

Comparative Study to Assess Clinical Efficacy of Leukotriene Receptor Antagonists and Antihistamines in the Treatment of Allergic Rhinitis

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ABSTRACT

Introduction

Pharmacologic treatment options for allergic rhinitis include intranasal corticosteroids, oral and topical antihistamines, decongestants, intranasal cromolyn, intranasal anticholinergics and leukotriene receptor antagonists. The present study was undertaken to compare the efficacy of leukotriene receptor antagonist and antihistamines in relieving nasal congestion/obstruction symptom and itching/irritation in eyes.

Material and Methods

The study was conducted among 125 patients clinically diagnosed to be suffering from allergic rhinitis. Patients were divided into 5 groups and were given oral treatment with oral antihistamines (chlorpheniramine maleate, levocetirizine, fexofenadine, desloratadine) and leukotriene receptor antagonist (montelukast) for a period of 6 weeks. The results were tabulated and analyzed by Chi-square and Kruskal-Wallis test with p value <0.05 as significant value.

Result

For relieving nasal obstruction, levocetirizine group showed maximum improvement at 2 weeks. However, at the end of 6 weeks montelukast group showed maximum relief followed by levocetirizine and desloratadine. In relieving eye itching/irritation, montelukast and levocetirizine were equally effective. Fexofenadine and desloratadine were less effective in relieving nasal obstruction and eye itching/irritation followed by chlorpheniramine maleate, which was least effective.

Conclusion

Allergic rhinitis affects the social and professional life of patient. Allergen avoidance should be the initial step in the management of allergic rhinitis. Montelukast and levocetirizine are more effective in relieving nasal obstruction and eye itching/irritation compared to fexofenadine, desloratadine and chlorpheniramine maleate.

Keywords

Rhinitis, Allergic, Seasonal; Histamine Antagonists; Leukotriene Antagonists.

Allergic rhinitis is clinically defined as a symptomatic disorder of the nose induced, after allergen exposure, by an IgE-mediated inflammation of the membranes lining the nose. It represents a global health problem affecting at least 10% to 40% of the population. Although it is not usually a severe disease, it alters the social life of patients and affects school performance and work productivity.¹ Histamine appears to be a major mediator released by mast cells in seasonal and perennial allergen exposure, but other mediators such as leukotrienes, prostaglandins and kinins may also contribute to the symptomatology through their interaction with neural and vascular

receptors.² Pharmacologic treatment options include intranasal corticosteroids, oral and topical antihistamines, decongestants, intranasal cromolyn (Nasal crom), intranasal anticholinergics and leukotriene receptor antagonists.³ The present study was undertaken to

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compare the efficacy of leukotriene receptor antagonist and antihistamines in relieving nasal congestion/obstruction symptom and itching/irritation in eyes.

Material and methods

The present prospective study was conducted among 125 patients attending the ENT outpatient Department. Patients clinically diagnosed suffering from allergic rhinitis of either sex with age range 10-60 years were randomly selected for the study. Patients with nasal congestion/obstruction and itching/irritation in eyes were selected for the study.

Informed consent was taken from the patients and ethical approval was obtained from the institute. This was an open study where the patient, the observer and the supervisor and co-supervisor were having a clear knowledge of the drugs used.

It was chosen as it avoided any psychological trauma to the patient as to what therapeutic trial is made on his/her by using the drug. Patients with previous treatment with leukotriene receptor antagonist and antihistamines over a period of one month were excluded from the study.

DAY TIME	RESULTS			
	0	1	2	3
Nasal Congestion/Obstruction	No	Mild	Moderate	Severe
Itching/Irritation in Eyes	No	Mild	Moderate	Severe

Patients were divided into 5 groups with 25 patients in each group and were given oral treatment with oral antihistamines (Chlorpheniramine maleate, Levocetirizine, Fexofenadine, Desloratadine) and leukotriene receptor antagonist (Montelukast) for a period of 6 weeks. The different 5 groups were compared

for symptoms of nasal congestion/ obstruction and itching/irritation in eyes recorded on day 1, 2 weeks, 4 weeks and 6 weeks of treatment and analysed. The result were interpreted on the basis of symptoms relieved.

The subjective assessment for the degree of relief of symptoms were done according to total symptom score (TSS) from 0 to 3 as given below. Each patient was followed up after 2 week and then, after 4 and 6 weeks.

The results were tabulated and analyzed by Chi-square and Kruskal-Wallis test with p value <0.05 as significant value.

Results

The number of patients residing in rural area (63.2%) was higher than in urban area (36.8%) (Table I).

Table II shows that in maximum number of patients, dust was the single most important predisposing factor (36%) followed by seasonal change (32.8%). However in 12% patients, no predisposing factor could be identified. The predisposing factors were identified from detailed history.

Table III shows that at 2nd week follow up Levocetirizine in Group 2 was significantly effective with 20% patients having zero (0) symptom score in nasal congestion/obstruction symptom and with mean rank 35.92 as compared to other drugs.

At 4th week, follow up montelukast in group 1 and Levocetirizine was more effective with 40% patients having zero symptom score in nasal congestion/obstruction symptom score and having mean rank 43.80 and 47.48 as compared to other drugs. At 6th week follow up montelukast in group 1 was significantly effective with 64% patients having zero symptom score in nasal congestion/obstruction symptom and having mean rank 42.62

Table IV shows that at 2nd & 4th week follow up Levocetirizine in Group 2 was significantly effective with 40% patients and 56% patients having zero (0) symptom score in itching /irritation in eyes symptom and with mean rank 46.08 and 51.40 as compared to other drugs. At 6th week follow up montelukast in group 1 and Levocetirizine in Group 2 were more effective with 56% patients having zero (0) symptom score in

Table I: Comparison of patients according to residential area

	GROUP					TOTAL
	1 Montelukast	2 Levocetirizine	3 Fexofenadine	4 Desloratadine	5 CPM	
RURAL	13 (52%)	16 (64%)	18 (72%)	15 (60%)	17 (68%)	79 (63.2%)
URBAN	12 (48%)	9 (36%)	7 (28%)	10 (40%)	8 (32%)	46 (36.8%)

SEM = Standard Error of Mean

itching / irritation in eyes symptom in group 1 and 2 with mean rank 58.62 in both groups as compared to other drugs.

Discussion

Allergic rhinitis is one of the diseases that affect health-related quality of life. Health-related quality of life is defined as the patient's perception of the effects of a specific disease or the use of a certain treatment on different aspects of his/her life, particularly the consequences for the patient's physical, emotional, and social well-being.⁴ The rapid increase in air pollution and climate change are reasonable explanations as risk factors for the marked increases in the occurrence and exacerbation of allergic rhinitis.⁵

Present study shows a slightly higher incidence of allergic rhinitis in rural areas (63.2%). It may be because people in rural areas are more exposed to house dust because of katcha houses and field dust as well as increased pollen exposure in fields.

Animal dander (Buffalo, cats, dogs and sheep) is also important in disease causation. Similar findings were

reported by Mygind N⁶ and Krouse GH⁷ who reported increased incidence of allergic rhinitis in rural area mainly due to pollens, grasses, house dust and animal danders.

In present series 36% percent of patients were allergic to house dust while 32.8% percent patients got their illness aggravated on exposure to various seasonal changes and some patients could identify other factors like smoke fumes, perfume, flowers, and cosmetics as the aggravating factors. 12% patients found no predisposing factor for causation of allergic symptoms.

Mygind N,⁷ Pawankar R⁸ identified house dust and house dust mite to be the most important allergen causing allergic rhinitis. Jones NS⁹ implicated house dust, animal emanations, perfumes and cosmetics to be important as the causative factors leading to allergic rhinitis symptoms.

In the present study, regarding nasal obstruction, levocetirizine was significantly better at 2 weeks with mean rank 35.92, followed by montelukast with mean rank 57.90, desloratidine with mean rank 65.84 is better than fexofenadine with mean rank 77.04. Chlorpheniramine maleate with mean rank 78.30 was least effective.

Table II : Statistical Analysis

		GROUP					TOTAL
		1 Montelukast	2 Levocetirizine	3 Fexofenadine	4 Desloratadine	5 CPM	
PREDISPOSING FACTORS	Cosmetics	0	1 (4%)	1 (4%)	1 (4%)	1 (4%)	4 (3.2%)
	Dust	7 (28%)	12 (48%)	5 (20%)	9 (36%)	12 (48%)	45 (36%)
	Flowers	1 (4%)	0	1 (4%)	1 (4%)	1 (4%)	4 (3.2%)
	No history	4 (16%)	2 (8%)	5 (20%)	3 (12%)	1 (4%)	15 (12%)
	Perfumes	1 (4%)	0	2 (8%)	0	0	3 (2.4%)
	Seasonal Change	8 (32%)	7 (28%)	9 (36%)	8 (32%)	9 (36%)	41 (32.8%)
	Smoke	4 (16%)	2 (8%)	1 (4%)	2 (8%)	1 (4%)	10 (8%)
	Wheat flour	0	1 (4%)	1 (4%)	1 (4%)	0	3 (2.4%)

At the end of 4th weeks levocetirizine with mean rank of 43.80 was better than montelukast with mean rank 47.48 while fexofenadine, desloratidine and chlorpheniramine maleate were very less effective in relieving nasal obstruction with mean rank of 64.44, 68.20 and 84.90 respectively.

At 6 weeks, montelukast (mean rank 42.62) was slightly better than levocetirizine (mean rank 46.98). Desloratidine (mean rank 68.32) though less effective in relieving nasal obstruction but it was better than fexofenadine (mean rank 74.20) and chlorpheniramine maleate (mean rank 75.14). Fexofenadine and chlorpheniramine maleate were very less effective in relieving nasal obstruction.

George P et al¹⁰ found that during the 4 weeks treatment with montelukast, patients showed improvement compared with patients treated with placebo for the primary end point day night symptom score and for individual nasal symptoms of rhinorrhoea, sneezing and nasal congestion. During the entire 6 weeks of treatment, treatment with montelukast showed a statistically significant improvement over treatment with placebo in rhinorrhoea, nasal congestion and sneezing, but no difference in itching.

In the present study, regarding relieving of itching/irritation in eyes, at 2 weeks levocetirizine in group 2 was significantly effective with mean rank 46.08 followed by montelukast and desloratidine with same

Table III : Comparison of Nasal congestion/Obstruction symptom score from day 1 presentation to 6 weeks follow-up

	SYMPTOM SCORE	GROUP					TOTAL
		Montelukast	Levocetirizine	Fexofenadine	Desloratadine	CPM	
OBSTRUCTION AT DAY 1 PRESENTATION	1	3(12%)	2(8%)	3(12%)	3(12%)	3(12%)	14(11.2%)
	2	12(48%)	11(44%)	12(48%)	12(48%)	12(48%)	59(47.2%)
	3	10(40%)	12(48%)	10(40%)	10(40%)	10(40%)	52(41.6%)
	Total	25	25	25	25	25	125
	Mean Rank	61.82	67.72	61.82	61.82	61.82	
	Sig. #	Chi Square 0.646; p value 0.958; Non Significant					
OBSTRUCTION AT 2 WEEKS FOLLOW-UP	0	0(0%)	5(20%)	1(4%)	1(4%)	0(0%)	7(5.6%)
	1	15(60%)	17(68%)	6(24%)	11(44%)	7(28%)	56 (44.8%)
	2	10(40%)	3(12%)	16(64%)	11(44%)	16(64%)	56 (44.8%)
	3	0(0%)	0(0%)	2(8%)	2(8%)	2(8%)	6(4.8%)
	Total	25	25	25	25	25	125
	Mean Rank	57.9	35.92	77.04	65.84	78.3	
	Sig. #	Chi Square 25.722; p value 0.000; Significant					
OBSTRUCTION AT 4 WEEKS FOLLOW-UP	0	10(40%)	10(40%)	4(16%)	5(20%)	0(0%)	29(24%)
	1	13(52%)	15(60%)	14(56%)	14(56%)	11(52.4%)	67(55.4%)
	2	2(8%)	0(0%)	7(28%)	6(24%)	10(47.6%)	25(20.7%)
	Total	25	25	25	25	21	121
	Mean Rank	47.48	43.8	68.2	64.44	84.9	
	Sig. #	Chi Square 25.722; p value 0.000; Significant					
OBSTRUCTION AT 6 WEEKS FOLLOW-UP	0	16(64%)	14(56%)	5(20%)	7(28%)	3(14.3%)	45(37.2%)
	1	9(36%)	11(44%)	15(60%)	14(56%)	15(71.4%)	64(52.9%)
	2	0(0%)	0(0%)	5(20%)	4(16%)	3(14.3%)	12(9.9%)
	Total	25	25	25	25	21	121
	Mean Rank	42.62	46.98	74.2	68.32	75.14	
	Sig. #	Chi Square 23.640; p value 0.000; Significant					

Table IV : Comparison of Itching /Irritation in eyes symptom score from day 1 presentation to 6 weeks follow-up

	SYMPTOM SCORE	GROUP					TOTAL
		Montelucast	Levocetirizine	Fexofenadine	Desloratadine	CPM	
ITCHING IN EYES AT DAY 1 PRESENTATION	0	1(4%)	1(4%)	1(4%)	1(4%)	1(4%)	5(4%)
	1	5(20%)	5(20%)	5(20%)	5(20%)	5(20%)	25(20%)
	2	16(64%)	16(64%)	16(64%)	16(64%)	16(64%)	80(64%)
	3	3(12%)	3(12%)	3(12%)	3(12%)	3(12%)	15(12%)
	Total	25	25	25	25	25	125
	Mean Rank	63	63	63	63	63	
	Sig. #	Chi Square 0.000; p value 1.000 Non Significant					
ITCHING AT 2 WEEKS FOLLOW-UP	0	5(20%)	10(40%)	4(16%)	4(16%)	3(12%)	26(20.8%)
	1	15(60%)	14(56%)	16(64%)	17(68%)	14(56%)	76 (60.8%)
	2	5(20%)	1(4%)	5(20%)	4(16%)	8(32%)	23 (18.4%)
	Total	25	25	25	25	25	125
	Mean Rank	64.2	46.08	66.24	64.26	74.22	
	Sig. #	Chi Square 10.668; p value 0.031; Significant					
ITCHING AT 4 WEEKS FOLLOW-UP	0	10(40%)	14(56%)	10(40%)	10(40%)	5(23.8%)	49(40.5%)
	1	15(60%)	11(44%)	15(60%)	15(60%)	15(71.4%)	71(58.7%)
	2	0(0%)	0(0%)	0(0%)	0(0%)	1(4.8%)	1(.8%)
	Total	25	25	25	25	21	121
	Mean Rank	61	51.4	61	61	72.43	
	Sig. #	Chi Square 5.608; p value 0.230; Non Significant					
ITCHING AT 6 WEEKS FOLLOW-UP	0	14(56%)	14(56%)	13(52%)	13(52%)	9(42.9%)	63(52.1%)
	1	11(44%)	11(44%)	12(48%)	12(48%)	12(57.1%)	58(47.9%)
	Total	25	25	25	25	21	121
	Mean Rank	58.62	58.62	61.04	61.04	66.57	
	Sig. #	Chi Square 1.015; p value 0.907; Non Significant					

mean rank 64.20, fexofenadine with mean rank 66.24 and chlorpheniramine maleate with mean rank 74.22.

In relieving eye itching/irritation at 4 weeks levocetirizine in group 2 was effective with mean rank 51.40 followed by montelukast, fexofenadine and desloratidine which were equally effective in relieving itching/irritation with same mean rank 61.00 which was least effective among the compared groups.

At 6 weeks, montelukast and levocetirizine were equally effective with mean rank of 58.62 in relieving itching/irritation in eyes followed by desloratidine and fexofenadine with same mean rank 61.04 and chlorpheniramine maleate with mean rank 66.57. Singh Franco D et al¹¹ found that in patients with moderate to severe perennial allergic rhinitis, levocetirizine 5 mg/d was associated with improvements in scores for rhinorrhoea, nasal and ocular pruritus, and sneezing at 4 to 6 weeks compared with placebo.

Nasal congestion scores improved within 1 week, an effect that was maintained over 4 to 6 weeks. Ralph M et al¹² revealed that effectiveness of modern antihistamines for treatment of allergic rhinitis (levocetirizine) improved the symptom score after 24 hours compared to Fexofenadine and Desloratidine, thus reported that levocetirizine is highly effective in reducing the total symptom score.

Allergen avoidance should be the initial step in the management of AR. Oral antihistamines are the first-line therapy for mild to moderate intermittent and mild persistent rhinitis and montelukast is as effective as antihistamines.¹³

Conclusion

Allergic rhinitis affects the social and professional life of patient. For relieving nasal obstruction, levocetirizine group showed maximum improvement at 2 weeks. However, at the end of 6 weeks montelukast group showed maximum relief followed by levocetirizine and desloratidine.

In relieving eye itching/irritation, montelukast and levocetirizine were equally effective. Fexofenadine and desloratidine were less effective in relieving nasal

obstruction and eye itching/irritation followed by chlorpheniramine maleate which was least effective.

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