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Original Research Article

A comparative study of efficacy and safety of Olopatadine and Levocetirizine in seasonal Allergic Rhinitis

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Abstract: Allergic rhinitis (AR) is one of the common prevalent diseases representing approximately 20% of the general population. Allergic rhinitis (AR) has a relevant impact on society because of its high prevalence, association with an impaired quality of life and the presence of co-morbidities such as atopy and asthma. The aim is to compare the therapeutic efficacy of Levocetirizine and Olopatadine in the treatment of Seasonal Allergic Rhinitis and to compare their safety in terms of incidence of adverse effects. The study was conducted on 90 patients of seasonal allergic rhinitis attending the Department of ENT, Prathima Institute of Medical Sciences, Nagunur, and Karimnagar. In this study 90 subjects suffering from Seasonal Allergic Rhinitis were included. At the first visit, after clinical evaluation and laboratory investigations (DC Eosinophil, Absolute Eosinophil Count, IgE levels), Olopatadine group**:** n=45 patients were in this group received Olapatadine 10 mg once daily for 2 weeks. Levocetirizine group: n=45 patients were in this group received Levocetirizine 10 mg once daily for 2 weeks. After 2 weeks, all laboratory investigations were repeated and clinical improvement was assessed in terms of change in TNSS scoring and laboratory parameters. TNSS was considered as primary outcome measure. Among 90 patients, 48 patients (53.33%) were female and 42 patients (46.66%) were male. There was a mean decrease of 294.77 in Absolute Eosinophil Count (AEC) in Olopatadine group in comparison to 176.56 in Levocetirizine group. Serum IgE levels (UI/ml) were measured before and after 2 weeks and the results in Olopatadine group there was a mean reduction of 92.04 (UI/ml) in IgE in comparison to 43.28 (UI/ml) in Levocetirizine group. The individual changes in both the groups were statistically significant (<0.001). Total Nasal Symptom Score [TNSS] was assessed. There was a mean decrease of 3.39 in TNSS in Olopatadine group whereas it was 2.92 in Levocetirizine group. Levocetirizine and Olopatadine have been found effective in symptomatic treatment of allergic rhinitis. However Olopatadine was found to have edge over levocetirizine because Olopatadine additionally suppresses LTs and TXA_2 release and PAF formation by reducing arachidonic acid release from membrane phospholipids, probably through interference with phospholipase A_2 (PLA_2). Both drugs have similar adverse effect profiles.
Keywords: Olopatadine, Levocetirizine, Allergic Rhinitis

INTRODUCTION

Allergic Rhinitis AR, an inflammatory condition of the nasal mucosa mediated by an IgE-associated response to indoor and outdoor environmental allergens, has traditionally been classified as being seasonal or perennial, depending on whether an individual is sensitized to cyclic pollens or year round allergens [1, 2]. Seasonal Allergic Rhinitis (SAR), Symptoms appear in or around a particular season when the pollens of particular plant, to which the patient is sensitive, are present in the air. Perennial Allergic Rhinitis (PAR) Symptoms present throughout the year [3]. Inhalant allergens are often to cause of allergic rhinitis. Pollen from trees and grasses, mould spores, house dust, debris from insects or house mite are common offenders. Food allergy is rarely an important cause. Genetic predisposition plays an important part. Chances of children developing allergy are 20% & 47% respectively if one or both parents suffer from allergic diathesis [4]. Inhaled allergen produces specific Ig-E class antibody in the genetically predisposed individuals. This antibody fixed to the Basophils or tissue mast cells by Fc end on subsequent exposure antigen combines with Ig-E antibody at its FAb end. This reaction produces degranulation of mast cells with release of several chemical mediators including histamine, leukotriene, prostaglandins some of which already exists in preformed state while others

synthesized as fresh. These mediators are responsible for symptomatology of allergic disease depended on the tissues involved there may be vasodilatation, mucosal edema, infiltration with eosinophils, excessive secretion from nasal glands or smooth muscle contraction [5, 6]. AR has been reported to affect approximately 17% of the general population in the United States, and in selected pediatric populations might be present in up to 42% [7]. Less information is available on the demographics of non allergic rhinitis in the general population. However, in an attempt to define the prevalence of various forms of rhinitis, the National Rhinitis Classification Task Force retrospectively analyzed 975 patients with rhinitis from a variety of allergy practices. They determined that in the surveyed cohort, 43% of patients had ‘‘pure’’ AR, 23% had ‘‘pure’’ non-allergic rhinitis, and 34% had mixed rhinitis. Thus 57% of the patients with rhinitis had non-allergic rhinitis either alone or of mixed form [1, 5, 8, 9]. Diagnosis is by typical history and typical symptoms, Rhinoscopy in acute cases shows maximal redness and swelling of nasal mucosa, obstruction of nasal cavity, profuse nasal discharge mucosa appears pale. Antihistamines substantially reduce symptoms of nasal itching and watery eyes and have moderate but clinically and statistically significant effects in reducing rhinorrhoea and sneezing. However these agents have minimal effects on the symptoms of nasal congestion [10]. Rarely patients with severe symptoms who do not have a response to or are intolerant of other medications, may be treated with either oral or injected systemic corticosteroids [11]. With this background we in the present study tried to evaluate the efficacy and safety of Olopatadine and Levocetirizine in seasonal allergic rhinitis.

MATERIALS AND METHODS

The present study is a randomized, open labeled (non-blinded), comparative clinical study between Levociterizine and Olopatadine in patients with seasonal allergic rhinitis conducted in a single centre. The study was conducted on 90 patients of seasonal allergic rhinitis attending the department of ENT, Prathima Institute of Medical Sciences, Nagunur, and Karimnagar. Procedures followed in this study are in accordance with the ethical standard laid down by ICMR’s Ethical guidelines for biomedical research on human subjects (2006). At the first visit, after clinical evaluation and laboratory investigations (DC eosinophil, Absolute Eosinophil Count, IgE level), in one group (Levocetirizine group) Levocetirizine at a dose of 10mg once daily and in another group (Olopatadine group) Olopatadine was prescribed at a dose of 10 mg once daily for a period of 2 weeks.

Inclusion criteria: Patients irrespective of sex, aged 18-65 years suffering from Seasonal Allergic Rhinitis with a history of SAR (requiring treatment) of 6 months or longer, and to have documented positive allergy skin test during the previous year.

Exclusion criteria: Use of concomitant medication(s) that could affect the assessment of efficacy of study treatment. Patients those who used antibiotics for acute conditions within 14 days of the first visit, or were treated with systemic corticosteroids within 2 months of study initiation, or were treated with topical corticosteroids in concentrations in excess of 1% hydrocortisone for dermatologic conditions within 1 month of study initiation and Pregnant and lactating women. After 2 weeks, all laboratory investigations were repeated and clinical improvement was assessed in terms of change in TNSS, scoring and laboratory parameters. TNSS was considered as primary outcome measure. In 2 weeks follow-up, 6 patients were lost in Levocetirizine group and in Olopatadine group 4 patients were lost. So finally, Total 80 patients (39 patients in Levocetirizine group and 41 patients in Olopatadine group) completed this study. Lab investigations done were, Total Leucocyte Count, Differential count, Absolute Eosinophil Count, Serum IgE level, Total Nasal Symptom Score (TNSS). Symptom severity was determined by the TNSS, which consisted of runny nose, sneezing, nasal itching, and nasal congestion scored on a severity scale from 0 to 3 (0 = none, 1 = mild, 2 = moderate, and 3 = severe), such that the maximum possible TNSS is 12.

RESULTS

The present study is a randomized (systematic), open, single centered, comparative clinical study between olopatadine and Levocetirizine in Seasonal Allergic Rhinitis. The baseline demographic data and clinical characteristics of all 90 patients of follow up study have been compared in the Table 1 and p values suggest that there is no statistically significant difference in between the study groups in the parameters studied in the first visit. This proves the homogeneity of our study subjects in two groups.

Table 1: Baseline demographic data and clinical characteristics

Characteristics	Olopatadine Group	Levocetirizine group	p value
Number of patients recruited	45	45	
Number of patients at follow-up	41	39	
Female sex (%)	23	25	
Male sex (%)	22	20	
Age (years)	30.51	31.17	
Duration of suffering (months)	16.71	15.53	
Total Leucocyte Count (TLC)	9488.04 ± 1453	9432 ± 1110.82	0.87
DC Neutrophil (%)	65.15 ± 5.1	64.12 ± 4.02	0.42
DC Eosinophil (%)	7.31 ± 1.56	7.64 ± 1.52	0.44

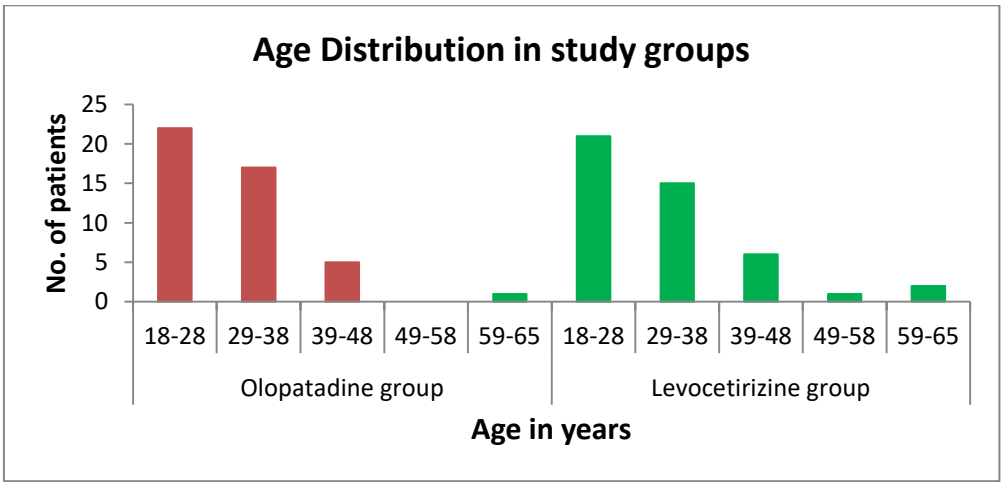

Fig 1: Age distribution of the patients

Among 90 patients, 48 patients (53.33%) were female and 42 patients (46.66%) were male. The male to female ratio was 1:1.1. The sex distribution of the study subjects has been given in the presented in the bar diagram. Total Leucocyte Count was done both at first and second visit in both study groups. The results in the Table 2 reveal that there was mean decrease of 431 in TLC in Olopatadine group in comparison to 428 in Levocetirizine group. The mean difference in two groups was compared by unpaired t-test, the change was not found to be statistically significant (0.84).

Table 2: Change in Total Leucocyte Count in study group

Variable	**Olopatadine group**			**Levocetirizine group**			
	1st Visit	**2nd Visit**	**p value**	**1st Visit**	**2nd Visit**	**Δ_L**	**p value**
Total Leucocyte count	9385 ± 1508	8954 ± 1141	<0.001*	9432 ± 1111	9004 ± 1508	428	0.005*

Data are in Mean ± SD, Δ Mean Difference, *statistically significant

The results in the Table 3 show that there was a mean decrease of 294.77 in Absolute Eosinophil Count (AEC) in Olopatadine group in comparison to 176.56 in Levocetirizine group. The change seen within Levocetirizine and Olopatadine groups was statistically significant (<0.001) and when the mean difference in two groups was compared by unpaired t-test, the change in Olopatadine group was found to be statistically significant (p=0.03).

Table 3: Change in Absolute Eosinophil Count in study groups

Variable	Olopatadine group			Levocetirizine group		
	1st Visit	2nd Visit	p value	1st Visit	2nd Visit	p value
DC Eosinophil	724 ± 203	430 ± 127	<0.001*	693 ± 186	517 ± 164	<0.001*

Data are in Mean ± SD *statistically significant.

Serum IgE levels (UI/ml) were measured at both visits and the results have been shown in the table 4. In Olopatadine group there was a mean reduction of 92.04 in IgE in comparison to 43.28 in Levocetirizine group. The individual changes in both the groups were statistically significant (<0.001). The comparative analysis of the mean difference in individual group also revealed to be statistically significant (p=0.004).

Table 4: Change in Serum IgE (UI/ml) Level in study groups

Variable	Olopatadine group			Levocetirizine group		
	1st Visit	2nd Visit	p value	1st Visit	2nd Visit	p value
Serum IgE	383 ± 63.24	290.77 ± 52.88	<0.001*	384.52 ± 71.23	341.24 ± 65.12	<0.001*

Total Nasal Symptom Score [TNSS] was assessed at both the visits. The results shown in table 5 reveal that there was a mean decrease of 3.39 in TNSS in Olopatadine group whereas it was 2.92 in Levocetirizine group and these changes in individual groups were statistically significant (p=<0.001). The comparison of the mean difference was also found to be statistically significant

Table 5: Change in Total Nasal Symptom Score [TNSS] in study groups

Variable	Olopatadine group			Levocetirizine group		
	1st Visit	2nd Visit	p value	1st Visit	2nd Visit	p value
Total Symptom Score	7.77 ± 1.09	4.38 ± 1.02	<0.001*	7.60 ± 1.68	5.12 ± 0.88	<0.001*

Assessment of safety was done in both the drugs were well tolerated without any new/ unpredictable / alarming side effects. In Olopatadine group, out of 5 patients who experienced adverse effects, 1 of them complained of drowsiness, 1 had headache, 2 had gastric irritation, and 1 patient had dryness of mouth. In Levocetirizine group out of 6 patients who experienced adverse effects, 2 of them complained of drowsiness, 2 had headache, 1 had gastric irritation, and 1 patient had dryness of mouth. The overall incidence of adverse effects was 20 % and 23.07 % in Olopatadine and Levocetirizine group respectively. By performing Fischer's exact test the p values obtained for drowsiness (p=0.5), headache (p=0.5), gastric irritation (p=0.5), and dryness of mouth (p=0.75) respectively were not found to be statistically significant.

DISCUSSION

Treating the symptoms of Seasonal Allergic Rhinitis and ensuring a decent quality of life to the patients is challenging to the physicians, an increasing understanding of the pathomechanisms in the last few decades as well as development of newer generations anti-histaminics in the treatment of Allergic Rhinitis. World Health Organization suggests that the treatment of allergic rhinitis make use of a combination of patient education, allergen avoidance, pharmacotherapy, and immunotherapy [12]. Histamine is the key mediator in allergic response; it causes muscle constriction, mucus secretion, increase vascular permeability and sensory nerve stimulation resulting in allergic rhinitis [13]. Levocetirizine is a Second generation antihistamine has more complex chemical structures that decrease their movement across blood-brain barrier reducing central nervous system adverse effects such as sedation [14]. Olopatadine hydrochloride a tricyclic compound is an orally-active Antiallergic / antihistaminic drug. In the

present study we prescribed oral levocetirizine and olopatadine at the dose of 10 mg once daily for 14 days. The pre and post treatment data regarding the Absolute Eosinophil count decreased from the pre treatment levels to post treatment levels in both groups. However the Decrease in Absolute Eosinophil count was more in olopatadine group as compared to levocetirizine group. The serum IgE levels also showed more decrease in olopatadine group than levocetirizine group. In one study by Dakhale G et al; comparing the efficacy safety of Olopadatine and Rupatidine in allergic rhinitis found that after weeks of treatment with both the drugs there were higher reductions in Absolute Eosinophil counts in olopatadine group as compared to rupatidine group [15]. This is in agreement with results of present study. Olopatadine is known as dual blocker since it blocks the actions of not only histamine but also of the other inflammatory mediators such as PAF, LTs and chemokines. The superiority of olopatadine over Levocetirizine may be attributed to facts that olopatadine can reduce the amount of cell associated PAF by 52.8% [16]. PAF is known to increase vascular permeability and an important mediator of inflammation. It suppresses LTS and TXA2 release and PAF formation by reducing arachidonic acid release from membrane phospholipids by interfering with phospholipase A2 [17]. In the present study we used TNSS score to assess the efficacy of treatment. TNSS is widely accepted as a toll to assess the efficacy of drug in the treatment of Allergic Rhinitis. We found in this study that the mean TNSS score pre-treatment in olopatadine group was 7.77 which decreased to 4.38 at the end of two weeks of therapy whereas the levocetirizine group had mean TNSS score 7.60 and decreased to 5.12 after two weeks of therapy. A decrease in the TNSS score suggests that there is an overall clinical improvement in the condition. We observed that the TNSS decrease was significant showing that the olopatadine group had better clinical outcomes. Similar observations were also noted by Dakhale G *et al.;* while comparing olopatadine and rupatidine in allergic rhinitis [15]. In the context of safety profile, both the drugs were well tolerated. Only 6 patients (15.38%) in Levocetirizine group and 5 patients (12.19%) in Olopatadine group complained of adverse effects. All the adverse effect complained were expected and no new/alarming side effects were recorded. Discontinuation of the drug or dose modulation was not required for those reported side effects in either group. By analyzing and comparing the side effect profile of both the drugs, it can be concluded that both drugs are equally safe.

CONCLUSION

Levocetirizine and Olopatadine have been found effective in symptomatic treatment of allergic rhinitis. However Olopatadine was found to have edge over levocetirizine because Olopatadine additionally suppresses LTs and TXA_2 release and PAF formation by reducing arachidonic acid release from membrane phospholipids, probably through interference with phospholipase A_2 (PLA_2). Both drugs have similar adverse effect profiles.

Conflict of interest: None

Source of support: Nil

Ethical Permission: Obtained

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