ANTIHISTAMINES

Quality of life studies to assess the efficacy and safety in allergic rhinitis in Punjab, India

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ABSTRACT: Objectives: Allergic rhinitis impairs social life, but it is not known whether quality of life may be improved when patient are treated with H 1 blockers. The present study evaluated the comparative efficacy and safety of cetirizine, loratidine and astemizole in patients of allergic rhinitis. **Material &Methods:** The design was open, randomized, parallel group comparison of three active treatment groups over a six week period. Sixty patients of either sex in the age group of 16 – 45 years, suffering from allergic rhinitis were selected randomly. The effect of cetirizine, loratidine and astemizole were observed on various parameters i.e., sneezing, nasal obstruction, watering of eyes, sedation and overall well being of the patients over a period of six weeks. The Visual Analogue Scale (VAS) was utilized as a quantitative measure of symptom relief. **Results:** An improvement in patient's discomfort as assessed by VAS was observed in all treatment groups, with cetirizine 10mg daily being significantly more effective than loratidine 10mg and astemizole 10mg. Cetirizine resulted in a significant reduction in sneezing and nasal obstruction as compared to loratidine and astemizole ($p<0.05$). Cetirizine and loratidine both were equally efficacious in relieving watering of eyes but cetirizine as well as loratidine were more efficacious as compared to astemizole ($p<0.05$). Sedation was found to be maximum with cetirizine followed by astemizole and loratidine over six weeks of study period. **Conclusion:** Cetirizine has been found to be most effective in relieving the symptoms of allergic rhinitis followed by loratidine and astemizole and it can also improve quality of life for patients with allergic rhinitis.

KEY WORDS: Allergic rhinitis, cetirizine, loratidine, astemizole.

INTRODUCTION

Patients with allergic rhinitis are bothered both by the nasal symptoms themselves and by associated symptoms such as headache and fatigue. The combination can produce quite severe impairment of day to day physical, emotional, occupational and social functioning and can cause emotional distress. This breadth of impairment of health-related quality of life in patients with rhinitis is often not recognized and is sometimes trivialized by some health care professionals. One of the aims of treating patients with rhinitis must be to ensure that all individual patient problems are recognized and treated appropriately. Treating with sedating antihistaminics can also compound the problem by hampering performance and cognition. Treatment of allergic rhinitis includes avoiding allergens, short-term decongestants, oral and/or topical H1 receptor antagonists, intranasal cromoglycate, intranasal corticosteroids, and allergen immunotherapy.

Histamine (H1) – receptor antagonists have been an established treatment for allergic disorders for many decades[1,2]. These agents are said to be better at treatment and are best suited for prophylaxis and long term therapy of allergic rhinitis. They are also less expensive than the newer treatment modalities.

The usefulness of the first generation antihistaminics was limited by the side effects like sedation and anticholinergic activity. Cetirizine, is a potent H1 histaminic receptor antagonist and has been shown in the double blind clinical trials to be effective in the treatment of seasonal allergic rhinitis[3,4]. Loratidine, another antihistaminic is effective in the treatment of allergic rhinitis[5]. Astemizole may be more appropriately used for a condition that requires a daily dose for a long period. One study suggests that astemizole may be more effective than loratidine in controlling the symptoms of allergic rhinitis[6].

The usual outcomes measured in clinical trials of allergic rhinitis have been symptoms, nasal patency and cytology. Each is important to the clinician in determining the clinical efficacy of the medication. It is now recognized that the treatment must also enable the patients both to feel better and to function better in their day to day lives. The aim of the present study was to compare the efficacy and safety of various antihistamines; cetirizine, loratidine and astemizole in the treatment of allergic rhinitis and also on the quality of life scores.

MATERIAL AND METHODS

Subjects

A total number of 60 patients of either sex in the age group of 16 – 45 years, suffering from allergic rhinitis were selected at random from those attending the outpatient department of ENT at tertiary care hospital, Amritsar. Patients of bronchial asthma, skin allergy, glaucoma, prostatic hyperplasia, atrophic rhinitis, steroid dependence and infections of the upper respiratory tract were excluded from the study. Women of childbearing potential were also excluded. Patients unable to understand the questionnaire were also excluded. The study protocol was approved by the ethical committee of the institution. Written informed consent was sought from all the patients before commencing the study.

Study design:

The study was open, randomized comparison between three parallel active treatment groups over a six week period. After meeting the initial entry criteria, potential subjects were included in the study only if they recorded the presence of at least two of the following symptoms; stuffy nose, runny nose, itchy nose and sneezing.

After this subjects were randomized to receive cetirizine, loratidine or astemizole. They were allocated to 3 groups of twenty patients each on the basis of antihistamines given.

Group I	Tab. Cetirizine 10mg orally OD.
Group II	Tab. Loratidine 10mg orally OD.
Group III	Tab. Astemizole 10mg orally OD.

The parameter evaluated in the present study were sneezing, nasal obstruction,, watering of eyes and sedation. After baseline recording of clinical signs & symptoms, the patients were given a week's supply of either drug and given a set of cards with filling instructions, to be produced on their next visit. The dose of medication and the set of cards were replenished on their weekly visits. On the cards patients were asked to record the severity of daily symptoms which included nasal symptoms, eye symptoms, practical problems and other symptoms.

The subjective assessment for the degree of relief of symptoms of the patient was done according to graded scale Visual analogue scale (VAS) marked 0 to10.

0 – being no relief from symptoms.
10 – Complete relief from symptoms.

The weekly score of common symptoms and overall well being of the patients with all the three drugs were recorded and tabulated over a period of six weeks on each weekly visit. Absolute eosinophil counts and nasal smear eosinophil counts from the nasal cytogram were carried out before the study and at weekly intervals for the rest of the study. The possible side effects like sedation, headache and dry mouth were also recorded.
The results were expressed as mean + SE and were analysed for statistically significant difference using one way ANOVA followed by Bonferroni's multiple comparison test with the level of significance set at 0.05.

RESULTS

Sixty patients were randomized and completed the study & were included in the analysis. Over the six weeks of treatment, all nasal symptoms of allergic rhinitis showed improvement in all the three groups as shown by mean VAS score (Tab 1,2,3,4 &5) There was statistical significant difference in the relief of symptoms of allergic rhinitis in all the three groups.

The relief in sneezing was found to be greater with cetirizine as compared to loratidine during 4th & 6th week ($p<0.05$) and as compared to astemizole throughtout the 6weeks ($p<0.05$), whereas with loratidine as compared to astemizole relief in sneezing was greater during 1st, 3rd & 6th weeks ($p<0.05$) (Table 6).

Table: 1 Effect of Cetirizine (Group I), Loratidine (Group II) & Astemizole (Group III) on sneezing over a period of 6 weeks.

Group	0 day	Ist week	2nd Week	3rd Week	4th Week	4th Week	5th Week
I	0	2.8±.26	4.55±.336.	6.05±.31	7.05±.21	7.4±.24	7.85±.21
I	0	2.65±.32	4.35±.29	5.15±.26	5.9±.29	6.45±.27	6.7±.32
II	0	1.45±.18	2.75±.19	3.9±.26	5.0±.18	5.4±.18	5.7±.23
One way ANOVA	F	6.73*	12.72*	14.0*	13.1*	17.7*	17.67*
	Df	2.57	2.57	2.57	2.57	2.57	2.57
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

* p<0.05 [F_{cal} is > F_{tab} i.e. 3.16 so difference is significant].
Values are expressed as mean + SE, n =20 in each group.

Table: 2 Effect of Cetirizine (Group I), Loratidine (Group II) & Astemizole (Group III) on Nasal obstruction over a period of 6 weeks.

Group	0 day	Ist week	2nd Week	3rd Week	4th Week	4th Week	5th Week
I	0	4.0±0.23	6.3±0.22	7.7±0.23	8.95±1.99	9.5±0.18	9.7±0.15
I	0	3.9±0.23	5.2±0.26	5.9±0.25	6.8±0.27	8.2±0.27	9.0±0.23
II	0	3.05±0.5	4.4±0.24	5.6±0.23	6.5±0.3	7.4±0.23	7.8±0.26
One way ANOVA	F	3.58*	17.0*	21.8*	25.7*	20.6*	18.0*
	Df	2.57	2.57	2.57	2.57	2.57	2.57
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

* p<0.05 [F_{cal} is > F_{tab} i.e. 3.16 so difference is significant].
Values are expressed as mean + SE, n =20 in each group.

Cetirizine resulted in greater reduction in nasal obstruction as compared to loratidine and astemizole (p<0.05). There was no statistical significant difference in patients of group I & II for watering of eyes over six weeks of study period whereas in patients of group I & III, and in group II & III significant difference was seen (Table 6).

In the present study, VAS was used as an instrument to demonstrate the sedative effects of cetirizine, loratidine and astemizole. Though the sedation was observed with all the three drugs but was found to be maximum with cetirizine followed by astemizole and loratidine.

Reduction in Absolute eosinophil counts was found with all the three drugs but maximum with cetirizine. Total number of eosinophils were also decreased in nasal smear with all the three drugs.

DISCUSSION

Allergic rhinitis is a common disorder seen in ENT practice. It occurs because of exposure of the individual to allergens which result in the release of a large number of vasoactive agents and secondary mediators. The disorder is characterized by mild to severe upper respiratory symptoms such as sneezing, rhinorrhoea,

Table: 3 Effect of Cetirizine (Group I), Loratidine (Group II) & Astemizole (Group III) on Watering of Eyes over a period of 6 weeks.

Group	0 day	Ist week	2nd Week	3rd Week	4th Week	4th Week	5th Week
I	0	3.0±0.33	5.1±0.31	6.4±0.21	7.25±0.24	8.35±0.25	9.2±0.24
I	0	2.7±0.39	4.6±0.31	5.6±0.31	6.6±0.33	7.8±0.32	8.6±0.34
II	0	2.3±0.4	3.7±0.27	4.6±0.34	5.65±.31	6.4±0.29	6.8±0.31
One way ANOVA	F	0.87	5.7*	8.77*	7.56*	11.97*	17.6*
	Df	2.57	2.57	2.57	2.57	2.57	2.57
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

* $p<0.05$ [F_{cal} is > F_{tab} i.e. 3.16 so difference is significant].
Values are expressed as mean + SE, n =20 in each group.

Table: 4 Effect of Cetirizine (Group I), Loratidine (Group II) & Astemizole (Group III) on Sedation over a period of 6 weeks.

Group	0 day	Ist week	2nd Week	3rd Week	4th Week	4th Week	5th Week
I	0	2.7±0.49	3.3±0.50	3.5±0.51	3.4±0.51	3.7±0.50	3.3±0.53
I	0	1.2±0.30	1.35±.25	1.9±0.28	1.8±0.26	1.85±.28	1.9±0.31
II	0	2.2±0.39	2.65±.41	2.8±o.34	2.7±0.38	2.6±0.38	2.8±0.44
One way ANOVA	F	3.60*	5.37*	4.5*	4.05*	5.41*	2.67
	Df	2.57	2.57	2.57	2.57	2.57	2.57
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

* $p<0.05$ [F_{cal} is > F_{tab} i.e. 3.16 so difference is significant].
Values are expressed as mean + SE, n =20 in each group.

Table: 5 Effect of Cetirizine (Group I), Loratidine (Group II), & Astemizole (Group III) on the overall well being of the patients over a period of 6 weeks.

Group	0 day	Ist week	2nd Week	3rd Week	4th Week	4th Week	5th Week
I	0	2.7±0.24	4.15±.15	4.9±0.17	6.4±0.21	6.9±0.16	7.3±0.13
I	0	3.35±.25	4.75±.17	6.15±.17	6.7±0/13	6.95±.09	7.4±0.13
II	0	1.15±.55	2.15±.24	2.75±.20	3.85±.21	4.35±.18	4.75±.16
One way ANOVA	F	38.7*	49.43*	86.5*	71.08*	72.66*	113.0
	Df	2.57	2.57	2.57	2.57	2.57	2.57
	p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

* $p<0.05$ [F_{cal} is > F_{tab} i.e. 3.16 so difference is significant]., Values are expressed as mean + SE, n =20 in each group.

obstruction of nasal passages, congestion of the conjunctiva, itching of nose & pharynx and watering of eyes. The patients' quality of life, work performance, physical and emotional well being are also affected to a large extent.

A large number of over the counter (OTC) drugs which consists of decongestants, antihistamines and antipyretics are available and are widely used without any medical supervision, for the symptomatic relief of allergic rhinitis. The H1 antihistamines are most commonly used for relieving the symptoms of allergic rhinitis. The first generation oral antihistaminics are safe but sedation and anticholinergic side effects may be troublesome. The second generation oral antihistamines do not have these side effects and are generally well tolerated. The presence of a large numbr of treatment modalities of allergic rhinitis indicates that no satisfactory treatment is as yet available.

The present study involved the comparison of the efficacy of three antihistaminics: cetirizine, loratidine and astemizole in allergic rhinitis. The common symptoms evaluated weekly over a period of six weeks were sneezing, nasal obstruction, watering of eyes, sedation and overall well being of the patients. The visual analogue scale (VAS) was utilized as a quantitative measure of symptom relief[7].

In the present study, the administration of cetirizine, loratidine and atemizole resulted in statistically significant reduction in the symptoms of allergic rhinitis. Cetirizine provided greater relief in sneezing followed by loratidine and astemizole. (Table Fig p) During the Ist and IInd week of study period, cetirizine & loratidine were found to be equally effective ($p<0.05$) whereas during the remaining four weeks, cetirizine was found to be more efficacious in relieving sneezing as compared to loratidine ($p<0.05$). These findings are in accordance with the observations made in the previous studies [8,9]. The relief in nasal obstruction was found to be maximum with cetirizine as compared to loratidine and astemizole. Statistical significant difference was observed in between cetirizine & loratidine ($p<0.05$) whereas no statistical difference was observed between loratidine & astemizole. Jobst et al in a comparative study found that cetirizine was more effective than placebo in controlling the five symptoms i.e. sneezing, nasal obstruction, nasal discharge, nasal pruritus and ocular pruritus[10].

Both cetirizine and loratidine were equally efficacious in relieving watering of eyes, and were more efficacious as compared to astemizole. These findings were consistent with the effects observed in another study in which both cetirizine and loratidine inhibited the symptoms of allergic rhinitis and conjunctivitis[11]. Dubuske in 1995 found that cetirizine was better than astemizole in relieving the symptoms of allergic rhinitis[12] while loratidine was found to be superior to a placebo and faster acting than astemizole13 by Ilaria et al in 1994.

other parameters evaluated were absolute eosinophil count and number of eosinophils in the nasal smear at 1st week and VIth week of study period. At VIth week, maximum reduction in the absolute eosinophil count was with cetirizine whereas nasal smear eosinophil count was reduced equally by cetirizine as well as by loratidine in this study. These findings were in accordance with the observations made in the previous studies which showed that both eosinophil and neutrophil numbers were decreased by cetirizine[14] and both loratidine and cetirizine significantly reduced eosinophil count and metachromatic cell infiltration[15].

On assessment of the overall clinical improvement of the patient, it was found that mean subject satisfaction score of cetirizine was greater than that of loratidine and astemizole. Cetirizine was found to improve quality of life as comparison with loratidine and astemizole. Bousquet found that after six weeks of treatment, percentage of days without symptoms of rhinitis or with only rhinitis was significantly greater with cetirizine than with a placebo ($p<0.0001$). He concluded that cetirizine can improve quality of life for patients with perennial allergic rhinitis[16].

Although the maximum sedation was observed with cetirizine, but it did not affect the work performance of patients, rather patients reported an improvement in

TABLE: 6 Statistical significance of various symptoms of allergic rhinitis (on the basis of Bonferroni's multiple comparison procedure) at weekly interval on the intergroup comparisons over a period of six weeks

Group	Symptoms	Ist week	2nd Week	3rd Week	4th Week	4th Week	5th Week
I v/s II	Sneezing	0.37	0.22	2.27	2.87*	1.77	3.18*
	Nasal obstruction	0.25	4.09*	5.78*	5.86*	3.95*	2.24
	Watering of eyes	0.56	1.19	1.91	1.56	1.46	1.42
	Sedation	2.64*	3.22*	2.91*	2.84*	3.28*	2.36
	Overall well bing	2.43*	2.19	5.17*	1.14	0.20	0.20
I v/s III	Sneezing	.35*	2.66*	5.80*	5.11*	3.74*	5.94*
	Nasal obstruction	2.44*	6.43*	6.68*	6.67*	6.38*	6.07*
	Watering of eyes	1.32	3.32*	4.30*	3.85*	4.74*	5.70*
	Sedation	0.88	1.07	1.27	1.24	1.77	0.87
	Overall well bing	8.21*	9.49*	13.03*	10.84*	10.52*	5.3*
II v/s III	Sneezing	2.73*	2.36	3.53*	2.24	2.13	2.76*
	Nasal obstruction	2.18	2.34	0.89	0.82	2.43*	3.19*
	Watering of eyes	0.75	2.14	2.39	2.40	3.41*	4.27*
	Sedation	1.76	2.14	1.64	1.59	1.33	1.45
	Overall well bing	5.78*	7.29*	7.85*	9,69*	10.32*	5.1*

* $p<0.05$ [Table shows t values. t_{cal} is > t_{tab} i.e. 2.41; difference is significant].

sociability and required lesser number of holidays for work. In 1996 Nightingale approved that cetirizine had sedative and anticholinergic effects, though to a lesser degree than the first generations antihistaminics[17]. Incidence of headache was higher with loratidine than with cetirizine. Somnolence was the commonest side effect with cetirizine.

CONCLUSIONS

The present study shows that cetirizine, loratidine and astemizole used for the treatment of allergic rhinitis are well tolerated and have minimum side effects. Cetirizine provided greater relief of allergic rhinitis symptoms as compared with both loratidine and astemizole.

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