

A comparative study to assess the efficacy and safety of bepotastine and cetirizine in allergic rhinitis**A. T. Priyanka¹, K. R. Mamatha^{1*}, G. M. Puttamadaiah²**

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Received: 04 August 2019
Accepted: 10 September 2019

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ABSTRACT

Background: Pharmacotherapy is the mainstay of allergic rhinitis and many caregivers use over-the-counter antihistamines. Bepotastine is a novel oral second generation non-sedative antihistamine and an effective treatment option for allergic rhinitis. The objectives of the present study were to evaluate the efficacy and safety of bepotastine versus cetirizine an over the counter drug.

Methods: A prospective, randomized, open-label, parallel-group study was conducted among 60 patients fulfilling the inclusion and exclusion criteria. Group A (n=30) received tablet cetirizine 10 mg once daily and Group B (n=30) received tablet bepotastine 10 mg once daily. Efficacy was assessed by mean change in total symptom score (TSS) which is the sum of total nasal symptom score and total ocular symptom score at the end of two weeks from baseline.

Results: At the end of two weeks of treatment, both groups showed statistically significant ($p < 0.005$) improvements from their baseline TSS. Mean TSS was reduced from 12.36 ± 2.12 to 4.2 ± 1.66 in group A and from 13.33 ± 3.039 to 3.033 ± 1.40 in Group B. Significant statistical difference in TSS was seen more in Group B than Group A ($p < 0.005$).

Conclusions: Both the groups showed a substantial therapeutic benefit in patients with allergic rhinitis, however bepotastine is more effective.

Keywords: Rhinitis, Cetirizine, Bepotastine

INTRODUCTION

Allergic rhinitis (AR) is a type 1 allergic disease of the nasal mucosa, characterized by a paroxysmal repetitive sneezing, watery rhinorrhoea, and nasal blockage with prevalence of 25% worldwide.¹ Over the previous decades, the prevalence of allergic disorders has risen to epidemic proportions. As a result of high and increasing occurrence, its significant impact on quality of life, its association with multiple comorbidities, the considerable costs in terms of use of healthcare resources, school or work absenteeism and loss of productivity, the disease represents a major global health concern.²

Numerous classes of pharmacological agents are available for treatment of AR. Although not fully an ideal treatment, second-generation antihistamines exhibit many desirable properties and provide an effective means of symptomatic treatment for allergic rhinitis.³

Cetirizine, a H₁ receptor antagonist that is available over-the-counter (OTC), has been shown to be well tolerated and effective in allergic rhinitis.⁴ In addition to its antihistaminic properties, cetirizine is considered to have broad anti-inflammatory effects, including the inhibition of leukocyte influx, the reduction of intercellular

adhesion molecule 1 expression, the augmentation of interleukin 10 and interferon gamma production.⁴

Bepotastine, a novel second-generation antihistamine has recently become available for clinical use. Along with its antihistamine action, this drug suppresses eosinophilic migration to nasal mucosa and controls day time and night time triggers, hence has proven to be effective in allergic rhinitis.⁵

Nevertheless, the burden and consequences of AR are often underestimated by healthcare providers, patients and their environment.⁶ Too often, the disease is underdiagnosed and remains mis- or un- (der) treated, which leads to uncontrolled symptoms affecting work, home and social life. The aim of this study was to add to the current knowledge regarding the efficacy and safety of cetirizine and bepotastine in treatment of AR.

METHODS

A prospective, open label, parallel group, comparative clinical study conducted at ENT OPD, attached to Bangalore Medical College and Research Institute, Bengaluru.

After obtaining clearance and approval from the Institutional ethics committee (reference no. BMCRI/PS/145/2018-19) and written informed consent, the study was carried out from November 2018 to May 2019 among 60 patients clinically diagnosed with moderate to severe allergic rhinitis of either sex, aged between 18-65 years. Patients with hypersensitivity to study medications, pregnant and lactating women were excluded.

Enrolled patients were randomly divided into two groups of 30 each and simple randomization was carried out using computer generated randomization sequence (www.randomization.com). Patients in Group A received tablet cetirizine 10 mg per oral once daily and Group B received tablet bepotastine 10 mg per oral once daily.

Demographic data, history of presenting illness, associated allergic disorders, concomitant medications, physical and clinical examination, nasal and ocular examination (nasal and ocular symptom scores), and details of the drug prescription were recorded at the baseline visit (visit 1). The patients received study medications for the period of two weeks irrespective of the symptom control and were followed up at the end of two weeks (visit 2). A deviation of ± 2 days for follow-up was accepted. Study subjects were evaluated for nasal symptoms (nasal congestion, rhinorrhea, nasal itching, and sneezing) and ocular symptoms (itching or burning eyes, tearing or watering eyes, and eye redness) on a 4-point scale. Efficacy was assessed by mean change in total symptom score (TSS) which is the sum of total nasal symptom score (TNSS) and total ocular symptom score (TOSS) at the end of the study. Safety was assessed by any adverse reactions reported by the patient as well as those observed by the physician.

Data was analyzed using descriptive statistics. Paired and unpaired student t tests were used to compare the results within the group and between the groups respectively. p value < 0.05 is considered statistically significant.

Sample size

Based on a study conducted by Kimihiro et al sample size of 60 was calculated to detect a difference in symptom scores of 0.070 ± 0.091 at 90% power and 5% significance level under two tailed tests of significance.⁷

RESULTS

Sixty participants were randomized into two study groups using computer generated randomization sequence in 1:1 ratio. These 60 participants were comparable at baseline with respect to age, sex and symptom scores (Table 1). The average age of study participants was 29.7 which included 21 males and 39 females showing female preponderance.

Table 1: Demographic details.

Characteristics	Cetirizine group (n=30)	Bepotastine group (n=30)	P* value
Mean age in years (SD)	29.3 (10.10)	30.06 (8.30)	0.75
Sex			0.58
Male	12	9	
Female	18	21	
Occupation history			0.45
Students	9	12	
Home makers	7	10	
Outdoor workers	9	5	
Others	5	3	
Family history	14 (46%)	12 (40%)	
History of asthma	5 (16.66%)	7 (23%)	0.59
Habits			
Smokers	2	3	
Non-smokers	28	27	

*: p value < 0.05 shows significant difference.

Efficacy analysis

Change in TSS

TSS was assessed at baseline and the end of 2 weeks for all the participants. Baseline mean TSS for Group A and Group B was 12.36±2.12 and 13.33±3.03 respectively, which was comparable (Figure 1). At the end of the treatment mean TSS reduced to 4.2±1.66 in Group A and 3.033±1.40 in Group B which was statistically significant from baseline (Figure 2). The change in between the study groups was statistically significant (Table 2).

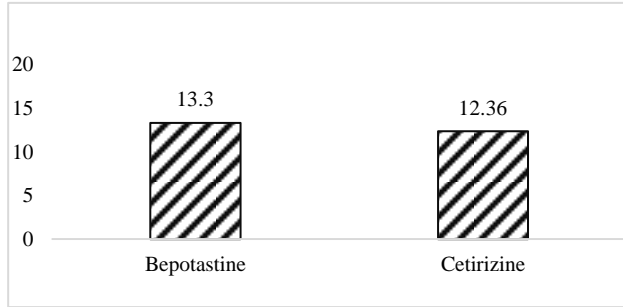


Figure 1: Baseline TSS for both treatment groups.

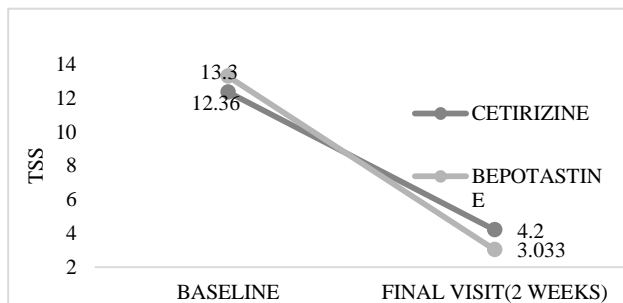


Figure 2: TSS between the two study groups at baseline and end of two weeks.

Change in TNSS

TNSS was evaluated at baseline and the end of 2 weeks for all the participants. Baseline TNSS for Group A and Group B was 9.2±1.54 and 9.13±1.56 respectively, which was comparable. At the end of 2 weeks of treatment, TNSS was 3.26±1.28 in Group A and 2.41±1.08 in Group B. The changes from the baseline in both the study groups were statistically significant (Figure 3). However, TNSS in Group B reduced to a greater extent than Group A which was statistically significant (Table 2 and 3).

Table 2: Baseline efficacy parameters.

	Cetirizine (n=30)	Bepotastine (n=30)	P value*
TSS	12.36 ± 2.12	13.33±3.03	0.18
TNSS	9.2±1.54	9.13±1.56	0.86
TOSS	3.23±1.04	4.41±0.59	0.058

*: p value<0.05 shows significant difference.

Comparison of symptom scores at baseline between the groups.

Table 3: Final efficacy parameters at the end of two weeks.

	Cetirizine (n=30)	Bepotastine (n=30)	p value*
TSS	4.2±1.66	3.033±1.40	0.048
TNSS	3.26±1.28	2.41±1.08	0.041
TOSS	0.93±0.78	0.71±0.80	0.21

*: p value<0.05 shows significant difference.

Comparison of symptom scores at the end of the study between the groups.

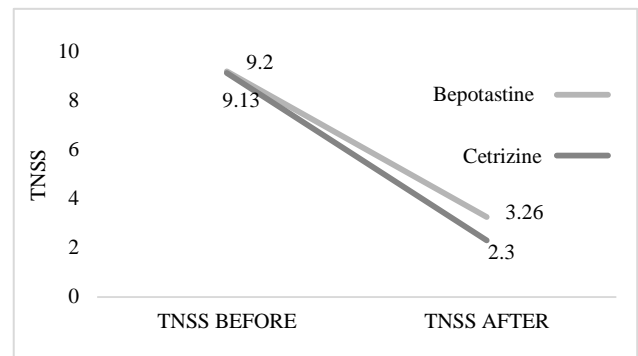


Figure 3: TNSS between the two study groups at baseline and end of two weeks.

Change in TOSS

Baseline TOSS for Group A and Group B was 3.23±1.04 and 4.41±0.59, respectively, which was comparable. At the end of 2 weeks of treatment, TOSS was 0.93±0.78 in Group A and 0.71±0.80 in Group B (Figure 4). This reduction in TOSS was comparable in between the study groups (Table 2 and 3).

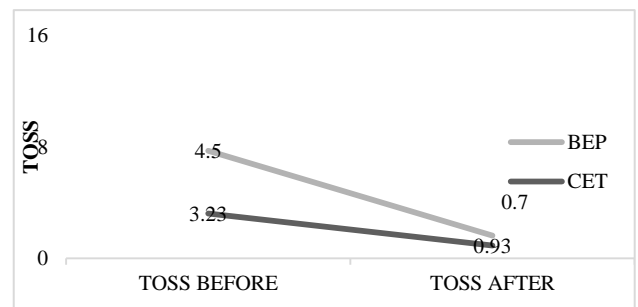


Figure 4: TOSS between the two study groups at baseline and end of two weeks.

Safety analysis

During the study period, we only encountered mild adverse drug reactions associated with both groups which did not require discontinuation of medication. The most

common adverse effect was sedation which was more in cetirizine group. No serious adverse events reported (Table 4).

Table 4: Safety profile.

Adverse effect	Bepotastine group (n=30)	Cetirizine group (n=30)
	N (%)	N (%)
Somnolence	4 (13.33)	7 (23.33)
Dizziness	3 (10)	4 (13.33)
Headache	1 (3.33)	1 (3.33)

DISCUSSION

Currently prevalence of allergic rhinitis is increasing and good epidemiologic studies suggest that 20 to 30% of adults and up to 40% of children are affected.⁸ Global climate changes leading to elevated levels of carbon dioxide increased plant productivity and increase in airborne pollen may explain the increasing prevalence.⁹ Symptoms can have significant negative impact on the patients' quality of life, often interfere with sleep and contribute to poor performance at work. Choosing correct treatment with minimal side effects still is a challenge for physicians.

In the past, allergic rhinitis was considered to be a disorder localized to the nose and nasal passages, but current evidence indicates that it may represent a component of a systemic airway disease involving the entire respiratory tract.¹⁰ IgE molecule has a prominent role in pathogenesis of allergic rhinitis, and adhering to a special receptors on the surface of mast cells and basophils results in degranulation and release of multiple mediators.¹¹ Histamine is one of these mediators that induces mucosal secretion, vascular dilation, increase vascular permeability, tissue edema, itching and sneezing.¹² In addition to allergen avoidance, suggested treatments for AR include H1 receptor antagonists (antihistamines), corticosteroids, immunotherapy, intranasal saline solutions and leukotriene receptor antagonists.¹³

Oral antihistamines frequently are used as OTC; therefore, it is important the physician should be sure the patient receives correct drug in enough dose with minimal side effects. Although the first-generation H1 antihistamines were developed and widely used clinically from the mid-1940s to the late 1970s; a comparably lower efficacy and association with particularly sedative and anticholinergic side effects have restricted their usefulness and subsequently led to the development of the more efficacious and safer second-generation antihistamines.¹⁴

Second-generation antihistamines are preferable in these disorders as they have got the dual mode of action both as histamine antagonist and mast cell stabilizer. They also

exert significantly less sedation as compared to the first-generation antihistamine while maintaining a higher efficacy.¹⁵ Hence, the focus of this study was to evaluate the use of cetirizine and bepotastine in management of AR.

In the present study the baseline data show no significant difference between the study groups with respect to demographic parameters. This proves the homogeneity of the study patients in the two groups. The efficacy of the study drugs was assessed by the total nasal symptom score, total ocular symptom score and total symptom score. Both the study drugs were administered in a dose of 10 mg once daily. At the end of two weeks there was a significant change in TNSS and TOSS parameters in both the study groups from the baseline. However, bepotastine had a greater reduction in total symptom score when compared to cetirizine and was found to be statistically significant ($p < 0.05$) as shown in Figure 2.

The results of our study have been in accordance with past study done by Deshmukh et al on "efficacy and safety of bepotastine, a newer 2nd generation antihistamine, compared to fexofenadine in allergic rhinitis".¹⁶ Bepotastine in twice daily dose regimen in adult population has been the focus of numerous clinical trials in patients suffering from allergic rhinitis.

Oral bepotastine is a highly selective second-generation histamine H1 receptor antagonist and has shown long lasting, dose-dependent antihistaminic and antiallergic activity in vitro and in vivo. H1-receptor blocking is not the only anti-allergic activity of bepotastine, it has inhibitory effects on eosinophilic inflammation in the respiratory tract and peripheral blood. Furthermore, bepotastine can stabilize mast cell function, inhibit IL-5 (Interleukin-5) production, and inhibit the activity of leukotrienes B4 and D4.⁵

Both the drugs were well tolerated. Sedation, dizziness and headache were common side effects. Over all adverse event rate has been very low showing good tolerance for bepotastine compared to cetirizine. Bepotastine has very low affinity to other cell receptors such as histamine H3, α 1-, α 2- and β -adrenergic, serotonin, muscarinic, and benzodiazepine receptors, which causes adverse effects to be few and uncommon.⁵ By reviewing the currently available literature and the results of the present study bepotastine which is now available in India seems to be a promising agent to combat allergic rhinitis due to its non-sedating profile, lesser to no adverse effects and dual mode of action on histamine and other inflammatory mediators.

CONCLUSION

In our study, both the treatment groups demonstrated significant therapeutic benefit in patients with AR. However, our data suggested that the efficacy of bepotastine, a novel second-generation antihistamine was

significantly more than cetirizine with respect to the TSS and TNSS, although there was no significant difference in TOSS. Further trials are needed to prove its use in the Indian population in different allergic conditions.

ACKNOWLEDGEMENTS

Authors would like to thank Head of the department and faculty of Department of Pharmacology and ENT for their guidance and support in completing their study.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Priyanka AT, Mamatha KR, Puttamadaiah GM. A comparative study to assess the efficacy and safety of bepotastine and cetirizine in allergic rhinitis. *Int J Basic Clin Pharmacol* 2019;8:2304-8.