To compare the efficacy of Olopatadine 0.1% and Alcaftadine 0.25% ophthalmic solution in ocular itch relief in Allergic conjunctivitis

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ABS TRACT

Allergic Conjunctivitis (AC) is the inflammation of conjunctiva in response to an allergen. It is one of the most common forms of conjunctivitis. Ocular allergies affect 6%-30% of the general population. Recent clinical observations suggests that ocular allergic response is not confined to conjunctiva but is a disease affecting the entire ocular surface including conjunctiva, lids(with their high content of mast cells), cornea, tear film(with its immunoglobulins) and lacrimal gland.

It is characterized by signs and symptoms ranging from itching, watering, redness, foreign body sensation, burning, photophobia, lid edema, conjunctival hyperemia, chemosis, watery or mucoid discharge, papillary reaction to severe sight threatening corneal complications.

The exposure of conjunctiva to an allergen initiates an immunological hypersensitivity reaction that heralds the onset of allergic eye disease. Early phase response occurs when allergen specific IgE binds to Fc receptors on surface of mast cells leading to its degranulation and release of pre formed mediators mainly histamine and newly synthesized mediators mainly PGD2. The released histamine binds to H1 receptor on cell surfaces of conjunctival tissue resulting in vasodilatation and increased vascular permeability which is responsible for itching, burning and tearing. Binding to H2 receptor results in increased mucus production at ocular surface. PGD2, considered being ten times more potent than histamine, increases conjunctival micro vascular permeability leading to redness, itching, chemosis and mucus production.

KEYWORDS
Acute AC, Seasonal AC (SAC), Perennial AC (PAC).

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INTRODUCTION

Allergic Conjunctivitis (AC) is the inflammation of conjunctiva in response to an allergen. It is one of the most common forms of conjunctivitis. Ocular allergies affect 6%-30% of the general population.[1] Recent clinical observations suggests that ocular allergic response is not confined to conjunctiva but is a disease affecting the entire ocular surface including conjunctiva, lids(with their high content of mast cells), cornea, tear film(with its immunoglobulins) and lacrimal gland.[2] The clinical profiles of AC may be described as follows:

- Acute AC
- Seasonal AC (SAC)
- Perennial AC (PAC)
- Vernal keratoconjunctivitis (VKC)
- Atopic keratoconjunctivitis (AKC)
- Giant papillary conjunctivitis. (GPC)

It is characterized by signs and symptoms ranging from itching, watering, redness, foreign body sensation, burning, photophobia, lid edema, conjunctival hyperemia, chemosis, watery or mucoid discharge, papillary reaction to severe sight threatening corneal complications.[3,4]

The exposure of conjunctiva to an allergen initiates an immunological hypersensitivity reaction that heralds the onset of allergic eye disease. Early phase response occurs when allergen specific IgE binds to Fc receptors on surface of mast cells leading to its degranulation and release of pre formed mediators mainly histamine and newly synthesized mediators mainly PGD2. The released histamine binds to H1 receptor on cell surfaces of conjunctival tissue resulting in vasodilatation and increased vascular permeability which is responsible for itching, burning and tearing. Binding to H2 receptor results in increased mucus production at ocular surface.[5] PGD2, considered being ten times more potent than histamine [6], increases conjunctival micro vascular permeability leading to redness, itching, chemosis and mucus production.

Late phase response is demonstrated by more severe disease characterized by interaction of allergen with T-cells and release of cytokines.

Management includes avoidance of allergen if known, topical mast cell stabilizers, topical anti histamines, topical steroids for acute exacerbation, systemic / topical cyclosporine to induce remission.[7] Commonly used topical anti-histamines are Olopatadine 0.1, 0.2 %, Alcaftadine 0.25 %. These newer anti allergic medications have combined anti histaminic and mast cell stabilization action [8] and help relieving acute symptoms in milder disease and reduce the use of topical steroids for the same. Olopatadine is a specific H1 inhibitor and has a rapid onset of action. Alcaftadine is an antagonist at H1, H2, and H4 receptor and has onset of action within fifteen minutes.[9, 10]

METHODS

Source of Data and Materials

Patients with Allergic conjunctivitis presenting at Minto ophthalmic hospital and research institute, attached to Bangalore Medical College and Research institute, Bangalore.

Method of Collection of Data

Study design: Randomized open label study.
Study period: 1.5 years
Study place: Minto ophthalmic hospital, Regional institute of ophthalmology
Sample size: Based on previous study by Stacey Ackerman et al[10], 78 % of subjects had minimal or no itch with Alcaftadine 0.25 % and less than 50 % had minimal or no itch with Olopatadine 0.1 %. Minimum expected difference between two groups will be 30 %. The sample size calculation is

$$N = \frac{(Z_\alpha + Z_{(1-\beta)})^2 [P_1(100-P_1) + P_2(100-P_2)]}{d^2}$$

Where Z_α = 1.96

$Z_{(1-\beta)}$ = 0.84

P_1 = 78%

P_2 = 50%

d = effect size

Thus n = 42 in each group
Rounding off to 50 in each group.

Inclusion criteria:

1. Patients ≥ 5 years and < 65 years of age with a history of allergic conjunctivitis.
2. Patients willing to give informed consent.
3. Patients with Signs and symptoms of clinically active allergic conjunctivitis (itching, foreign body sensation, conjunctival redness, chemosis, papillae) in either eye.

Exclusion criteria:

1. Patients not willing to give informed consent.
2. History of allergy or sensitivity to the study medications.
3. Prior participation with Alcaftadine and Olopatadine ophthalmic solution within 1 week.
4. Patients requiring topical immunosuppressant or topical steroids.
5. Contact lens users.
6. Patients planning for any ocular surgery during the study period.
7. Other clinically diagnosed ocular conditions like active ocular infection, narrow-angle glaucoma, pterygium, iritis, retinal diseases.
8. Pregnancy and lactating women.

Methodology:

After obtaining approval and clearance from the institutional ethics committee, the patients fulfilling the inclusion and exclusion criteria were enrolled for the study after obtaining informed consent. Patients were asked to fill a symptom questionnaire for baseline evaluation of symptoms and their severity. Assessment of clinical symptoms was done using subjective grading using a four point grading scale with respect to ocular itch, foreign body sensation, discharge, photophobia, conjunctival redness and papillae was assessed based of size. Complete ophthalmic evaluation was performed including Slit lamp bio microscopy to evaluate the baseline signs and their severity. One group received 0.1 % Olopatadine ophthalmic solution and the other group 0.25 % Alcaftadine ophthalmic solution. Symptom and sign relief was assessed after 15 minutes of instillation of eye drops. A follow up visit was scheduled after one day, one week and one month where symptoms and sign relief were assessed using slit lamp bio microscopy.

RESULTS

During the study period of 1.5 years, a total of 100 AC patients were evaluated. Their initial symptoms and signs and relief of same after initiation of treatment and its associated side effects were analyzed.

Age Distribution

Age	Number	Percentage
5-19 years	33	33
20-34 years	37	37
35-49 years	24	24
50-65 years	6	6
Total	100	100
Mean +/- SD		

Table Number 1: Age Distribution Of Study Participants

Most of the patients were young belonging to 20-34 year age group and 5-19 year age group, while the least belonged to 50-65 year age group.

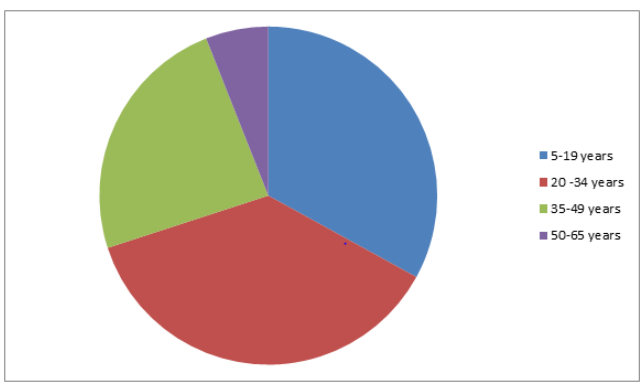

Figure 1: Age Distribution of Study Participants.

Sex Distribution

Gender	Number	Percentage
Male	47	47
Female	53	53
Total	100	100

Table Number 2: Gender Distribution Of Study Participants

Almost equal distribution of gender was observed in this study with females (53 %) being slightly preponderant than males (47 %).

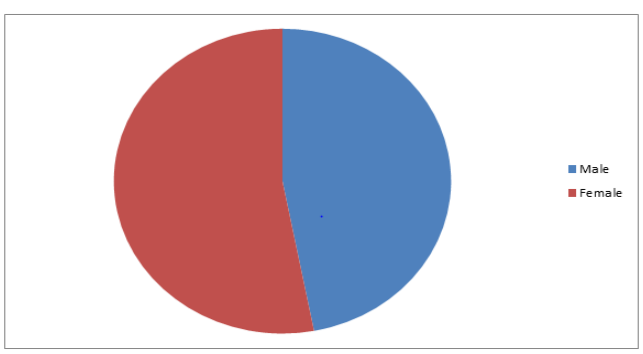

Figure 2: Gender Distribution of Study Participants

		DRUG		
		Alcaftadine	Olopatadine	Total
ocular itch	no	Count	2	6	8
		% within DRUG	4.00%	12.00%	8.00%
	yes	Count	48	44	92
		% within DRUG	96.00%	88.00%	92.00%

Table Number 3: Distribution Of Ocular Itch In Study Participants

Distribution of Ocular Itch in Study Participants

Comparison of Mean Itch Score

	Alcaftadine Mean ± SD	Olopatadine Mean ± SD	P value
At presentation	2.460 ± 0.7060	2.520 ± 0.8142	0.695
After 15 minutes	1.680 ± 0.7677	1.760 ± 0.6565	0.577
After 1 day	1.840 ± 0.7656	1.640 ± 0.5628	0.14
After 1 week	1.360 ± 0.7762	1.200 ± 0.4949	0.222
After 1 month	1.180 ± 0.6289	1.160 ± 0.4677	0.857

Table Number 4: Comparision Of Mean Itch Score

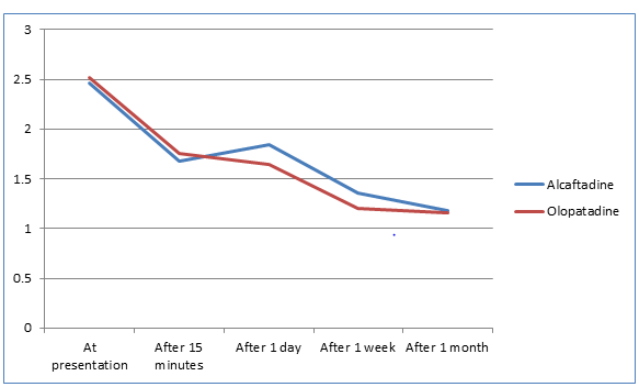

Figure 3: Comparison of Mean Itch Score between Groups.

DISCUSSION

Allergic conjunctivitis is the inflammation of conjunctiva in response to an allergen. It is characterized by signs and symptoms ranging from itching, tearing, discharge, redness to severe sight threatening corneal complications. Appropriate management alleviates symptoms and signs and improves quality of life.

Age Distribution

Most of the patients were young belonging to 20 - 34 year age group (37 %), second most common age group was 5-19 years (33 %) while the least belonged to 50 - 65 year age group (6 %). The mean age of presentation was 28.66 ± 9.12 in both alcaftadine and olopatadine group, in the study, Comparative analysis of safety and efficacy of Alcaftadine 0.25 %, Olopatadine hydrochloride 0.2 % and Bepotastine besilate 1.5 % in allergic conjunctivitis conducted by Ayyappanavar et al in 2021.[11]

Sex Distribution

Almost equal distribution of gender was observed in this study with females (53 %) being slightly preponderant than males (47 %).

In the Alcaftadine group, 29 % were females and 21 % were males. In the Olopatadine group, 24 % were females and 26 % were males. In the study conducted by Ayyappanavar et al in 2021, 38 were males and 22 were females in Alcaftadine group and 32 were males and 28 were females in Olopatadine group.[11]

Distribution and Scoring Of Ocular Itch

92% of patients had ocular itching. Majority of the population had ocular itch score of 2 (43 %) and 3 (41 %).

Comparison of Mean Itch Scores

The mean baseline itch score (at presentation) in the Alcaftadine group was 2.46 ± 0.7060 and 2.520 ± 0.8142 in the Olopatadine group. After day 1, there was substantial decrease in the mean itch scores in both groups – mean itch score in Alcaftadine group was 1.840 ± 0.7656 and in Olopatadine group was 1.640 ± 0.5628 indicating a mean decrease of 0. 62 in Alcaftadine group and 0.88 in Olopatadine group. After 7 days, mean itch score in Alcaftadine group was 1.360 ± 0.7762 and in Olopatadine group was 1.200 ± 0.4949 indicating a mean decrease of 1.1 in Alcaftadine group and 1.32 Olopatadine group from the baseline scores. After 1 month, mean itch score in Alcaftadine group was 1.180 ± 0.6289 and 1.160 ± 0.4677 in the Olopatadine group, indicating a mean decrease of 1.28 Alcaftadine group and 1.36 in Olopatadine group. Thus the mean decrease in the itch scores from baseline to after 1 month is significant in both groups. The reduction in mean itch scores between two groups at various time intervals was comparable with no statistically significant difference (p value > 0.05).

Our study corroborated with the study done by lakshey dudeja et.al, showing significant symptom relief in both groups with effect starting within minutes of instillation and almost complete relief at the end of one month.[12]

CONCLUSION

Both the study drugs resulted in significant decrease in ocular itch scores.

Thus both topical Alcaftadine 0.25 % and Olopatadine 0.1 % ophthalmic solutions are equally effective in relieving ocular itch in Allergic conjunctivitis.

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