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A COMPARATIVE, RANDOMIZED, DOUBLE BLIND, PARALLEL GROUP AND NON CROSSOVER MULTICENTRIC CLINICAL STUDY WITH BEPOTASTINE BESILATE OPHTHALMIC SOLUTION VS. OLOPATADINE HYDROCHLORIDE OPHTHALMIC SOLUTION IN SUBJECTS SUFFERING FROM ALLERGIC CONJUNCTIVITIS

[1]*Dr. Shailesh Singh, [2]Dr. Ravindra Mote, [3]Dr. Sarita Shukla, [4]Abhijit Mali and [5]Khushwant Khatri

[1]Vice President, Ajanta Pharma Limited, Advent Research Centre, Plot No. 43 AB & 44 BCD, Govt. Industrial Estate, Charkop, Kandivali (W), Mumbai – 400067.
[2]Assistant Manager, Ajanta Pharma Limited, Advent Research Centre, Plot No. 43 AB & 44 BCD, Govt. Industrial Estate, Charkop, Kandivali (W), Mumbai – 400067.
[3]Assistant Manager, Ajanta Pharma Limited, Advent Research Centre, Plot No. 43 AB & 44 BCD, Govt. Industrial Estate, Charkop, Kandivali (W), Mumbai – 400067.
[4]Senior Officer, Ajanta Pharma Limited, Advent Research Centre, Plot No. 43 AB & 44 BCD, Govt. Industrial Estate, Charkop, Kandivali (W), Mumbai – 400067.
[5]Executive, Ajanta Pharma Limited, Advent Research Centre, Plot No. 43 AB & 44 BCD, Govt. Industrial Estate, Charkop, Kandivali (W), Mumbai – 400067.

***Corresponding Author: Dr. Shailesh Singh**
Vice President, Ajanta Pharma Limited, Advent Research Centre, Plot No. 43 AB & 44 BCD, Govt. Industrial Estate, Charkop, Kandivali (W), Mumbai – 400067.

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ABSTRACT

Background: This study was designed to evaluate the efficacy, safety and tolerability of Bepotastine Besilate Ophthalmic Solution 1.5% w/v (Arm A) Vs. Olopatadine Hydrochloride Ophthalmic Solution 0.1% w/v (Arm B) in Subjects suffering from Allergic Conjunctivitis. The main objective of this study was to compare subjects-perceived relief from the symptoms of ocular itching, conjunctival redness, tearing (watery eyes), eyelid swelling and eye discharge. **Method:** It was a comparative, randomized, double blind, parallel group, non-crossover, active control multi-centric clinical trial conducted in 12 centers across India in subjects with signs and symptoms of allergic conjunctivitis. The recruitment has been started from Dec 31, 2014 to Nov 24, 2015. Total 200 patient (aged 10 – 60 years) were randomized with 99 enrolled in Arm A and 101 in Arm B. All the subject were advised to instil one drop twice a day into the affected eye of either Bepotastine or Olopatadine as per randomization. The treatment continued for 21 days with periodic follow-up on 7th, 14th and 21st day from start of treatment. **Results:** The current study showed the mean change in ocular itching and conjunctival redness score from baseline to visit 4 for Bepotastine and Olopatadine as (-2.5, -2.5 P=0.8793) & (-2.5, -2.3 P= 0.2249) respectively. There were 08 clinical adverse events reported (Bepotastine: 03, Olopatadine: 05) which were mild in nature. **Conclusion:** Bepotastine Besilate Ophthalmic Solution is equivalent in all primary efficacy variables and has equal efficacy in improving the clinical features of Allergic Conjunctivitis when compared with Olopatadine and as safe as Olopatadine.

KEYWORDS: Alcaftadine, Olopatadine, conjunctival redness.

INTRODUCTION

Allergic conjunctivitis is a condition who affects the conjunctiva, eyelids and cornea, and it is often associated with nonocular symptoms and signs of rhinitis or sinusitis.[1] In India, 20-30 % of population suffers from at least one allergic disease and its prevalence has been increasing over past years.[2] Seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC) are the most common forms of ocular allergies. In allergic conjunctivitis, allergen-induced inflammatory response is produced by interaction of allergens with IgE which is bound to sensitized mast cells resulting in the clinical ocular allergic expression. Activation of mast cells induces enhanced tear levels of histamine, tryptase, prostaglandins and leukotriene, this immediate or early inflammatory responses lasts clinically 20–30 min.[3]

Mast cell degranulation also induces activation of vascular endothelial cells, which in turn expresses chemokines and adhesion molecules such as intercellular adhesion molecule (ICAM), vascular cell adhesion molecule (VCAM). Other chemokines secreted include

regulated upon activation normal T cell expressed and secreted (RANTES) chemokines, monocyte chemo attractant protein (MCP), interleukin (IL)- 8, eotaxin, macrophage inflammatory protein (MIP)-1 alpha. These factors initiate the recruitment phase of inflammatory cells in the conjunctival mucosa, which leads to the ocular late-phase reaction.[3]

SAC is usually caused by airborne pollens and commonly occurring form of allergic conjunctivitis, followed by PAC. Signs and symptoms usually occur in the spring and summer, and generally abate during the winter months. PAC can occur throughout the year with exposure to perennial allergens. Diagnostic features of SAC and PAC consist of itching, redness, and swelling of the conjunctiva. Redness, or conjunctival injection, tends to be mild to moderate. Conjunctival swelling, or chemosis, tends to be moderate, and somewhat more prominent than one would expect for a mild amount of redness. Itching is a fairly consistent symptom of SAC and PAC. Corneal involvement is rare.[4]

Allergic conjunctivitis can be treated with a variety of drugs, including topical antihistamines, mast cell stabilizers, nonsteroidal anti-inflammatory drugs and corticosteroids.[1] Ocular allergies are very common and range in intensity from mild, self-resolving, acute conditions to serious, chronic disease that can severely affect vision. Treatment should be simple, comfortable and very safe. They should be able to respond to an ongoing attack but also provide long-term relief from symptoms.[5]

Bepotastine Besilate Ophthalmic Solution 1.5% w/v is a novel anti-allergic agent with histamine H1 receptor antagonistic activity. Bepotastine Besilate Ophthalmic Solution 1.5% w/v has H1 antagonistic and inhibitory action on eosinophilic infiltration to inflammatory sites. Bepotastine Besilate has three primary mechanisms of actions viz. act as a non – sedating, selective antagonist of the histamine 1 (H1) receptor, has a stabilizing effect on mast cells and suppresses the migration of eosinophils into inflamed tissues.[6]

Since Bepotastine Besilate has a strong histamine antagonistic action as well as an inhibitory action of migration of eosinophils to inflamed tissues, it was expected to be effective against main symptoms such as itching in seasonal allergic conjunctivitis caused by pollens as well as perennial allergic conjunctivitis caused by house dusts etc. Bepotastine Besilate has rich water solubility and suitable for applying eye-drop products.[6]

The increasing prevalence of allergic conjunctivitis and its deleterious effects on vision and ocular comfort necessitates the use of a safe, highly effective and comfortable topical medicine. However, the current literatures are lacking comparative data to assist the eye care professionals in selecting the appropriate initial topical treatment for allergic conjunctivitis. Hence, Comparative, Randomized, Double blind, Parallel group and Non Crossover Multi-centric Clinical Study with Bepotastine Besilate Ophthalmic Solution Vs. Olopatadine Hydrochloride Ophthalmic Solution was planned in subjects suffering from Allergic Conjunctivitis.

MATERIALS AND METHODOLOGY

Study Design

This study was a comparative, randomized, double blind, parallel group and non-crossover multi-centric clinical study conducted between Dec 31, 2014 to Dec 10, 2015 in 12 centres across India in subjects suffering from Allergic Conjunctivitis (CTRI No.:- CTRI/2015/01/005399).

All procedures followed the tenets of the Declaration of Helsinki, were in accordance with all regulatory standards, were approved by an Institutional Review Board and all subjects signed an informed consent form. Protocols and Inform consent were approved by Indian Regulatory authority and Institutional Ethical Committee.

Subjects

Both male and female subjects suffering from allergic conjunctivitis were included in the study for the duration of 21 days. They were randomized (simple block randomization) by computer generated system to either of the study arms in 1:1 proportion (Test: Reference).

Study Eligibility Criteria

Subjects of age ≥ 10 years and ≤ 60 years, with sign and symptoms of allergic conjunctivitis like ocular itching, eye lid swelling, tearing, photophobia, watery discharge, diagnosis of allergic conjunctivitis were confirmed by conjunctival smear examination. Also, freshly diagnosed subject or subjects who are previously diagnosed and on treatment of allergic conjunctivitis and have undergone for 3 days wash out were included in this study.

Informed consent form (ICF) were willingly signed by each participated subjects prior to any screening procedure. Minor subjects (age below 18 years) participation in the clinical trial was undertaken with provision of Legally Acceptable Representative (LAR) with assent form.

Potential subjects were excluded based upon criteria established prior to the study. Subjects who took systemic administration of corticosteroids or immunosuppressive agents, or used ophthalmic ointments of corticosteroids within 1 week before instillation of the investigational drugs were excluded. Subjects who were blind or having single eye, planned surgery during trial period, suffering with dry eyes and Schirmer <10 excluded from the study. Also, subjects who had Vernal Keratoconjunctivitis, corneal epithelial detachment or corneal ulcer in the target eye, require to wear contact lens during the study period, pregnant or

may be pregnant or lactating. Subjects who had participated in other clinical studies within 3 months, suffered with any ocular condition that, in the opinion of the investigator, could affect the subject's safety or trial parameters, uses disallowed medications during the period indicated prior to study enrolment or during the study, known contraindications or sensitivities to the study medication or its components and inappropriate for the study participation by the opinion of the investigator/sub investigator.

Treatment and Compliance

One drop of either Bepotastine Besilate Ophthalmic Solution 1.5% w/v or Olopatadine Hydrochloride Ophthalmic Solution 0.1% w/v were administered twice daily in subjects with Allergic Conjunctivitis for 21 days with periodical follow-up on 7th, 14th and 21st day from start of treatment.

The compliance was observed through drug accountability and subject diary. Adherence to assigned regimen was assessed by recording the amount of returned investigational products at the end of study treatment. Treatment compliance was considered adequate, when provided patients have used at least 75% of scheduled doses.

Time and Events Schedule

After fulfilling inclusion and exclusion criteria and pathological assessment at screening visit, subject was enrolled for the study. At the baseline visit subjects had been undergo tests for the assessment of safety and efficacy parameters. There were 5 visits in the study such as Screening Visit, Baseline/ Randomization Visit (Day 0), Visit 2 (Day 7), Visit 3 (Day 14) and Visit 4/ Final Visit (Day 21). The study medication either Bepotastine Besilate Ophthalmic Solution 1.5% w/v or Olopatadine Hydrochloride Ophthalmic Solution 0.1% w/v were handed over to randomized subjects on Day '0' (Visit - 1) as per randomization schedule and instructed for their direction of use (Figure 1).

Demographical variables (age, sex, race, height and weight), medical history, physical examination including vital signs and electrocardiogram (ECG) was done at screening visit; laboratory investigations such as haematology and blood chemistry, Schirmer's Tear Test and Tonometry Test were performed at both screening and final visit (Day 21).

Assessment of primary and secondary efficacy parameters and Slit Lamp Biomicroscopy observations were recorded on baseline visit to each follow up visit. Visual Acuity (VA) was measured at each visit except screening visit. At the Day 21, overall response of clinical cure and overall global assessment (based on total score of signs and symptoms) had been done by Subjects and Investigators.

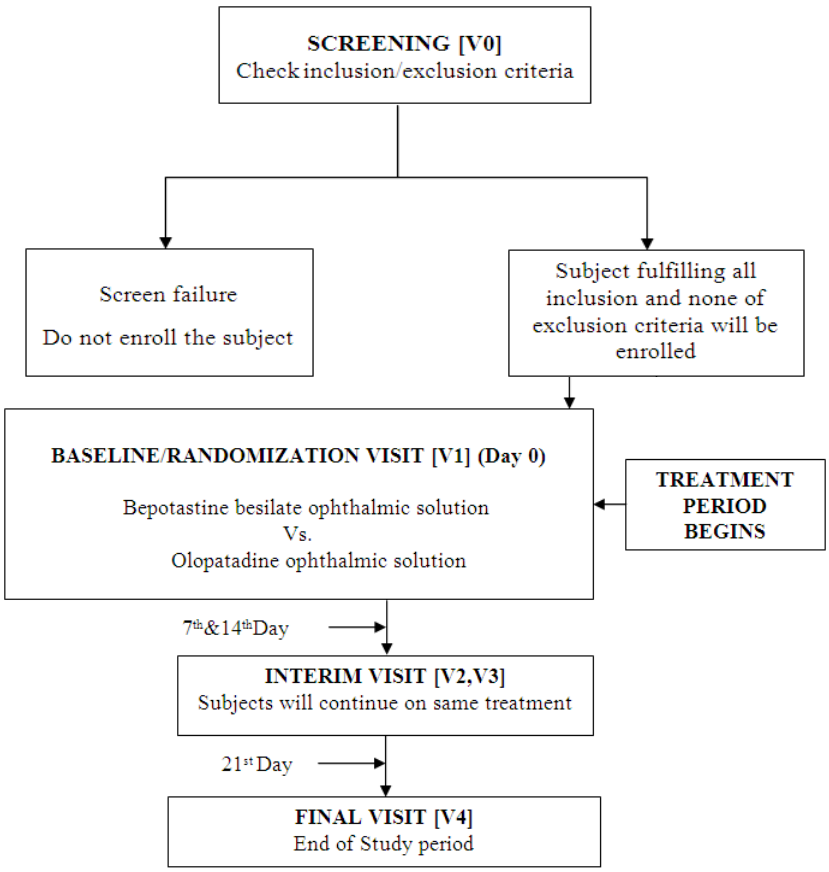

Figure 1: Study Flowchart.

Efficacy and Safety Parameters

Efficacy of the study medications i.e. Bepotastine Besilate Ophthalmic Solution 1.5% w/v and Olopatadine Hydrochloride Ophthalmic Solution 0.1% w/v were analysed on the basis of comparison of scores of Allergic Conjunctivitis symptoms. Allergic Conjunctivitis score comprised of ocular itching (0-4), conjunctival redness (0-4), tearing (0-3), eye lid swelling (0-3) and stringy eye discharge (0-3). Safety of both study medications were assessed by evaluating ocular sign and symptoms, Tonometry, Visual Acuity, Slit Lamp Biomicroscopy and Schirmer's Tear Test.

Adverse Events (AEs) and Serious Adverse Events (SAEs) were summarized by counting both the number of separate events and the number of subjects experiencing any of these events during the study period was recorded. Furthermore, similar summaries were provided and stratified according to the seriousness, severity and relationship to the study medication.

The data were collected on electronic case record form (eCRF). The data analysis was performed for predefined parameters to correspond with primary endpoint outcome measures. The subjects were excluded for safety analysis unless there was consent withdrawal / termination pertaining to adverse event.

Statistical methods

Statistical analysis was done using SAS 9.2. Continuous variables were statistically tested using 2-Sample T Test, Wilcoxon Rank Sum Test, Paired T test and Wilcoxon Signed Rank Test. Primary efficacy analysis was done using Wilcoxon Signed Rank Test and Mann Whitney U Test. Secondary efficacy analysis was done using Pearson's Chi-Square and Fisher's Exact Test. Overall global assessment was analysed by Pearson's Chi-Square Test and Fisher's Exact Test. All safety parameters were analysed by Chi Square Test.

RESULTS

Total 215 subjects were randomized to the study. 15 subjects (8 subjects from test arm and 7 subjects from reference arm) were discontinued from the study due to lost to follow up. None subject terminated from the study due to adverse event. The subjects who lost to follow up for Non-AE reason (2 subjects) were taken as safety population for efficacy analysis and were excluded from safety analysis. Total 99 subjects in Test and 101 Subjects in reference arm completed the study, constituting a complete sample size of 200 (Table No. 1).

Table No. 1: Overall Subject Disposition by Treatment Group.

	Bepotastine Besilate (N=107)	Olopatadine (N=108)	Total (N=215)
Total Pre-Screened			231
Eligible for Randomization			221
Total Randomized Participants to Study	107	108	215
Completed Participants	99 (92.5%)	101 (93.5%)	200 (93.0%)
Not Completed Participants	8 (7.5%)	7 (6.5%)	15 (7.0%)
Reason for Early Termination			
Protocol violation	0 (00.0%)	0 (00.0%)	0 (00.0%)
At the discretion of the Investigator	0 (00.0%)	0 (00.0%)	0 (00.0%)
Lack of efficacy	0 (00.0%)	0 (00.0%)	0 (00.0%)
Adverse Events/AE	1 (01.0%)	0 (00.0%)	1 (0.5%)
Disease progression/recurrence	0 (00.0%)	0 (00.0%)	0 (00.0%)
Inter-current illness that prevents further administration of treatment	0 (00.0%)	0 (00.0%)	0 (00.0%)
Lost to follow Up	8 (06.5%)	7 (06.5%)	14 (6.5%)
Death	0 (00.0%)	0 (00.0%)	0 (00.0%)
Change in the subject's condition rendering the subject unacceptable for further treatment in the judgment of the investigator.	0 (00.0%)	0 (00.0%)	0 (00.0%)
Others	0 (00.0%)	0 (00.0%)	0 (00.0%)

Demographic characteristics of both the groups were comparable. All subjects were in range of 10 to 60 years of age as per protocol. Average body weight was comparable with an average of 60.3 in Olopatadine group and 62.6 in Bepotastine group. 197 Subjects in the study were Asian. 1 subject in Olopatadine group was African American and 2 subjects in Bepotastine group were Caucasian (Table No. 2).

Table No. 2: Baseline Demographics Characteristics by Treatment Group.

Characteristics	Bepotastine Besilate (N=99)	Olopatadine (N=101)	Overall (N=200)
Age (Years)			
N	99	101	200
Mean (SD)	35.2 (11.9)	29.8 (11.5)	32.5 (12.0)
Median (Min-Max)	33.1 (18.3- 59.9)	26.2 (11.7 – 58.9)	29.2 (11.7 – 59.9)
Race, n(%)			
Asian	97 (97.9%)	100 (99.0%)	197 (98.5%)
African American	00 (00.0%)	01 (01.0%)	01 (00.5%)
Alaska Native	00 (00.0%)	00 (00.0%)	00 (00.0%)
Caucasian	02 (02.1%)	00 (00.0%)	02 (01.0%)
Other pacific islander	00 (00.0%)	00 (00.0%)	00 (00.0%)
Other	00 (00.0%)	00 (00.0%)	00 (00.0%)
Gender, n(%)			
Female	26 (26.2%)	29 (28.7%)	55(27.5%)
Male	73 (73.7%)	72 (71.3%)	145 (72.5%)
Height (in cms)			
N	99	101	200
Mean (SD)	161.7 (8.9)	162.5 (12.0)	162.1 (10.6)
Median (Min-Max)	162.0 (138 -182)	166.0 (126 -188)	164.0 (126 – 188)
Weight (kg)			
N	99	101	200
Mean (SD)	62.6 (9.6)	60.3 (11.5)	61.4 (10.6)
Median (Min-Max)	62.0 (32 – 84)	60.3 (30 – 90)	61.0 (30 – 90)

EFFICACY ANALYSIS

Ocular Itching and Conjunctival Redness Score

Ocular Itching score was reduced by the treatment of both Bepotastine and Olopatadine. At the end of the treatment, mean change in ocular itching score of subjects treated with both Bepotastine and Olopatadine were found to be 2.5 (±1.3) and 2.5 (±1.1) respectively ($p < 0.001$). Treatment of Bepotastine and Olopatadine were shown equivalent improvement in conjunctival redness. Mean change of conjunctival redness score at day 21 were 2.5 (±1.0) and 2.3 (±1.0) for subjects treated with Bepotastine and Olopatadine respectively (Table No. 3).

Table No. 3: Assessment of Ocular Itching and Conjunctival Redness Score.

Assessment	Change from Baseline to V2		Change from Baseline to V3		Change from Baseline to V4	
	Bepotastine	Olopatadine	Bepotastine	Olopatadine	Bepotastine	Olopatadine
N	99	101	99	101	99	101
Ocular Itching Score						
Change Score (Mean (SD))	-1.2 (0.9)	-1.0 (0.7)	-2.0 (1.1)	-1.8 (0.9)	-2.5 (1.3)	-2.5 (1.1)
Median (Min – Max)	-1.0 (-3.5 - 1)	-1.0 (-3 - 0)	-2.0 (-4 - 0)	-2.0 (-4 - 0)	-3.0 (-4 - 2)	-3.0 (-4 - -0.5)
95% CI	(-0.46, 0.01)		(-0.5, 0.1)		(-0.3, 0.3)	
p Value	0.0610		0.1725		0.8793	
Conjunctival redness Test						
Change Score (Mean (SD))	-1.2 (0.8)	-0.9 (0.7)	-1.9 (0.9)	-1.7 (0.8)	-2.5 (1.0)	-2.3 (1.0)
Median (Min – Max)	-1 (-4 - 0)	-1 (-3 - 0)	-2 (-4 - 0)	-2 (-4 - 0)	-3 (-4 - 0)	-3 (-4 - 0)
95% CI	(-1.4, -1.0)	(-1.1, -0.8)	(-2.1, -1.7)	(-1.9, -1.5)	(-2.7, -2.3)	(-2.5,-2.1)
p Value	0.0285		0.0747		0.2249	

Tearing Test, Eye Lid Swelling and Stringy Eye Discharge were the secondary efficacy parameters which were used to evaluate changes in excessive tearing, eye lid swelling and eye discharge, before and after the treatment. Bepotastine was equivalent to Olopatadine in reducing symptoms like Tearing, Eyelid Swelling and Stringy Eye Discharge (Table No. 4).

Table No. 4: Eye Lid Swelling, Tearing Test and Stringy Eye Discharge Test with observed abnormalities - Change from Baseline Visit.

Abnormality	Change from Baseline to V2		Change from Baseline to V3		Change from Baseline to V4	
	Bepotastine	Olopatadine	Bepotastine	Olopatadine	Bepotastine	Olopatadine
	(N = 99)	(N = 101)	(N = 99)	(N = 101)	(N = 99)	(N = 101)
Eye Lid Swelling						
No change (n (%))	80 (80.8)	88 (87.1)	62 (62.4)	70 (69.3)	45 (45.5)	46 (45.5)
Normal to Abnormal (n (%))	2 (2.0)	3 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abnormal to Normal (n(%))	17 (17.2)	10 (9.9)	37 (37.6)	31 (30.7)	54 (54.5)	55 (54.5)
Abnormal to Normal (proportion)	0.17	0.10	0.37	0.31	0.54	0.55
95% CI for Abnormal to Normal	(0.10, 0.26)	(0.05, 0.17)	(0.29, 0.50)	(0.22, 0.41)	(0.46, 0.67)	(0.46, 0.67)
Within Group p1	<0.0001	<0.0001	0.0586	0.0002	0.2132	0.2181
Between Group p2	0.1392		0.2152		0.9837	
Tearing (N)						
No change (n (%))	81 (81.8)	87 (86.1)	56 (56.5)	56 (55.4)	17 (17.1)	15 (14.8)
Normal to Abnormal (n (%))	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abnormal to Normal (n(%))	17 (17.2)	14 (13.9)	43 (43.5)	45 (44.6)	82 (82.9)	86 (85.2)
Abnormal to Normal (proportion)	0.17	0.14	0.43	0.44	0.83	0.86
95% CI for Abnormal to Normal	(0.10, 0.30)	(0.08, 0.23)	(0.33, 0.54)	(0.33, 0.53)	(0.75, 0.90)	(0.78, 0.92)
Within Group p1	<0.0001	<0.0001	0.2945	0.2229	<0.0001	<0.0001
Between Group p2	0.6695		0.9277		0.6378	
Stringy Eye Discharge						
No change (n (%))	77 (77.8)	87 (86.1)	47 (47.5)	49 (48.5)	24 (24.3)	19 (18.8)
Normal to Abnormal (n (%))	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abnormal to Normal (n(%))	22 (22.2)	14 (13.9)	52 (52.5)	52 (51.5)	75 (75.7)	82 (81.2)
Abnormal to Normal (proportion)	0.22	0.14	0.53	0.52	0.76	0.83
95% CI for Abnormal to Normal	(0.14, 0.32)	(0.08, 0.22)	(0.42, 0.65)	(0.43, 0.63)	(0.67, 0.85)	(0.74, 0.89)
Within Group p1	<0.0001	<0.0001	0.2082	0.5426	<0.0001	<0.0001
Between Group p2	0.1314		0.6261		0.2948	

p1-values for within-intervention group shifts in abnormality status calculated using exact binomial test; p2-values for difference between groups in distribution of shifts from abnormal to normal vs. no change or normal to abnormal calculated using chi square test.

Global assessment done at the final visit by subject and investigators showed non-significant difference in results as presented in Chart 1. The results were equivalent to Olopatadine as the mean difference with total study population was slightly less than 5%.

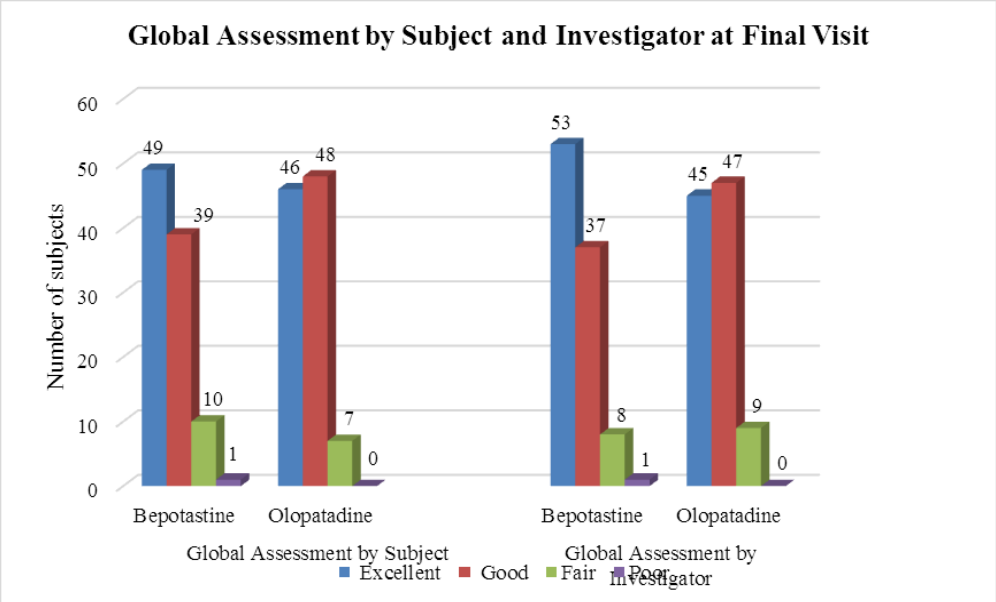

Chart 1: Global Assessment by Subject and Investigator at Final Visit

Safety Analysis

Visual Acuity test was the first attribute observed for safety analysis of the investigational medicinal products. The Visual acuity test evaluated vision of both eyes at all visits to assess safety of the investigational product. Bepotastine arm found to be significantly safe when compared with itself before (0.9) and after (0.0) the treatment as well as with Olopatadine arm. Results were equivalent to Olopatadine as the mean difference with total study population was slightly less than 5% ($p < 0.001$) (Chart 2).

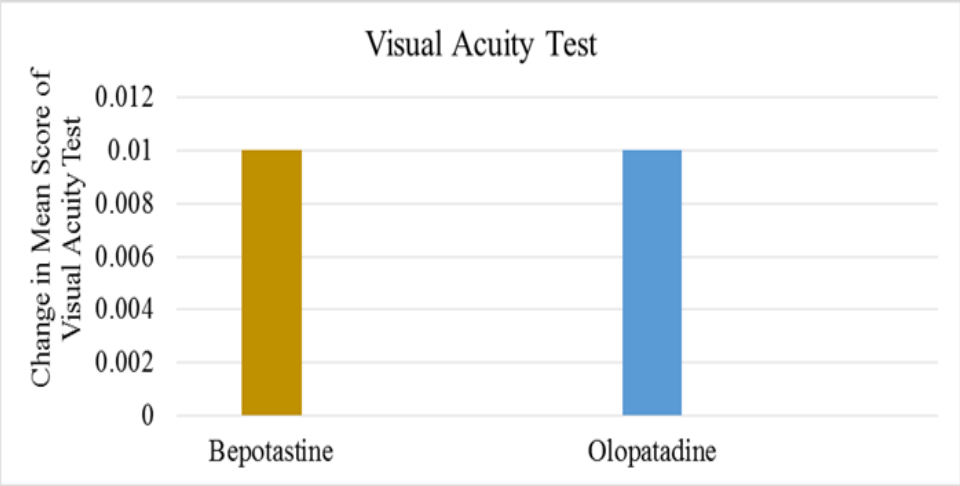

Chart 2: Visual Acuity Test.

Tonometry test was the second attribute observed for safety analysis of the investigational medicinal products. The Tonometry test was used to evaluate intra ocular pressure in eyes at final visit. Tonometry test showed safety in Bepotastine group when compared with itself before and after the treatment as well as with Olopatadine group. Results were equivalent to Olopatadine as the mean difference with total study population was less than 5% ($p < 0.001$).

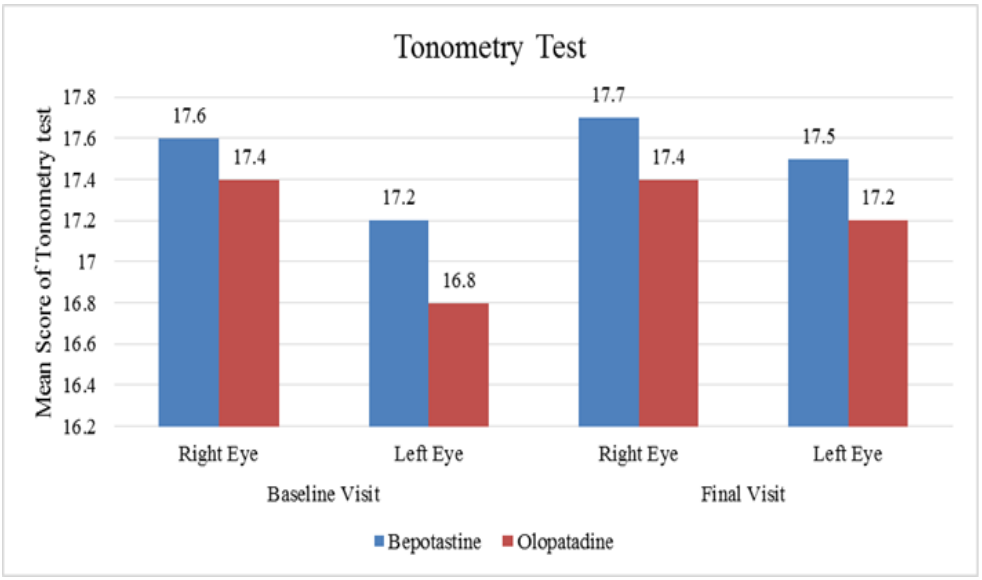

Chart 3: Tonometry Test.

Schirmer's Tear test was the third attribute observed for safety analysis of the investigational medicinal products. The Schirmer's tear test evaluated moisture/tear in eyes at baseline and final visit. Schirmer's tear test showed safety in Bepotastine arm when compared with Olopatadine. The results were equivalent to Olopatadine (Chart 4).

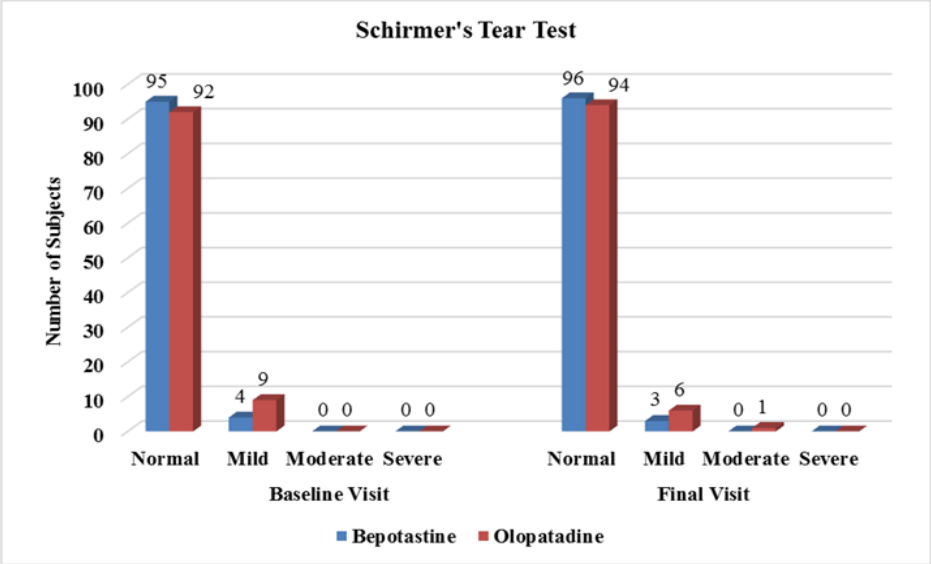

Chart 4: Schirmer's Tear Test.

Slit lamp biomicroscopy was done to assess the safety by evaluating any change in the structure of anterior of the eye and retina after use of investigational drugs. There were no changes in anterior structure of the eye as well as in retina before and after the study in both arms. Hence, it can be concluded that investigational product does not cause any change in anatomical structures of the eye.

Most clinical adverse events were ocular and respiratory related in Bepotastine and Olopatadine group respectively. All the AEs were mild. Most of the subjects who experienced adverse events had burning sensation in eyes, redness of eyes and eye discharge. In Olopatadine group some AEs were sore throat, throat infection and cough (Table No. 5).

Table No. 5: Summary of Adverse Events by Enrolment Group.

	Bepotastine (N=99)	Olopatadine (N=101)	Total (N=200)
Number of Events/Participants			
Number of Adverse Events	4	5	9
Participants with at least one AE	4 (4.0%)	4 (4.0%)	8 (4.0%)
Number of SAEs	3	0	3
Participants with at least one SAE	1 (1.0%)	0 (0.0%)	1 (0.5%)
Severity (All AEs)			
Mild	4	5	9
Moderate	0	0	0
Severe	0	0	0
Highest Severity Per Participant			
Mild	4	5	9
Moderate	0	0	0
Severe	0	0	0
Relationship (All AEs)			
Not related	3	5	8
Related	1	0	1
Strongest Relationship Per Participant			
Not related	3	4	7
Related	1	0	1
Severity (All SAEs)			
Mild	3	0	3
Relationship (All SAEs)			
Not related	3	0	3

In Allergic conjunctivitis subjects, Bepotastine was found to be equivalent to Olopatadine in safety parameters as per the clinical and laboratory evaluations.

Both Olopatadine and Bepotastine have no effect on hepatic and haematological profile. Intra ocular pressure, moisture, anterior eye structure, retina and vision of both

eyes were demonstrated by Tonometry, Schirmer's Test, Slit Lamp Biomicroscopy and Visual Acuity test and found to be normal after completion of the treatment. The clinical events of Bepotastine and Olopatadine includes routine mild burning sensation in eye. For the given clinical trial, it was seen that Bepotastine is as safe as Olopatadine. There were no deaths or prolonged hospitalizations in both Bepotastine and Olopatadine group.

DISCUSSION

This double blind, parallel group, non-crossover and multicentric clinical trial assessed for the efficacy and safety of Bepotastine Besilate Ophthalmic Solution 1.5% w/v compared with Olopatadine Hydrochloride Ophthalmic Solution 0.1% w/v for the treatment of subjects suffering from allergic conjunctivitis. We found that Bepotastine Besilate Ophthalmic Solution 1.5% w/v was shown equivalent efficacy with respect to Olopatadine Hydrochloride Ophthalmic Solution 0.1% w/v for the treatment of allergic conjunctivitis.

This clinical trial showed the safety and benefit of Bepotastine Besilate Ophthalmic Solution 1.5% w/v administered twice daily for 21 days in alleviating ocular itching and conjunctival redness associated with AC. The efficacy end points, change from baseline for reduction of ocular itching and conjunctival redness were significant over the 21 days treatment period in the Bepotastine Besilate Ophthalmic Solution 1.5% w/v subjects compared with the Olopatadine Hydrochloride Ophthalmic Solution 0.1% w/v administered subjects.

These results suggest that twice daily use of Bepotastine Besilate Ophthalmic Solution 1.5% w/v provides sustained ocular itching and conjunctival redness relief.[5] This study confirms the efficacy findings for Bepotastine Besilate Ophthalmic Solution 1.5% w/v from studies using the CAC model.[7, 8] As previously mentioned, the ocular symptoms of AC can affect the quality of life of patients.[9] Bepotastine Besilate Ophthalmic Solution 1.5% w/v fulfills the need for a treatment that provides complete symptom relief.

Furthermore, Bepotastine Besilate Ophthalmic Solution 1.5% w/v given twice daily showed reduced stringy eye discharge, chemosis and tearing compared with Olopatadine Hydrochloride Ophthalmic Solution 0.1% w/v, at the onset of action and upto 24 hours. These findings are important, because allergen concentrations vary throughout the 24-hour day–night cycle, peaking at different times depending on the allergen and local environmental conditions.

Based on the review of AEs and ocular safety parameters, no safety concerns were identified for Bepotastine Besilate Ophthalmic Solution 1.5% w/v after twice daily dosing for 21 days in adults with allergic conjunctivitis. Evidence from previous studies demonstrates that Bepotastine Besilate Ophthalmic Solution 1.5% w/v and Olopatadine Hydrochloride Ophthalmic Solution 0.1% w/v is well tolerated in subjects with a history of allergic conjunctivitis.[10-12] This study showed that the safety profile of Bepotastine Besilate Ophthalmic Solution 1.5% w/v is comparable with that of its vehicle, as well as Olopatadine Hydrochloride Ophthalmic Solution 0.1% w/v. The safety profile is also consistent with that of Bepotastine Besilate Ophthalmic Solution 1.5% w/v as previously established.

CONCLUSION

Bepotastine Besilate Ophthalmic Solution 1.5% w/v is an effective treatment of allergen-mediated ocular itching and conjunctival redness. The relief from ocular itching and conjunctival redness provided by Bepotastine Besilate Ophthalmic Solution 1.5% w/v is maintained throughout, supporting twice daily dosing of Bepotastine Besilate Ophthalmic Solution 1.5% w/v in the treatment of ocular itching and conjunctival redness associated with allergic conjunctivitis. This study showed that the benefit–risk profile for Bepotastine Besilate Ophthalmic Solution 1.5% w/v is superior to Olopatadine Hydrochloride Ophthalmic Solution 0.1% w/v for the treatment of allergic conjunctivitis associated ocular itching and conjunctival redness when both are dosed twice daily.

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