

# Comparative efficacy of steroid nasal spray versus antihistamine nasal spray in allergic rhinitis

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## ABSTRACT

This prospective randomized case controlled study was conducted to determine the efficacy of antihistamine (azelastine) nasal spray and compare it to steroid ( beclomethasone) nasal spray on the symptoms of allergic rhinitis. Seventy five symptomatic patients of allergic rhinitis were included in this study. Diagnosis was made on the basis of history and physical examination. The patients were divided into three groups randomly. **Group A** was treated with Azelastine nasal spray, **Group B** was treated with Beclomethasone nasal spray and **Group C** was control group and only treated with steam inhalation. Efficacy of the treatment was assessed in the terms of 'Total Rhinitis Symptom Complex' (TSC) scores and individual symptom score which was calculated on the basis of Okuda's grading system. Base line total symptom complex (TSC) scores were reduced in group A and group B by 84.0% after 4 week treatment whereas in group C it was reduced by only 38.0%. Decrease in mean score for sneezing was 95.0% in group A and group B whereas it was only 28.3% in group C. Similarly decrease in mean score for rhinorrhoea in azelastine group was 94.4% and in beclomethasone group was 95.3% in comparison to steam inhalation group where it was 25.0%. Only the beclomethasone reduced nasal stuffiness score significantly by 95.0%. No significant adverse effects of the drugs were observed. The present study establishes the relative efficacy and tolerability of azelastine nasal spray as compared to beclomethasone nasal spray in symptomatic patients of allergic rhinitis.

**Keywords:** Allergic rhinitis, azelastine, beclomethasone, nasal spray.

## INTRODUCTION

Allergic rhinitis, which is best, defined as that adverse pathophysiological response of the nose and adjacent organs, that results from the interaction of allergen with antibody in a host sensitized by previous exposure to that allergen.<sup>1</sup> It is one of the most common respiratory problems encountered in the clinical practice. Estimates of the prevalence of the allergic rhinitis in different countries vary from 0.5% to 28.0%.

Common manifestations of the allergic rhinitis include paroxysmal sneezing, nasal blockage, and watery nasal discharge. In clinical examination there may be pale or bluish boggy inferior turbinates with watery nasal discharge. The conjunctivae may be hyperemic and edematous.

The best treatment for allergic rhinitis is avoidance of the inciting antigen(s). However, because this is often impractical symptomatic relief may be sought from pharmacotherapy. Pharmacotherapy consists of decongestant drugs, mast cell stabilizers, anticholinergics, antihistamines, corticosteroids and newly developed leukotriene antagonists (montelukast). Understanding of pathomechanism of allergic rhinitis has cleared that, preformed mediators like histamine and mediators synthesized from arachidonic acid are responsible for the most of the allergic symptoms and signs. The inflammatory basis of rhinitis has also important implications for therapy. That may be the cause, even today two major categories of drugs namely antihistamines and corticosteroids are in common use, despite of development of various drugs.

In order to avoid possible systemic effects while concentrating the therapeutic effect on the diseased tissue, the topical nasal administration of drugs has become popular. Corticosteroid nasal spray in allergic rhinitis is an established treatment modality for more than 2 decades. But the side effects of the corticosteroid may limit its use in diabetic, hypertensive and young patients. The other major group of drugs used in allergic rhinitis is antihistamines. But systemic use of this drug may cause sedation. Topical antihistamine nasal spray (Azelastine) was introduced to minimize these problems. Azelastine nasal spray was approved by FDA in November of 1996.

The objective of this study was to determine whether the intranasal topical antihistamine (Azelastine) nasal spray is effective in decreasing the symptoms of allergic rhinitis and to compare the clinical efficacy of this drug to steroid (Beclomethasone) nasal spray on the symptoms of allergic rhinitis. Clinically detectable adverse effects of both drugs during the treatment of allergic rhinitis were also considered

## MATERIALS AND METHODS

Seventy five patients with symptomatic allergic rhinitis attending at OPD, Dept. of ENT, BPKIHS, Dharan were included in the study. Diagnosis was made on the basis of history and physical examination. A detailed history was taken with reference to sneezing, itching, nasal discharge, nasal obstruction which are generally the chief symptoms of allergic rhinitis. An enquiry was made about the history of allergens from the patient. Presence of pale or blue nasal mucosa and hypertrophied boggy turbinates with watery nasal discharge was considered in diagnosing the allergic rhinitis.

The patients were divided into three groups randomly:- Group A , Group B and Group C.

**Group A :** treated with azelastine ( Azep) nasal spray 2 puffs into each nostril BID ( 0.56 mg bid).

**Group B:** treated with beclomethasone (Beclate )nasal spray 2 puffs into each nostril BID (0.2 mg bid).

**Group C:** taken as a control group. Patients of this group were advised for only steam inhalation twice daily.

All the patients of all three groups were advised for avoidance of exposure to allergens and irritants as far as possible.

Duration of the treatment was 4 weeks.

All antihistaminic/antiallergic, sympathomimetics, decongestant and other systemic or topical corticosteroids were prohibited throughout the study. No additional drugs for rhinitis were given during the treatment period.

**Evaluation:** patient's symptoms and signs were evaluated on the basis of Okuda's grading system (Table-1). Efficacy of the treatment was assessed in the terms of total rhinitis symptom complex (TSC) scores which was calculated on the basis of Okuda's grading system.

Other symptoms and signs like eye/ear/palate itching, headache, fullness of ear, allergic shiners were also assessed during the follow up period.

**Follow up:** every patient was followed up weekly for 4 weeks during the treatment. During the therapy, patients were carefully observed for any side effects and patients were also asked to record any unpleasant experience with the drugs and attend at ENT OPD if necessary.

Patients with marked septal deviation, polyps, pregnancy, and those patients receiving any medication, likely to affect the treatment or course of rhinitis are excluded from this study.

## RESULTS

Seventy five patients, 39 (52.0%) male and 36 (48.0%) female were included in this study. Among the total number of patients 29.2% were students and 26.4% were housewives. In this present study the age of the patients varied from 12- 69 years; median is 27years. IQ range is 20 to 30 years. The model age group affected by allergic rhinitis is 21-30 years of age.

**Treatment response:** Seventy five patients were randomly divided into three sub-groups with 25 patients' of each group: group A, B and C. They were treated with azelastine nasal spray, beclomethasone nasal spray and steam inhalation respectively.

It was observed that in both azelastine and beclomethasone group significant decrease in mean 'Total Rhinitis Symptom Complex (TSC)' scores has been observed in comparison to steam inhalation group ( $p < 0.05$ ). No significant difference was observed in between the azelastine and beclomethasone treated patients. Decrease in TSC scores, calculated in 1<sup>st</sup> and 4<sup>th</sup> follow up in all three treatment groups has been given in Fig. 1.

Improvement in mean scores for Sneezing in different treatment groups are shown in Fig.2. Decrease in mean score after 4 week treatment for sneezing in azelastine and beclomethasone group was 95.0% in comparison to steam inhalation group where it was only 28.3%. Azelastine improved sneezing more potently than beclomethasone in 1<sup>st</sup> follow up but after 4 week treatment results are same.

Decrease in mean score for Rhinorrhoea after 4 week of treatment in azelastine group was 94.4% and in beclomethasone group was 95.3% in comparison to steam inhalation group where it was 25.0% (Fig.3). ( $p < 0.05$  for both azelastine and beclomethasone in comparison to steam inhalation).

Decrease in mean score for Stuffiness after 4 week of treatment in azelastine group was 65.0% and in beclomethasone group was 94.5% in comparison to steam inhalation group where it was 60.8%. (Fig.4.).

Hence in this study beclomethasone appears to more potent than azelastine in decreasing the stuffiness of nose. Statistical significance could not be shown in between the treatment groups.

Most of the symptoms and signs improved in azelastine treated patient within 2 days whereas in beclomethasone treated patients it was within 4 days.

Side effects of the drug was noted and given in Table-2.

## DISCUSSION

Azelastine, a phtalazinone derivative, is an antiallergic drug with multiple activities. In fact, azelastine demonstrate histamine H<sub>1</sub>- receptor antagonist action and also inhibits histamine release from both human and animal mast cells in response to a variety of stimuli. By in vitro and in vivo studies azelastine was demonstrated to prevent the activation of inflammatory cells (e.g. basophils, neutrophils eosinophils, polymorphonuclear cells, and macrophages) and to inhibit the synthesis and/or release of different mediators (e.g. leukotriens, superoxide anion, oxygen free radical and platelet activating factor). In particular azelastine inhibits antigen induced production of leukotrienes (LTC<sub>4</sub> and LTD<sub>4</sub>), which inhibits the 5-lipoxygenase pathway of arachidonic acid metabolism.<sup>2,3</sup>

Azelastine nasal spray on inflammatory changes after allergen specific nasal challenge. After azelastine administration, significant decrease in total symptom score, eosinophilic and neutrophilic infiltration and intercellular adhesion molecule -1 (ICAM-1) expression were observed during both early and late phase reactions. Furthermore serum eosinophil cationic protein levels decreased during the late phase reaction.<sup>4</sup>

Maximum plasma concentrations of azelastine were achieved approximately 2.5 hours after intranasal azelastine administration. The systemic bioavailability after intranasal azelastine administration was approximately 40.0%.<sup>5</sup>

Results of the present clinical trial demonstrated the efficacy of intranasal azelastine in the treatment of symptomatic allergic rhinitis, showing it to be superior to control group with steam inhalation ( $p < 0.05$ ).

In our study baseline total symptom complex (TSC) scores were reduced by 60.0% after 1 week treatment and by 84.0% after 4 week treatment in patients treated with azelastine.

Similar results were obtained by Gastpar *et al*<sup>3</sup> in their study, 70.0% improvement in TSC scores was achieved after 1<sup>st</sup> week of treatment and after 6 week of treatment improvement in TSC score was 80.0%.

Similarly in Germany, Mosges<sup>6</sup> had studied the efficacy of azelastine in 4000 patients. After 4 week treatment symptom scores was markedly reduced by up to 95.0%. In particular, frequent occurrence of sneezing was reduced in 94.0% of patients.

Beclomethasone is basically a corticosteroid which prevents mediator release by inhibiting the phospholipase A<sub>2</sub> and so prevents the breakdown of arachidonic acid on the cell membrane, thus blocking the first step in the production of leukotriens and prostaglandins. They also decrease the population of mast cells and other inflammatory cells.

Beclomethasone in present study reduced the base line total symptom (TSC) score by 60.8% in first week and by 83.4% after the end of 4 week treatment. This reduction in base line total symptom score is significantly greater than the reduction obtained by steam inhalation. ( $p < 0.05$ )

Comparing to the beclomethasone it was observed that there was no significant difference in reducing the TSC scores in between beclomethasone treated patients and azelastine treated patients. Davis<sup>7</sup> and Pelucchi<sup>8</sup> reported similar results in their two different studies. Results did not show any significant difference in responses in between the azelastine and beclomethasone. But it was found that both of the drugs were superior to placebo ( $p < 0.05$ ).

It was however found that azelastine improved the rhinitis symptoms faster than the beclomethasone. On the basis of patients' subjective feelings, it was found that most of the symptoms improved within 2 days in azelastine treated patients. In beclomethasone treated patients it was observed that only after 4 days most of the symptoms were improved. Newson<sup>9</sup> also observed in his study with 243 patients that azelastine had faster action than the beclomethasone. The cause of faster action of azelastine may be due to its different pharmacokinetic properties (faster absorption from nasal mucosa, rapid achievement of maximum plasma concentration) than the beclomethasone.

Symptom scores for sneezing were reduced by 81.0% after 1 week treatment and by 95.0% after 4 week of treatment in azelastine group. In comparison to steam inhalation the effect is significant ( $p > 0.05$ ). Similarly beclomethasone was also more effective in reducing the symptom score for sneezing (after 1<sup>st</sup> week: 73.0%, after 4 week: 95.0%) than the control group ( $p < 0.05$ ). It was observed that azelastine was slightly more potent in improving the sneezing than beclomethasone after 1week therapy but after the 4 week treatment there was no difference in it. Similar results were observed by Gastpar<sup>3</sup> in his study.

Symptom scores for rhinorrhoea were also more potently reduced by both azelastine and beclomethasone in comparison to control group with steam inhalation ( $p < 0.05$ ). But there is no significant difference in between azelastine and beclomethasone in improving the rhinorrhoea.

Symptoms score for stuffiness was reduced in all three groups. Beclomethasone reduced the stuffiness more effectively than azelastine and steam inhalation. After 4 week of treatment, beclomethasone reduced the symptom score by 94.5%. Azelastine and steam inhalation reduced the scores by 65.0% and 60.8% respectively. Johnston<sup>10</sup> found that nasal hyperthermia reduced allergen induced nasal blockage and vascular leakage, but no effect on sneezing, rhinorrhoea or tryptase levels.<sup>10</sup> The most likely mechanism underlying the

beneficial effect of steam inhalation in reduction of stuffiness may be the modification of nasal mucosal temperature or reduction of osmolality of nasal secretion.

In azelastine group 28.0% of the patients reported adverse effects. In study done by Dorrow<sup>2</sup> it was 11.0%. A study by Lassig<sup>11</sup> in paediatric patients adverse effects were found to be 13.5%. In our study the adverse effects are reported in more patients although the side effects were relatively minor. Most frequently reported adverse effect was sneezing or irritation of the nasal mucosa immediately after the drug use which being a subjective symptom depends upon the individual tolerance of persons also. Slightly high percentage of adverse effects observed in our patients may be due to lack of knowledge in using the nasal spray properly.

Sedation was not reported with any drug in this series.

In beclomethasone group 20.0% of the patients reported as the adverse affects, all were minor in nature. In this group dryness of the nose was most frequently reported as the adverse effect and may be due to its more potent effect as local anti-inflammatory response.

Results of this study clearly demonstrate the excellent efficacy and tolerability of intranasal azelastine in treatment of allergic rhinitis. Azelastine appears to be faster in action and reduce more efficiently the symptoms of itchy eye, dry cough and conjunctival injection. It has however relatively low efficacy in reducing the stuffiness of nose and hyposmia where beclomethasone appears to be more potent. Regarding the side effects only minor adverse effects were reported in both azealastine and beclomethasone treated patients.

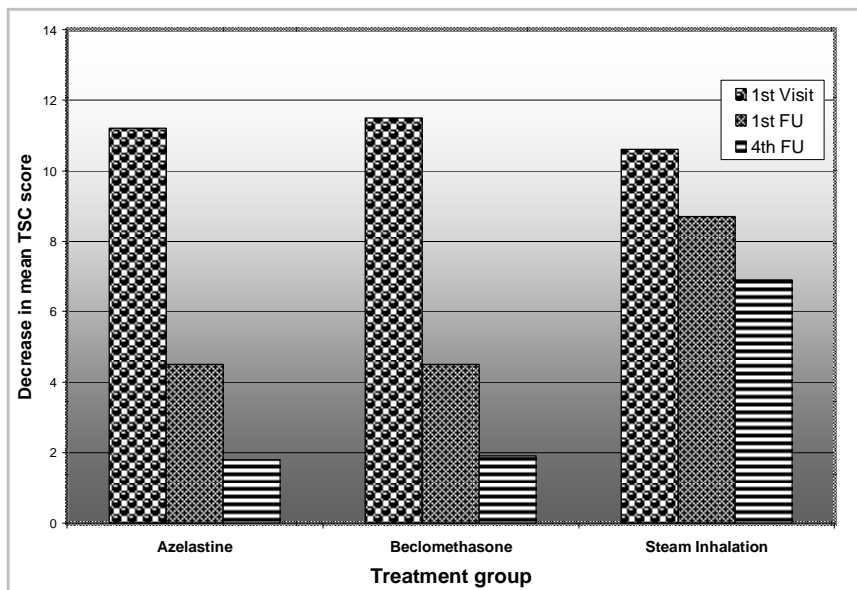
In patients where the steroid is contraindicated, antihistamine nasal spray may be an alternative for treatment of allergic rhinitis

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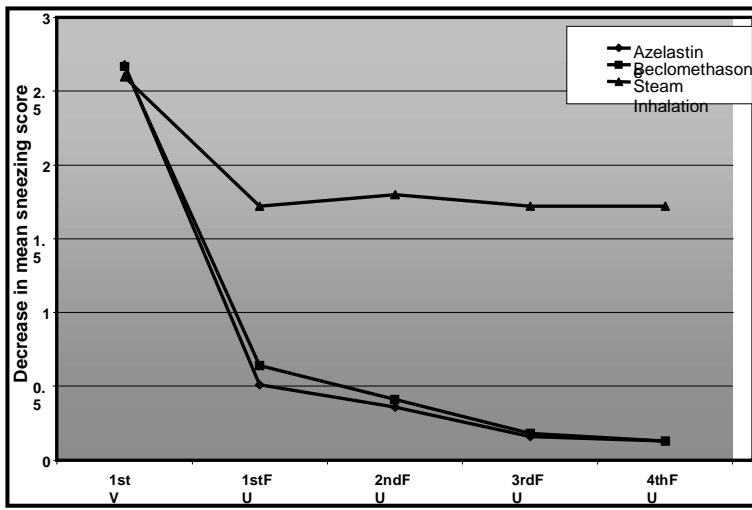
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**Table-1: Okuda's grading system**

Nasal symptoms and Signs	Severe (3+)	Moderate (2+)	Mild(1+)	None (-)
Nasal stuffiness	Predominant mouth breathing	Occasional mouth breathing	No mouth breathing Sensation of blockage	(-)
Rhinorrhoea (Blows per day)	>10 blows	6-10 blows	1-5 blows	(-)
Sneezing (attacks per day)	>10 sneezes	6-10 sneezes	1-5 sneezes	(-)
Congestion of inferior Turbinate	No visible of Middle turbinate	between severe and mild	visible over half of middle turbinate	(-)
Nasal discharge	Filled in full	between severe and mild	only attached to turbinates	(-)

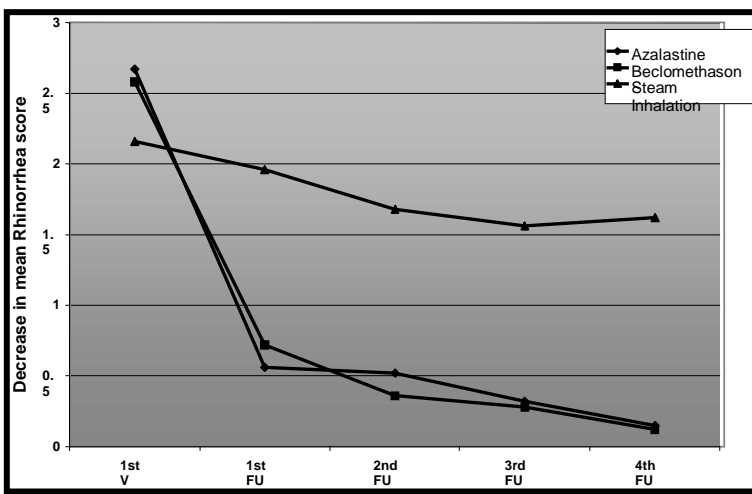


**Fig. 1.** Decrease in 'total rhinitis Symptom complex (TSC)' scores in different treatment groups



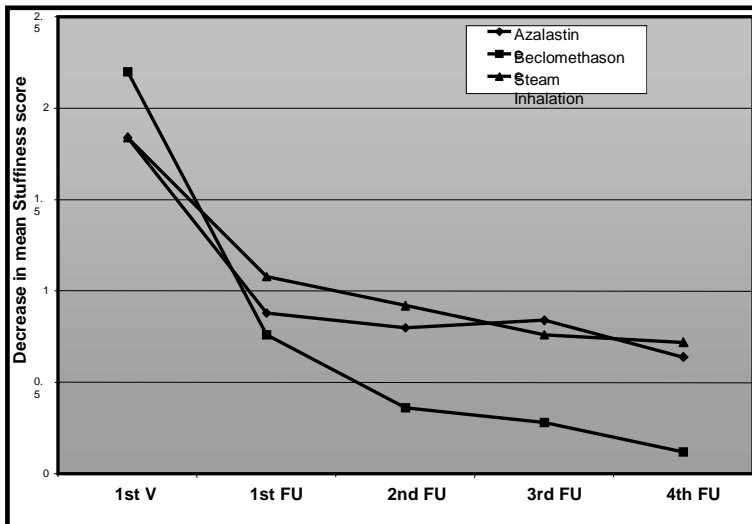
\*V- visit, FU - follow up

**Fig. 2.** Decrease in mean sneezing score in different treatment groups



\* V- visit, FU - follow up

**Fig. 3.** Decrease in mean rhinorrhea score in different treatment groups



\* V- visit, FU - follow up

**Fig. 4.** Decrease in mean stuffiness score in different treatment groups

**Table-2:** Side effects in different treatment groups

<b>Side Effects</b>	<b>No.of patients in azelastine group</b>	<b>No. of patients in beclomethasone group</b>
Irritation after the Drug Usage	4(16.0%)	2(8.0%)
Dryness of nose	1(4.0%)	3(12.0%)
Pain in nose	1(4.0%)	-
Bitter and unpleasant Taste	1(4.0%)	-