

## To Compare the Safety, Efficacy and Quality of Life in Patients with Allergic Rhinitis Treated with Levocetirizine and Desloratadine

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### Abstract

**Background:** Allergic Rhinitis (AR) is a very common disease that affects almost 10-30% of the world's population. Second-generation H<sub>1</sub> antihistaminics are the preferred drugs for treatment of patients with AR. Levocetirizine and desloratadine are commonly prescribed newer non-sedating second-generation antihistaminics. Various studies show no difference in efficacy and quality of life (QOL) between the two drugs desloratadine and levocetirizine and that the drugs are quiet safe; however, some studies show negative impact on patients' QOL with these drugs. Studies comparing the two drugs were insufficient in India; hence, this study was designed to evaluate and compare the efficacy, safety and QOL of patients with AR, following treatment with levocetirizine or desloratadine, in the Indian scenario.

**Methods:** This 2-month randomized, prospective study was performed in 60 patients with AR visiting the department of Otorhinolaryngology. Patients were randomized into one of the two treatment groups, and prescribed levocetirizine 5 mg once daily for two weeks or desloratadine 5 mg once daily for two weeks. The outcome measures for the severity of AR symptoms used were Total Nasal Symptom Score (TNSS); and QOL was assessed using Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) Score.

**Results:** Data from 54 patients who completed the study shows that both levocetirizine and desloratadine significantly ( $p < 0.05$ ) improved the AR symptoms and QOL at the end of 2 weeks study period, analyzed using TNSS and RQLQ scores, respectively. However, statistically non-significant differences in analysis of TNSS score between levocetirizine and desloratadine showed that the two drugs may be equally effective in patients with AR, with patients on levocetirizine showing slightly better response. The adverse events were low in patients on levocetirizine and no adverse event was seen with desloratadine. At baseline visit, rhinorrhoea was the most common and severe symptom, whereas nasal itching was the least common and severe symptom.

**Conclusion:** Study findings showed that both levocetirizine and desloratadine were equally effective in patients with AR, however, desloratadine group showed better safety profile. The drugs were safe and well tolerated.

**Keywords:** Allergic rhinitis; Levocetirizine; Desloratadine; Efficacy; Tolerability; QOL; TNSS; RQLQ

### Introduction

Allergic Rhinitis (AR) is a very common disease that affects almost 10-30% of the world's population [1]. It is an IgE mediated immunologic response of the nasal mucosa to the air borne allergens and is characterized by rhinorrhoea (watery nasal discharge), nasal congestion or obstruction, sneezing and itching in nose and/ or eyes. AR was earlier classified based upon the time of allergic exposure into seasonal allergic rhinitis (SAR), that occurs at the same time each year or perennial allergic rhinitis (PAR), a year-round (perennial) allergy that occurs any time during the year. These definitions do not entirely reflect patterns of AR symptoms in patients, as for example many patients with PAR do not show symptoms throughout the year, and in

certain areas, pollens and molds are perennial allergens. The World Health Organization (WHO) and Allergic Rhinitis and its Impact on Asthma (ARIA) workshop group has thus developed a new classification of AR based on the duration of symptoms, into Intermittent allergic rhinitis (IAR) defined by the AR symptoms for less than four days or less than four weeks a year, and persistent allergic rhinitis (PER) defined by the occurrence of AR symptoms for more than four days or at least four consecutive weeks a year. The severity of AR can be classified as mild or moderate/severe [2].

The most common causes of AR are inhalant allergens, which include pollens from trees, grasses, or weeds, house dust, dust or house mites, animal dander, cockroaches, or mold. In SAR, causative agents are commonly outdoor allergens (pollens and mold); and in case of PAR, the most common causes of perennial allergies are indoor allergens (dust mites, animal dander, cockroaches, or mold) [2,3].

The symptoms associated with AR may also influence cognitive and emotional functions, resulting in impaired functioning at work or school and disrupts sleep, thus has negative impact on the quality of life (QOL) of patient [4-6]. A study involving patients with AR in five European countries reported that 84.2% of patients had a deleterious effect on daily activities [6]. Among the symptoms of AR, nasal blockage is considered to be the most bothersome symptom that affects the QOL of patients as it leads to breathing through the mouth, disrupts sleep, causes night time awakening, resulting in consequent daytime somnolence, impaired mood, alters memory, and decreases productivity at school and work [7-10]. Disruption of sleep leads to increased consumption of sedatives, which deteriorates the problem [2,10].

Management of patients with AR involves avoidance of allergen (if allergen is known), and/or drug therapy. The drugs used for the treatment of patients with AR include antihistaminics, corticosteroids, sympathomimetics and mast cell stabilizers. Among these H<sub>1</sub> antihistaminics are the most preferred drugs [2]. H<sub>1</sub> antihistaminics include first-generation and second-generation antihistaminics. Sedation is the major side effect of first generation antihistaminics, and so the less-sedating second-generation antihistaminics are preferred for AR. Also, the newer second-generation antihistaminics have rapid onset of action, are highly effective on symptoms such as rhinorrhoea, sneezing, and nasal pruritis, and are relatively safe [11]. Levocetirizine and desloratadine are now commonly prescribed newer non-sedating second generation antihistaminics, highly selective for histamine H<sub>1</sub>- receptors, and are highly effective in controlling the symptoms of AR, without causing much adverse effects at therapeutic doses, as shown by several studies [12-18].

Drugs used in AR often impair the QOL of the patients and produces various adverse effects like sedation and drowsiness. XPERT study showed levocetirizine significantly improved the QOL of patients with AR [12]. Another study by Ciebiada et al. showed that therapy with placebo, or montelukast, desloratadine and levocetirizine, either as monotherapy or in combination significantly improved QOL of patients suffering from persistent allergic rhinitis [13]. Desloratadine and levocetirizine have been shown in various studies to significantly improve the QOL in patients with AR [4]. Also, some antihistamines can cause adverse events such as somnolence and can have an additional negative impact on QOL [2,12-14]. Thus, drugs used for AR should not only be efficacious in improving the symptoms, but also the QOL of patients.

Potter et al. reported significant improvement in total four symptom scores (T4SS) after four weeks of treatment (56.0 vs 29.2%; P<0.001) in patients with PAR who were treated with levocetirizine, when compared to patients on placebo [15]. In another study, patients on cetirizine reported greater reductions in total symptom scores (TSS) after 12 weeks of treatment, compared to levocetirizine and placebo treatment groups (5.54 vs 3.30 and 0.18, respectively; P<0.05). No difference was seen in QOL between patients receiving cetirizine or levocetirizine [14].

A study by Simons et al. conducted over four weeks on 676 patients showed statistically significant improvement in symptoms in patients on desloratadine when compared to placebo [16]. Another study by Kim et al. showed desloratadine to be more effective than placebo at reducing symptoms of PAR, as it caused a significant reduction in total symptom scores (TSS) when compared to those treated with placebo (26.6 vs 22.3%; P=0.001) [17].

Various studies show no difference in efficacy between the two drugs desloratadine and levocetirizine and that the drugs are quiet safe; however, some studies show negative impact on patients' QOL with these drugs [18]. For our research purpose, we selected levocetirizine and desloratadine, newer non-sedating second generation antihistaminics that are commonly used for symptomatic relief of AR. The studies comparing these drugs were insufficient in India and thus, this study was designed to evaluate and compare the efficacy, safety and QOL of patients with AR, following treatment with levocetirizine or desloratadine, in the Indian scenario.

## Material and Methods

### Study population

Patients with AR who fulfilled the following inclusion and exclusion criteria were enrolled in the study. Patients of both sexes in the age group of 18-70 years and who were willing to give written informed consent were included in the study. Exclusion criteria of the study were: Pregnant and/or lactating females, history or laboratory evidence of renal, hepatic or cardiovascular disease, subjects treated with systemic steroids or topical steroids during the previous 30 days, subjects treated with oral / topical antihistamine / decongestant during the past 7 days, subjects with nasal structural abnormalities that significantly interfered with nasal airflow, including large nasal polyps and marked deviation of nasal septum, history of hypersensitivity to any or all of drugs being used in the study, history of upper respiratory tract infection within 14 days prior to start of study.

### Study design

The study was a randomized, prospective, open-label (non-blinded), parallel group comparative study in patients with AR visiting the outpatient Ear, Nose, and Throat (ENT) Department of Gian Sagar Medical College and Hospital, Patiala during the period from June 2012 to July 2012. The study was conducted in association of ENT Department and Department of Pharmacology, Gian Sagar Medical College and Hospital, Patiala.

Before the commencement of the study, the study protocol and informed consent were got approved by the Institutional Ethics Committee of Gian Sagar Medical College and Hospital. Written informed consent was obtained from each subject prior to their enrolment in the study. The procedures followed in this study were in accordance with the ethical standard established by the Ethical Guidelines for Biomedical Research on Human Subjects (Indian Council of Medical Research, 2006).

Patient visit to the ENT OPD were planned as per the following schedule: During the first baseline visit (Visit 1), detailed history of the patient, their Total Nasal Symptom Score [TNSS] and Rhinoconjunctivitis Quality of Life Questionnaire [RQLQ] scoring were performed and physical examination for nasal secretion and turbinate swelling were done. The subsequent visits were after 1 week (Visit 2) and 2 weeks (Visit 3) of starting the treatment. At the end of 2 weeks treatment period, the symptoms were recorded and clinical improvement was assessed in terms of change in TNSS and change in patients' QOL using RQLQ score. Physical examination for nasal secretion and turbinate swelling were done at each visit. The patients were randomized into 2 treatment groups as per random number table: 30 patients in group A and 30 patients in group B. Subjects in

Group A were prescribed tablet desloratadine 5 mg once daily for 2 weeks whereas Group B received tablet levocetirizine 5 mg once daily for 2 weeks.

**Outcome measurements**

The outcome measure used for efficacy variable was mean change in TNSS, from baseline to day 14 of the study period. TNSS is used to assess the severity of AR symptoms (runny nose, sneezing, nasal itching, and nasal congestion), scored on a severity scale from 0 to 3 (0=no symptoms, 1=mild, 2=moderate, and 3=severe). The TNSS is the sum of all the four symptom scores, with TNSS ranging from 0 (no symptoms) to maximum symptom intensity of 12 and has high prognostic value [19].

The outcome measure that was used to assess the improvement in patients’ QOL was mean change in RQLQ scoring, from baseline to day 14 of the study period. RQLQ is a disease specific QOL questionnaire that has been developed for the measurement of physical, emotional, and social problems in adults with allergic diseases. It consists of 28 questions in 7 domains. The questionnaire has 3 ‘patient-specific’ questions in the activity domain which allow patients to select 3 activities in which they are most limited by their AR. Patients recall how bothered they have been by their AR during the previous week and to respond to each question on a 7-point scale (0=not impaired at all - 6=severely impaired). The overall RQLQ score is the mean of all 28 responses and the individual domain scores are the means of the items in that domains [20]. The completion time for the questionnaire was from 10-15 minutes.

**Statistical analysis**

The results were analyzed using paired t test, unpaired t test, fisher’s exact test and Chi-square test, using InStat Graphpad 3.10 version software. A p-value <0.05 was considered statistically significant.

**Results**

Of the total 60 patients (29 on levocetirizine, i.e. Group A and 31 on desloratadine, i.e. Group B) who were enrolled in the study, 54 patients (27 in Group A and 27 in Group B) completed the study. 6 patients, 2 in group A and 4 in group B did not come for follow-up or could not be contacted. So, we calculated data for these 54 patients (23 M, 31 F) who completed the study.

**Demographic and baseline data**

On statistical analysis, the mean demographic characteristics of the two treatment groups were comparable at baseline (Table 1). At the

Treatment groups	Baseline TNSS	TNSS at the end of 2-week study	Mean change from baseline	Mean percentage change from baseline	Statistical analysis
Group A (Levocetirizine 5 mg)	7.37 ± 0.93	4.96 ± 0.90	-2.41 ± 0.80	- 32.7%	p<0.001, highly significant
Group B (Desloratadine 5 mg)	7.11 ± 1.16	5.37 ± 0.79	-1.74 ± 0.80	- 24.5%	p<0.001, highly significant

**Table 2:** Changes in TNSS among the treatment groups over the study period.

baseline visit (Visit 1), TNSS and RQLQ scores were non-significant (p>0.05) between the two groups. There was no significant difference between the treatment groups at baseline. Rhinorrhoea was the most common and severe symptom, whereas nasal itching was the least common and severe symptom at baseline visit.

Characteristics	Group A (Levocetirizine 5 mg)	Group B (Desloratadine 5 mg)
No. of patients	27	27
Age in years (Mean ± SD)	35.96 ± 14.31	32.33 ± 11.49
Male/ Female	13 (48.15%)/14 (51.85%)	10 (37.04%)/17 (62.96%)
TNSS	7.37 ± 0.93	7.11 ± 1.16
RQLQ score	4.17 ± 0.5	4.27 ± 0.63

**Table 1:** Demographic and clinical characteristics of the two treatment groups at baseline visit.

**Total nasal symptom score (TNSS)**

Both treatments significantly decreased TNSS (-2.41 ± 0.80, p<0.001 for levocetirizine group A; -1.74 ± 0.80, p<0.001 for desloratadine group B) over the course of 2 weeks treatment (Table 2). However, the difference between the two treatment groups was not-significant (p>0.05) although levocetirizine (32.7% vs 24.5%) decreased TNSS scores slightly more than desloratadine (Table 2).

**Rhinoconjunctivitis quality of life questionnaire (RQLQ) scoring**

Mean change in RQLQ scoring, from baseline to day 14 of the study period is used to assess the improvement in patients’ QOL. Both treatments significantly decreased RQLQ score (-0.58 ± 0.31, p<0.001 for levocetirizine group A; -0.50 ± 0.29, p<0.001 for desloratadine group B) over the course of 2 weeks treatment (Table 3). The inter-group difference between the two treatment groups A and B was not-significant (p>0.05) although levocetirizine (13.91% vs 11.71%) decreased RQLQ scores slightly more than desloratadine (Table 2).

Treatment groups	Baseline RQLQ	RQLQ at the end of 2-week study	Mean change from baseline	Mean percentage change from baseline	Statistical analysis
Group A (Levocetirizine 5 mg)	4.17 ± 0.5	3.59 ± 0.33	- 0.58 ± 0.31	- 13.91%	p<0.001, highly significant
Group B (Desloratadine 5 mg)	4.27 ± 0.63	3.76 ± 0.49	- 0.50 ± 0.29	- 11.71%	p<0.001, highly significant

**Table 3:** Changes in RQLQ over the treatment period.

### Safety

Of the 54 patients who completed the study, only 2 patients (0.07%) in the levocetirizine 5 mg group developed adverse effects with the drug. One patient (0.04%) in levocetirizine group reported sedation and one (0.04%) complained of fatigue with the drug. No adverse effects were reported by patients in the desloratadine group.

### Discussion

The current study shows that both levocetirizine and desloratadine significantly improved the symptoms and QOL as shown by TNSS score and RQLQ scores, respectively in patients with AR, both IAR or PER. Statistically non-significant differences in analysis of TNSS score between levocetirizine and desloratadine showed that the two drugs may be equally effective in patients with AR, with slightly favorable results for levocetirizine. The adverse events were low in patients on levocetirizine and no adverse event was seen with desloratadine.

The newer studies usually follow the newer classification as IAR or PER, whereas other relatively older studies quoted their observation as SAR or PAR. It thus became difficult to compare these findings, as these do not fully represent one another. Also, there are very few studies that directly compare levocetirizine and desloratadine in patients with AR.

Our study shows that levocetirizine significantly improved the symptoms as shown by TNSS score in patients with AR. Similar results were also reported in various studies with levocetirizine in patients with AR [21,22]. A study by Benninger et al., over 2 weeks, showed median percent reduction from baseline in TNSS for patients with SAR by 23.5% and PAR by 51.4%, for patients receiving oral antihistamines [23].

A study on 440 patients comparing desloratadine 5 mg per day showed significant decrease (p<0.05) in TNSS score by 17.5% over 2-weeks. It also caused somnolence in 1% of the patients. Our study showed highly significant decrease (p<0.001) in TNSS score by 24.5% over 2-weeks, and no adverse-effect with desloratadine. These differences may be due to much lesser number of patients in our study, and the other study was Intention-to-treat study [24]. In another study by Kim et al., performed over 4 weeks, reductions from baseline in TNSS were greater with desloratadine compared to placebo (2.1 [23.7%] vs 1.8 [19.8%]; P=0.004) [17]. Similar results were seen in another study by Simons et al. and Raphael et al. [16,25].

The results of the current study show statistically non-significant differences in TNSS score between levocetirizine and desloratadine, with slightly in favour for levocetirizine. Similar results were seen in a study by Shimal Khan et.al. [26]. However, the study differs in duration as it was performed over 4 weeks in contrast to our 2-week, and better results were seen at 4-week than at 2-week. Another study that compared levocetirizine or desloratadine alone or in combination

with montelukast in patients with PER had similar results. However, the study duration was 6 weeks [27]. Another study showed levocetirizine to be better than desloratadine in symptoms control [28].

AR does not merely cause nasal discomfort due to persistent nasal symptoms, but also leads to losses in concentration and headaches, which can affect sleep, social interaction, school work, and even workplace productivity, leading to socioeconomic losses [29]. Studies have shown improvement in QOL using various parameters including RQLQ, which was used in our study. Our study shows improvement in QOL with significant decrease in RQLQ score (-0.58 ± 0.31, p<0.001 for levocetirizine group A; -0.50 ± 0.29, p<0.001 for desloratadine group B) over the course of 2 weeks treatment. However, there was non-significant difference in treatment between the two groups. Previous studies have also shown improvement in QOL with these drugs, however desloratadine is theoretically thought to improve the QOL more as it causes greater effect on nasal congestion, although studies do not show much difference between the two drugs. Our study however shows deviation in improvement in QOL by a slight margin in favour of levocetirizine, though not statistically significant improvement.

To conclude both levocetirizine and desloratadine showed significant (p<0.05) improvement in patients symptoms and QOL in patients with AR at the end of 2 weeks study period, with levocetirizine showing slightly better response in symptoms and QOL at the end of 2 weeks. However, desloratadine group showed better safety profile. The drugs were safe and well tolerated.

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