fluticasone furoate decrease the TSS, TNSS and TOSS significantly from baseline in 7 days and 14 days ( $p < 0.001$ ). But when compared between azelastine and fluticasone furoate, no significant difference found at any point of time. **Conclusions:** Azelastine and fluticasone furoate are equally effective in treatment of AR. Both are safely tolerated in AR patients.

**KEYWORDS:** Azelastine, Fluticasone Furoate, Allergic Rhinitis.

**INTRODUCTION**

Allergic rhinitis (AR) is a common disease affecting over 500 million people worldwide.<sup>[1]</sup> AR is an IgE mediated inflammation after allergen exposure to the nasal membrane and is characterized by symptoms like runny/stuffy/itchy nose, sneezing and red/watery/itchy eye. AR influences the quality of life of the patient through impairment of daily activities, social function, emotions, and sleep patterns, although it is not a life-threatening disease.<sup>[2-5]</sup> Moreover, AR is a social burden in terms of medical expenditure. Treatment guidelines from the Joint Task Force and WHO recommend that antihistamines, both topical (eg, Azelastine) and oral second-generation (eg, Loratadine, Desloratadine, Fexofenadine or Cetirizine) be used as first-line therapy for AR. Intranasal corticosteroids (eg, Fluticasone Propionate, Fluticasone Furoate, Mometasone Furoate) may also be considered as initial therapy for AR in patients with more severe symptoms, particularly nasal congestion.<sup>[6-8]</sup>

Azelastine, is a second generation histamine H1 receptor antagonist which has shown clinical efficacy in relieving the symptoms of allergic rhinitis when administered as

intranasal formulation.<sup>[9]</sup> It is thought to improve both the early and late phase symptoms of rhinitis through a combination of antihistaminic, antiallergic and anti-inflammatory mechanisms.<sup>[10]</sup>

Fluticasone Furoate (FF) is a new topical glucocorticoid with a high relative receptor affinity, selectivity and potency as well as a long duration of anti-inflammatory activity in comparison to other glucocorticoids currently in usage.<sup>[11,12]</sup> Fluticasone Furoate nasal spray (FFNS) has been studied extensively in allergic disease and found to demonstrate consistent efficacy and safety in seasonal as well as perennial allergic rhinitis.<sup>[13]</sup>

This study was thus aimed to compare the efficacy and safety of Fluticasone Furoate nasal spray versus Azelastine as anti-allergic, anti-inflammatory in allergic rhinitis.

**REVIEW OF LITERATURE**

Fluticasone Furoate (FF) is a new, topical, intranasal, enhanced-affinity trifluorinated glucocorticoid, with potent anti-inflammatory activity and low systemic exposure. Fluticasone Furoate nasal spray (FFNS) has

been studied extensively in allergic disease and found to demonstrate consistent efficacy and safety in seasonal as well as perennial allergic rhinitis.<sup>[13]</sup> It has a low absolute systemic bioavailability after intranasal administration<sup>[14]</sup> and does not affect hypothalamic-pituitary-adrenal (HPA) axis function at recommended doses in children 2 years of age to adults.<sup>[15,16]</sup> It has also been shown not to interfere with growth in pre-pubertal children in a short term study.<sup>[17]</sup> Several placebo controlled clinical trials have shown that FF consistently improves nasal as well as ocular symptoms of seasonal/perennial allergic rhinitis at an optimal dose of 110 µg/day.<sup>[18,19]</sup> The efficacy and safety of FF is well established internationally in adults, adolescents and children aged ≥ 2 years.<sup>[20]</sup>

Azelastine is a potent, second-generation, selective, histamine antagonist (histamine-H<sub>1</sub>-receptor antagonist). Azelastine has shown clinical efficacy in relieving the symptoms of allergic rhinitis when administered as intranasal formulation.<sup>[9]</sup> It is thought to improve both the early and late phase symptoms of rhinitis through a combination of antihistaminic, antiallergic and anti-inflammatory mechanisms.<sup>[10]</sup> In SAR patients azelastine therapy (two sprays per nostril twice daily), improved both total symptom and major symptom complex scores to a significantly greater extent than placebo.<sup>[21-23]</sup> Similarly, in PR patients, azelastine nasal spray significantly improved sleeping, reduced daytime somnolence and nasal congestion compared with placebo.<sup>[24]</sup>

## MATERIALS AND METHODS

### Aims and objectives

Objectives of the study are –

- To compare the efficacy and safety of Fluticasone Furoate versus Azelastine nasal spray in allergic rhinitis.
- To assess the improvement in Quality of life.

### Study design

Open label, prospective, unicentric, randomized study with two parallel treatment groups.

**Study period:** March 2014 to August 2014 (6 months)

### Study population

Screening for eligibility of the patient is to be performed based on following criteria:

#### Inclusion criteria

- Patients of either sex, aged between 12 years to 60 years.
- Confirmative diagnosis of IAR or PER (as definitions from ARIA 2008) by medical history, symptoms.
- Subjects must be symptomatic at the time of screening
- Willing to maintain same environment throughout the study

- Willing to give written informed consent and able to comply with study procedure.

#### Exclusion criteria

- patients with active asthma that required therapy with oral corticosteroids or long-term β-agonist
- patients with drug induced rhinitis, vasomotor rhinitis, rhinitis with eosinophilia or concomitant nasal disease other than rhinitis or eye disease
- patients with history of operation or damage on nasal or ocular region
- patients with history of bacterial/viral infection of upper respiratory tract which requires antibiotic therapy within the previous 14 days
- Patients with lung disease including COPD
- patients administered with corticosteroid within the previous 3 months
- Having significant uncontrolled systemic diseases
- History of hypersensitivity to study medications
- Pregnant women or lactating mother
- Patients who participated in another study within 3 months before screening
- Patients taking any non-permitted medication

**Definition of control group:** Not applicable.

**Whether vulnerable population involved:** No.

#### Site of study

ENT (Otorhinolaryngology) Outpatient Department, Medical College, Kolkata.

#### Sample size and its calculation

Assuming 5% type I error and 80% power of study the estimated sample size will be 60 patients in total (30 in each group). Considering 20% dropout, the final sample size would be 72 patients in total.

**Statistical methods to be used:** Two tailed unpaired t-test.

**Funding/ sponsor:** None.

**Conflict of interest:** None.

**Case report form/ data collection form:** Attached.

**Informed consent form:** Attached.

#### Additional points for clinical trials

- Blinding:** Not applicable.
- Randomization method:** Computer generated.
- Allocation concealment:** Yes.
- Allocation concealment method:** Sequentially numbered, opaque, sealed envelope.
- Method of recruitment of study subjects:** Randomized recruitment on the basis of inclusion / exclusion criteria.
- Compensation statement in case of injury:** Mentioned in patient information sheet.

**Regulatory permission:** Obtained from IEC.

**RESULTS**

- Azelastine group : n = 10 (3 lost to follow up)  
Fluticasone group : n = 12 (1 lost to follow up)
- Baseline parameters (age, sex, Body mass index) : comparable in both groups

	Azelastine group (n = 10)	Fluticasone group (n = 12)	p value
Mean age	33.08 ± 8.63	34.05 ± 7.46	0.78
Male : Female	4 : 6	5 : 7	0.94
TSS	15.0 ± 2.27	15.54 ± 5.43	0.77
TNSS	11.08 ± 1.26	11.15 ± 2.41	0.93
TOSS	3.92 ± 1.85	4.38 ± 3.55	0.71

- **TSS score: No significant difference found between 2 groups at any point of observation.**

	Baseline	1 weeks	2 weeks	P value
Azelastine group (n = 10)	15.0 ± 2.27	6.55 ± 2.62	1.40 ± 1.26	< 0.001
Fluticasone group (n = 12)	15.54 ± 5.43	6.0 ± 2.58	0.92 ± 1.08	< 0.001
p value	0.77	0.62	0.34	

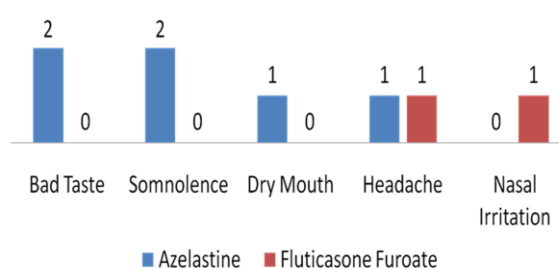
- **TNSS score: No significant difference found between 2 groups at any point of observation.**

	Baseline	1 weeks	2 weeks	P value
Azelastine group (n = 10)	11.08 ± 1.26	4.45 ± 1.44	0.08 ± 1.23	< 0.001
Fluticasone group (n = 12)	11.15 ± 2.41	4.15 ± 1.57	0.75 ± 0.97	< 0.001
p value	0.93	0.64	0.92	

- **TOSS score: No significant difference found between 2 groups at any point of observation.**

	Baseline	1 weeks	2 weeks	P value
Azelastine group (n = 10)	3.92 ± 1.85	2.09 ± 1.58	0.60 ± 0.70	< 0.001
Fluticasone group (n = 12)	4.38 ± 3.55	1.85 ± 1.72	0.17 ± 0.39	< 0.001
p value	0.71	0.74	0.08	

- **Adverse Drug Reaction: tolerability of Fluticasone Furoate appears to be significantly superior than Azelastine [2(16.67%) versus 6(60%), p = 0.048].**
- **No serious adverse event in either group was seen**



Individual Adverse events from 2 groups

**DISCUSSION**

Allergic rhinitis is a condition caused by IgE<sup>[25]</sup> mediated histamine release leading to various signs and symptoms like runny/stuffy/itchy nose, sneezing and red/watery/itchy eye. These conditions are treated with anti-histaminics, corticosteroids, leukotriene receptor antagonist, nasal decongestants, mast cell stabilizer and anti-cholinergic agents.<sup>[26]</sup> Of these various agents said above mild to moderate allergic rhinitis is treated by oral antihistaminic drugs and intra-nasal corticosteroids are preferred in moderate to severe conditions.<sup>[27]</sup> First generation anti-histaminics produces more sedation compared to newer one though newer anti-histaminics have modest effect on nasal symptoms.<sup>[27]</sup> Systematic review done by Weiner et al. showed that intra-nasal corticosteroids are superior to oral anti-histaminic drugs in controlling symptoms of AR.<sup>[28]</sup>

Here unicentric, open label study was done in which intra-nasal corticosteroid Fluticasone Furoate is compared with Azelastine nasal spray. Previous studies mostly compared various corticosteroids among themselves or corticosteroid vs oral anti-histaminics and it was found that intra-nasal corticosteroids are superior to oral anti-histaminics.<sup>[28]</sup> But in this study azelastine, an anti-histaminic drug, administered as nasal spray and it was seen that symptom scores improved significantly in both the groups. Intra-nasal Fluticasone Furoate and intra nasal Azelastine were found to be equally efficacious as difference between the two study groups were not significant.

Though efficacy was comparable between the two groups it was seen that fluticasone furoate is better tolerated compared to azelastine nasal spray. Bad taste, somnolence, dry mouth was reported more in the azelastine group whereas fluticasone furoate was preferred by the patients as it has mild fruity odour. On the other hand, following drug administration in fluticasone group, some people reported nasal irritation which can be due to preservatives like benzalkonium

chloride.<sup>[29]</sup> No serious adverse event in either group was seen.

## CONCLUSION

- Both Azelastine and Fluticasone Furoate nasal spray are appearing to be equally efficacious in allergic rhinitis.
- Fluticasone Furoate nasal spray appears to be better tolerated than Azelastine nasal spray.
- Unicentric, open label nature of this study involving small number of subjects necessitates further studies to confirm this observation.

## Citation of references in text

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