

Efficacy and Safety of Azelastine and Levocetirizine in Allergic Rhinitis

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ABSTRACT

BACKGROUND: Allergic rhinitis is an inflammatory disease with worldwide prevalence of 10-40%. Clinically, the condition manifests as nasal itching (pruritus), sneezing, rhinorrhea, congestion and itchy eyes. The second generation antihistamines are commonly used either as nasal sprays (azelastine) or orally (levocetirizine). Studies have demonstrated equal efficacy of azelastine and levocetirizine, but the data on Indian population is lacking. Hence, we designed this study to evaluate the effectiveness and safety of azelastine in comparison to levocetirizine in patients with allergic rhinitis.

METHODS: This prospective, randomized, parallel group study was conducted in the otorhinolaryngology outpatient department. Both male and female patients between the ages of 18 to 55 years were enrolled in the study after informed consent. Patients were randomized into two groups. Subjects in group 1 received azelastine whereas group 2 received levocetirizine. Clinic visits were scheduled at baseline and after every 2

weeks of treatment for 4 weeks. The primary outcome measure was mean change in the total daytime nasal symptom scores (PDS) and secondary outcomes were mean change in the nighttime nasal symptom scores (PNTS) and composite symptom scores (PCS).

RESULTS: We enrolled 40 patients, 20 in each group. Both groups were comparable at baseline and tolerated treatment well. There was significant ($p < 0.05$) improvement in mean PDS, PNTS and PCS scores in both groups from second week onwards. There was significant ($p < 0.05$) improvement in patients in group 1 at 4 weeks in the mean PDS and PCS score. There was no significant difference in mean PNTS scores in both groups. There were no reported adverse events.

CONCLUSION: In our study, both azelastine and levocetirizine improved the symptoms of patients with allergic rhinitis but azelastine showed better improvement in symptoms at the end of 4 weeks.

Keywords: Allergic rhinitis; Antihistamines; Azelastine; Levocetirizine

INTRODUCTION

Allergic rhinitis (AR) has high prevalence worldwide, varying from 10-40% [1]. Allergic rhinitis affects approximately 40 to 50 million people in the United States [2]. The prevalence of allergic rhinitis may vary within and among countries. This may be due to geographic differences in types and potency of different allergens and overall aeroallergen burden [2]. A recent survey in India shows that 20-30% of the population suffers from AR and that 15% has

asthma [3].

AR involves inflammation of mucous membranes of nose, eyes, eustachian tubes, middle ear, sinuses, and pharynx, and is characterized by a complex interaction of inflammatory mediators but ultimately is triggered by an immunoglobulin E (IgE)-mediated response to an extrinsic antigen [1]. Clinically, the condition manifests as nasal itching (pruritus), sneezing, rhinorrhea (runny nose), congestion and itchy eyes [1, 4].

Management of the disease involves allergen

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avoidance, specific immunotherapy and controlling symptoms with pharmacotherapy. The first-line treatment for symptom reduction is administration of antihistamines (H1-receptor antagonists) [5]. H1-receptor antagonists are prescribed to relieve or prevent the symptoms of allergies. The second generation antihistamines, characterized by their non-sedating effects, are available as nasal sprays (azelastine, olopatadine) and oral preparation (desloratadine, levocetirizine) [6, 7].

Azelastine, a selective antagonist of histamine H1-receptor, also inhibits synthesis and release of other chemical mediators participating in allergic reactions [8]. A trial by Shah et al and Berger et al showed that azelastine hydrochloride nasal spray was significantly more effective than oral cetirizine in relieving various symptoms associated with allergic rhinitis [9]. Another study demonstrated superiority of azelastine nasal spray over oral cetirizine [8]. Moreover, superior efficacy and distinctly earlier onset of action of azelastine strongly emphasizes the usefulness of nasal spray for symptomatic treatment of seasonal AR [8]. Several studies [8, 9] have demonstrated the superior efficacy of azelastine over cetirizine, but the data on Indian population is lacking. Hence, we designed this study to evaluate the effectiveness and safety of azelastine in comparison to levocetirizine in Indian patients with allergic rhinitis.

METHODS AND MATERIALS

Study design: This prospective, randomized, open, parallel group study (with a 4 week treatment period) was conducted in the outpatient department (OPD) of Gian Sagar Medical College and Hospital, District Patiala from June 2012 to July 2012. The study protocol and informed consent was reviewed and approved by the Institutional Ethics Committee (IEC) before study initiation.

Patient Selection: A total of 40 patients between the ages of 18 to 55 years with allergic rhinitis who gave written informed consent were recruited in the study. Subjects with physical signs and symptoms suggestive of renal, hepatic or cardiovascular disease, treated with systemic steroids or topical steroids during the previous 30 days, treated with oral/ topical antihistamine/decongestant during the past 7 days, with polyps in nose or significantly displaced septum, and upper respiratory tract infection within 14 days of start of study were excluded from the study.

Females planning pregnancy and lactating mothers were also excluded from the study.

Procedure: Clinic visits were scheduled at screening (visit 1), and after every 2 weeks of treatment according to randomization for 4 weeks (visit 2 and 3). The subjects were randomized into two groups as per random number table. Subjects in group 1 received topical azelastine (0.1%) nasal spray 1 puff in each nostril twice daily for 4 weeks whereas subjects in group 2 received oral levocetirizine (2.5-5 mg/day) daily for 4 weeks. A physical examination for nasal secretion and turbinate swelling was also done at each visit.

Outcome measurements: The primary outcome measure was mean change of the daytime nasal symptom scores (PDTS), defined as average score of four daytime nasal symptoms. The secondary outcomes were mean changes of nighttime nasal symptom scores (PNTS), and composite symptom scores (PCS) (average score of daytime and nighttime nasal symptom score).

Daily rhinitis diary card: The patient recorded the symptoms on the daily diary card, on a 4-point scale (0 to 3) for both daytime (diary card completed in the evening) and nighttime (diary card completed on awakening). The daytime nasal (rhinorrhea, sneezing, itching, and congestion), nighttime nasal (nasal congestion upon awakening, difficulty going to sleep, and nighttime awakening) symptoms and their ratings were described to every patient by researcher. The ratings of the symptom were: 0 = not noticeable, 1 = mild symptoms, 2 = moderate symptoms, 3 = severe symptoms. The rating was performed by the patients themselves to increase the credibility of the subjective scale. Safety evaluation includes spontaneously reported adverse events throughout the study.

Statistical analysis: The data was tabulated as mean \pm standard deviation (SD) (95% confidence interval). Results were analyzed using chi-square test and two tailed student t-test. A $p < 0.05$ was considered statistically significant.

RESULTS

A total of 40 patients were recruited in the study and divided into 2 groups. Of the 40 patients recruited in the study, 35 patients completed the entire 4 weeks of study. Two patients in group 1 and 3 patients in group 2 were lost to follow-up.

One patient in group 1 was lost to follow-up at 2 weeks and another at 4 weeks. In group 2, two patients did not come for follow-up visit at 2 weeks and one patient did not turn up at the end of 4 weeks.

The baseline characteristics of patients in both groups were comparable (Table 1). The mean daytime nasal symptom score was 1.76 ± 0.46 (1.55-1.98) versus 1.74 ± 0.47 (1.52-1.96) in group 1 and 2, respectively.

Group 1: There was a significant improvement in mean daytime nasal symptom score in patients in group 1 at the subsequent visits. The mean PDTS score at 0 weeks was 1.76 ± 0.46 which reduced significantly ($p < 0.05$) to 0.50 ± 0.30 (0.36-0.64) at the end of 4 weeks (visit 3). There was also a significant reduction of mean PDTS at 4 weeks as compared to after 2 weeks. The mean PNTS score at 0 weeks was 1.48 ± 1.03 (1.0-1.97) which reduced significantly to 0.38 ± 0.25 (0.27-0.50) at the end of 4 weeks (visit 3). There was also significant reduction of mean PNTS at 4 weeks as compared to after 2 weeks. The mean PCS score at 0 weeks was 1.62 ± 0.64 (1.32-1.92) which reduced significantly to 0.44 ± 0.23 (0.34-0.55) at the end of 4 weeks (visit 3). There was also significant reduction of mean PCS at 4 weeks as compared to after 2 weeks.

Group 2: There was a significant improvement in mean daytime nasal symptom score in patients in group 2 at the subsequent visits. The mean PDTS score at 0 weeks was 1.74 ± 0.47 which reduced significantly ($p < 0.05$) to 0.84 ± 0.53 (0.59-1.09) at the end of 4 weeks (visit 3). There was also significant reduction of mean PDTS at 4 weeks as compared to after 2 weeks. The mean PNTS score at 0 weeks was 1.18 ± 1.03 (0.73-1.64) which reduced significantly to 0.52 ± 0.48 (0.29-0.74) at the end of 4 weeks (visit 3). There was also a significant reduction of mean PNTS at 4 weeks as compared to after 2 weeks. The mean PCS score at 0 weeks was 1.46 ± 0.65 (1.16-1.76) which reduced significantly to 0.68 ± 0.43 (0.47-0.88) at the end of 4 weeks (visit 3). There was also significant reduction of mean PCS at 4 weeks as compared to after 2 weeks.

Daytime nasal symptom (PDTS) scores: Group 1 and group 2 had comparable reduction in PDTS scores at 2 weeks, though group 1 had slightly greater reduction in mean scores but it was not statistically significant (Figure 1). There was a statistically significant ($p < 0.05$) decrease in the mean PDTS scores in group 1 (0.50 ± 0.30)

Table 1: Baseline data in both groups

Characteristics	Group 1	Group 2	p-value
Age in years (Mean \pm SD)	27.4 \pm 9.1	26.7 \pm 7.7	0.78*
Sex (M:F)	11:9	9:11	0.75#
Daytime nasal symptom scores (PDTS) (Mean \pm SD)	1.76 \pm 0.46	1.74 \pm 0.47	0.87*
Nighttime nasal symptom scores (PNTS) (Mean \pm SD)	1.48 \pm 1.03	1.18 \pm 1.03	0.35*
Composite symptom scores (PCS) (Mean \pm SD)	1.62 \pm 0.64	1.46 \pm 0.65	0.43*

Both the groups were comparable ($p > 0.05$) at baseline

*using two tailed independent student t-test

using chi-square test

as compared to group 2 (0.84 ± 0.53) at the end of 4 weeks.

Nighttime nasal symptom (PNTS) scores: Group 1 and group 2 had comparable reduction in PNTS scores at 2 weeks, although group 2 had slightly greater reduction in mean scores but it was not statistically significant (Figure 2). Group 1 and group 2 had comparable reduction in PNTS scores at 4 weeks, although group 1 (0.38 ± 0.25 versus 0.52 ± 0.48) had slightly greater reduction in mean scores but it was not statistically significant.

Composite symptom (PCS) scores: Group 1 and group 2 had comparable reduction in PCS scores at 2 weeks, although group 1 had slightly greater reduction in mean scores but it was not statistically significant (Figure 3). There was a statistically significant ($p < 0.05$) decrease in the mean PCS scores in group 1 (0.44 ± 0.23) as compared to group 2 (0.68 ± 0.43) at the end of 4 weeks.

Safety: No serious adverse event was reported in both groups. The incidence of adverse events which were reported in group 2 was more as compared to that in group 1, but none of the adverse events which were reported were severe enough to warrant termination of the treatment. The adverse events which were reported in both groups did not require a reduction in dose or any therapy for their treatment. The patients complained about bitter taste, headache, nasal burning, somnolence, mouth dryness, and

Figure 1: Comparison of daytime nasal symptom scores in both groups

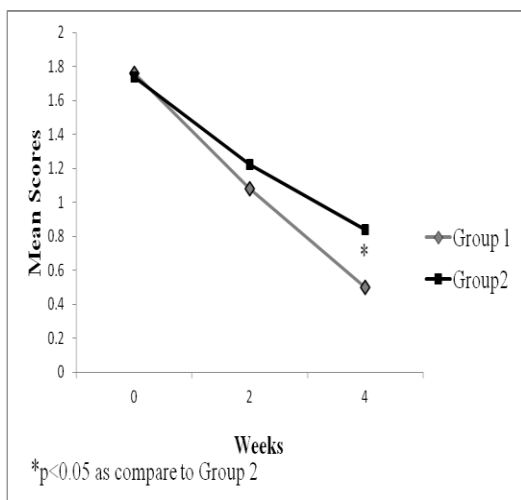


Figure 2: Comparison of nighttime nasal symptom scores in both groups

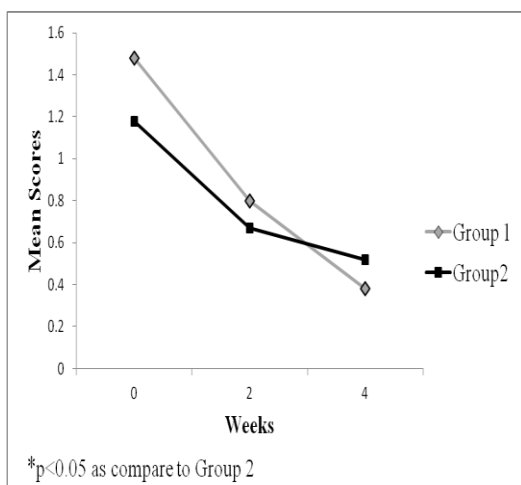
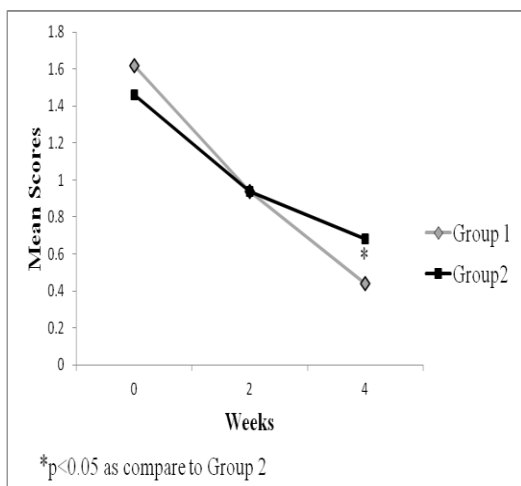


Figure 3: Comparison of composite symptom scores in both groups



light-headedness. Two patients in group 2 complained of somnolence and headache, whereas one patient in group 1 reported of bitter taste and nasal burning.

DISCUSSION

A number of therapeutic choices are available for the treatment of allergic rhinitis, which includes oral and intranasal H1 antihistamines, intranasal corticosteroids, oral and intranasal decongestants, intranasal anticholinergics and intranasal cromolyn and leukotriene receptor antagonists [10-12]. Antihistamines are helpful in relieving itching, sneezing, runny nose, and other symptoms unrelated to rhinitis, including hives and some rashes [8]. In the present study, both azelastine and levocetirizine significantly improved the PDTS, PNTS and PCS scores at subsequent visits at week 2 and week 4. However, azelastine significantly improved scores of PDTS and PCS at the end of 4 weeks as compared to levocetirizine. Patients on levocetirizine reported greater number of side effects but none of them was serious.

The results of our study are in agreement with previous studies [8, 9] where efficacy of azelastine nasal spray was significantly superior and treatment had more pronounced improvement of nasal symptom severity. Earlier studies have shown significant improvement of azelastine on total nasal symptom score from baseline. Another trial by Berger et al showed that azelastine hydrochloride nasal spray was significantly more effective than oral cetirizine in relieving various symptom scores associated with allergic rhinitis [9]. Moreover, superior efficacy and distinctly earlier onset of action of azelastine strongly emphasized the usefulness of nasal spray for symptomatic treatment of seasonal AR [8, 13, 14, 15].

Our study showed that although levocetirizine was effective in reducing the nasal symptom score at subsequent visits, it had significantly lesser reduction in nasal symptom scores as compared to azelastine.

There are certain limitations of our study; first, the sample size is small. The sample size could have been large but the time limit of two months would not have been sufficient for the study. Each patient recruited in the study had to come for follow-up every 2 weeks and 4 weeks and in the set time frame increasing the sample size would have compromised the feasibility. Secondly a placebo arm could have helped, but adding another arm to the study would have

increased the number of participants and would have compromised with the feasibility.

CONCLUSION

The results of our study showed that both the treatment regimens, group 1 treated with azelastine and group 2 treated with levocetirizine, improved the nasal symptoms of the patients suffering from allergic rhinitis. Both the treatment arms showed a significant reduction in the PDTS, PNTS and PCS scores as compared to baseline. There was a significant reduction in the scores at week 2 and week 4. Patients treated with azelastine showed a significant improvement in the PDTS and PCS scores as compared to levocetirizine group at the end of 4 weeks. The PNTS scores were comparable in both groups at 4 weeks. Azelastine was more safe and efficacious as compared to cetirizine in patients suffering from allergic rhinitis.

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