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RETROSPECTIVE ANALYSIS ON THE EFFICACY OF ALCAFTADINE 0.25% AND BEPOTASTINE BESILATE 1.5% OPHTHALMIC SOLUTIONS IN THE MANAGEMENT OF ALLERGIC CONJUNCTIVITIS

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Abstract

The treatment strategies used in the management of allergic conjunctivitis (AC) are antihistamines, mast cell stabilizers, and sometimes antihistamine–mast cell stabilizer combinations or dual action drugs. The current study aims to analyze the symptomatic relief of AC in patients treated with Alcaftadine 0.25% and Bepotastine Besilate 1.5% ophthalmic solutions. A retrospective cohort study was conducted at the ophthalmology department of a tertiary care hospital with a study population of 80 patients affected by AC. The recruited patients were categorized into two groups; Group A was treated with Alcaftadine 0.25% once daily for one week, and group B was treated with Bepotastine Besilate 1.5% twice daily for one week. The symptoms of the patients were assessed using the Severity Index scale at different durations (baseline-at visit, after 15 minutes, one day, and one week). The response scores collected were tabulated, and statistically analyzed to determine the efficacy of the test drugs. The study showed that both patients taking Alcaftadine and Bepotastine were equally efficacious in ameliorating the symptoms of AC. However, Alcaftadine provided statistically significant results in relieving the itching and redness symptoms compared to Bepotastine. Patients were also more compliant in group A, as the frequency of drug administration was only once per day. No treatment-related adverse effects were reported in the groups. It was found that both Alcaftadine and Bepotastine were equally efficacious in ameliorating the symptoms of AC. However, Alcaftadine provided better relief for itching and redness symptoms.

Key words: Alcaftadine; allergic conjunctivitis; Bepotastine Besilate; severity index

Introduction

Around the globe, about 40% of people suffer from allergic conjunctivitis (AC). In India, approximately 25.5% of the population is affected by AC due to high levels of pollution in the country[1]. The inflammation of the conjunctiva is specified as conjunctivitis, which can be either infectious or non-infectious. Bacteria (60%), viruses (20%), along with fungi, chlamydia, and parasites constitute infectious conjunctivitis, whereas non-infectious conjunctivitis is mainly caused by allergens[2]. This study aims to assess and compare the efficacy of Alcaftadine 0.25% and Bepotastine Besilate 1.5% in the symptomatic management of AC.

Allergic conjunctivitis is an inflammation of the conjunctiva caused due to IgE or non-IgE mediated immune response to external allergens[3]. The clinical features of AC include itching, watery discharge, chemosis, edema, keratitis, blurred vision, allergic rhinitis, and foreign body sensation[4]. There are many factors that contribute to the symptoms such as genetics, air pollution, immune regulation mechanisms, environment, and ocular microbiota[5].

Allergic conjunctivitis includes seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC) which are acute forms of AC. Vernal keratoconjunctivitis (VKC), atopic keratoconjunctivitis (AKC), phlyctenular keratoconjunctivitis (PKC), and giant papillary conjunctivitis (GPC) constitute the chronic form of AC[6]. The SAC and PAC affects about 15-20% of the population each year, and are thereby the most common type of AC. They are typically provoked by airborne allergens such as pollen, grass, weed, and animal dander[7–9].

The overwhelming number of different pharmacologic agents to manage AC makes it difficult for ophthalmologists to choose the right therapeutic agent. The management of AC primarily includes eye drops/ophthalmic solutions and tear supplements[10]. Various clinical studies have been done to determine the safety and efficacy of topical antihistamines that are used in the management of AC. Most ophthalmic solutions in the market are from two categories; mast cell stabilizers – which keep the mast cell from releasing histamine, and antihistamines – which keep the histamines from interacting with H1 receptors[11]. The other classes of drugs used to treat AC are non-steroidal anti-inflammatory drugs and corticosteroids[12]. The most commonly used antihistamines are Emedastine, Difumarate, Epinastine, Azelastine, Bepotastine Besilate, Alcaftadine, and the recently approved Cetirizine Ophthalmic solution[2, 13]. The commonly used mast cell stabilizers are Lodoxamide tromethamine, Olopatadine, Ketotifen, and Nedocromil. The current treatment strategies for the management of AC include a variety of combinations of different classes of drugs, including antihistamine-vasoconstrictor combinations, antihistamine-mast cell stabilizers, corticosteroids, nonsteroidal anti-inflammatory drugs, antihistamines, and antihistamine-mast cell stabilizer combinations[14–17]. Recently, in India, the use of dual-acting antihistamine-mast cell stabilizers has become the first-line agents in the management of AC as they provide faster relief from acute ocular symptoms such as itching, redness, and swelling[18].

Methods

A retrospective study was conducted on AC patients treated with Alcaftadine 0.25% and Bepotastine Besilate 1.5% to analyze their efficacy in managing various symptoms of AC.

For the purpose of the study, 80 patients were recruited as per inclusion and exclusion criteria. The majority of the patients were enrolled from the outpatients (OP) of the ophthalmology department of Vinayaka missions' Kirupananda Variyar Medical College and Hospital, Salem, Tamil Nadu. The patients were diagnosed with AC and were prescribed with either Alcaftadine 0.25% or Bepotastine Besilate 1.5% by the treating ophthalmologist. The study protocol was approved by the ethical committee of our institute. A total of 80 patients were recruited and grouped based on the ophthalmic solution they were prescribed. The patients in group A were treated with Alcaftadine 0.25% and the ones in group B were treated with Bepotastine Besilate 1.5% for managing to present ocular symptoms. Group A was asked by the treating the ophthalmologist to administer Alcaftadine 0.25% for the next one week once a day, and Group B was advised to administer Bepotastine Besilate 1.5% for the next one week twice a day.

The patients in the study with a history of ocular allergies agreed to avoid disallowed medications during the study period. The subjects who agreed to discontinue wearing contact lenses during the study period were also included in the study. Subjects with any known allergy or contraindication to the study medications, patients who have had ocular or refractive surgery within three to six months' time period, subjects who are pregnant or planning to get pregnant during the study period, patients who have used any H1 antagonist within 72 h of the study, and subjects under the age of five are excluded from the study population.

A total of 80 patients who satisfied the inclusion and exclusion criteria were enrolled in the study. The demographic details were collected from all the subjects. The enrolled patients were randomly divided into two groups (Group A and Group B).

Allergic conjunctivitis symptoms of Group A patients were treated with one drop of Alcaftadine 0.25% in the affected eye once a day. Group B patients were administrated with one drop of Bepotastine Besilate 1.5% in the affected eye twice a day for one week. The response for each group was collected at different time intervals after recording the baseline response prior to administration of the drugs. The response scores were collected as per the severity index as given in Table 1 at 15 min, one day, and one week. The response scores collected from both groups were itch score, discharge score, swelling scores, tearing scores, and redness scores. The severity of nasal symptoms such as allergic rhinitis was also obtained from both groups.

The data were collected, tabulated, and statistically analyzed using MINITAB version 19. Student T-test was used to compare and analyze the differences in the various mean scores of severity parameters between the two groups of the study population. The P-value was calculated at a confidence interval of 95% with an α value of 0.05. The P-value is significant at ≤0.05, highly significant at P≤0.01, and very highly significant at P≤0.001.

Results

Among the 80 patients in the study population, 24 female and 29 male patients were in the age group of 10-20, 7 female and 16 male patients were in the range of 21-30, and 3 female and male patients were in the age range of 31-40. Thus, the total number of patients in the age group 10-20 was 53 (66.25%), 21-30 age group was 23 (28.75%), and 31-40 age range comprised of 4 (5.00%) patients in total, which is shown in Table 2.

Ocular symptoms such as itching, tearing, redness, discharge, the swelling was assessed using the severity index scale with reference to Table 1[19]. The initial/baseline response was collected for the groups prior to administration of the test drugs. The test drug Alcaftadine 0.25% and Bepotastine Besilate 1.5% were administrated to group A and group B respectively, the response scores were collected after 15 minutes, one day, and one week. The mean symptom scores were calculated, and were compared using a two-sample paired t-test.

At baseline, there is no statistically significant difference between the two groups for all the symptoms. The mean and standard deviation of the collected data is shown in Table 3 and the comparison of each symptom in the test groups is graphically represented in Figure 1.

At 15 min, the mean itch score was 1.675 and 1.925 for group A and Group B respectively, the p-value of 0.029 indicates that there is a significant difference in the means of group A and B. The mean itch score after one day were 0.875 and 1.1 for group A and group B respectively, and the p-value of 0.097 indicates no significant difference. After one week, the mean itch scores are 0.025 and 0.225 for Group A and B respectively, and the p-value of 0.007 indicates a highly significant difference in the means of itch scores of groups A and B.

The mean tear score at 15 minutes was 1.800 and 1.950 for group A and Group B respectively, and the p-value of 0.121 indicates that there is no significant difference in the means of group A and B. The mean tear score after one day was 1.225 and 1.275 for group A and group B respectively, and the p-value of 0.715 indicates no significant difference. After one week, the mean Tear scores were found to be 0.175 and 0.175 for Group A and B respectively, and the p-

value of 1.000 indicates no significant difference in the means of tear scores of groups A and B.

The mean discharge score was 1.150 and 1.175 for group A and Group B respectively when collected at 15 minutes, and the p-value of 0.765 indicates that there is no significant difference in the means of group A and B. The mean discharge score after one day was 1.050 and 1.100 for group A and group B respectively, and the p-value of 0.403 indicates no significant difference. After one week, the mean discharge scores are 0 and 0.1 for Group A and B respectively.

About 15 minutes after the administration of drugs, the mean swelling score was 1.150 and 1.175 for group A and Group B respectively, and the p-value of 0.765 indicates that there is no significant difference in the means of group A and B. The mean swelling score after one day was 1.025 and 1.100 for group A and group B, and the p-value of 0.171 indicates no significant difference. After one week, the mean swelling scores were 0.125 and 0.200 for Group A and B correspondingly, and the p-value of 0.370 indicates an insignificant difference in the means of swelling scores of groups A and B.

The mean redness score was 1.675 and 1.950 for group A and Group B respectively at 15 minutes, and the p-value of 0.010 indicates that there is a significant difference in the means of group A and B. The mean redness score after one day was 1.025 and 1.275 for group A and group B respectively, and the p-value of 0.080 indicates an insignificant difference[20]. After one week the mean redness scores were 0.125 and 0.450 for Group A and B respectively, the p-value of 0.001 indicates a highly significant difference in the mean redness scores of groups A and B.

Nasal symptoms were also assessed for both groups in the study population. There was an assessment of allergic rhinitis in the study population, and in Group A 6 (7.50%) patients and in Group B 12 (15.00%) patients showed symptoms of allergic rhinitis. The symptoms were assessed at the end of one week of treatment.

Discussion

Understanding the underlying physiological and pathological mechanisms that trigger ocular allergy is very crucial in the management of AC. This would help the ophthalmologist to choose appropriate drugs for managing various symptoms associated with AC. In the study population, 66.75% (53) of patients were in the age range of 10-20 years, which suggests that AC is predominantly associated with this age group. A comprehensive review by La Rosa, Mario *et al.* reported that AC is under-reported in adult cases; however, cases of AC in young patients are reported more often[21]. Alcaftadine is a direct H1 receptor antagonist which inhibits histamine release from mast cells, indicated for the management of itching associated with AC. Bepotastine Besilate is a newer selective H1 receptor antagonist and mast cell stabilizer which was recently introduced in India in the management of AC[22].

In this study, each drug is administrated to different groups in managing various symptoms of AC such as itching (pruritus), tearing (epiphora), redness, discharge (Rheum), swelling/edema. From this study, it was observed that both the drugs are equally effective in managing tearing, discharge, and swelling symptoms associated with AC. However, itching and redness scores were found to be significantly different among the groups A and B. After 15 minutes of administration of Alcaftadine and Bepotastine Besilate, the mean itch scores were significantly different as indicated by the P-value of 0.029. A similar difference in itch score was also found after one week of treatment, indicated by a P-value of 0.007. This data suggests that Alcaftadine was significantly better when compared to Bepotastine in treating ocular itching, suggested by the P-values of 0.010 and 0.001 at 15 minutes and one week respectively. The study found that Alcaftadine provided better relief from itching and redness symptoms, which was also reported in a study conducted by Dudeja, Lakshey *et al*[23].

It may be concluded that both Alcaftadine and Bepotastine Besilate are safe and effective in managing AC. Alcaftadine performed better in reducing ocular itching and redness. Alcaftadine also has the advantage of once-daily dosing compared to Bepotastine which has to be given twice daily.

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SEVERITY INDEX SCORE				
Ocular symptoms	**0**	**1**	**2**	**3**
Itching	No itching	Mid itching occasionally	Mild itching persists all day	Severe itching
Tearing	Absent	Humid, No epiphora	Intermittent epiphora	Constant epiphora
Discharge	No discharge	Moistens the lesion	Mild discharge on scratching	Profuse discharge on scratching
Swelling	Absent	Mild swelling	Severe swelling with partial eyes closed	Severe swelling with eyes completely closed
Redness	No redness	Mild reddish eyes	Moderately red	Intense redness in the eye

Table 1: Severity index scale for assessing the ocular symptoms associated with allergic conjunctivitis

Age group	Female	Male	Total no of patients	Percentage
10-20	24	29	53	66.25%
21-30	7	16	23	28.75%
31-40	3	1	4	5.00%
Total	**34**	**46**	**80**	**100.00%**

Table 2: Gender diversity of different age groups in the study population