Efficacy of 0.05% Cyclosporine A Eye Drops in Allergic Conjunctivitis in terms of Improvement in Ocular Itching Score

Muhammad Saleh Faisal¹, Kashif Ur Rehman Khalil², Mian Asim Shah³

ABSTRACT

BACKGROUND: While corticosteroids serve an effective therapy against severe cases of allergic conjunctivitis, their long-term use is restricted due to adverse effects.

OBJECTIVE: To determine the efficacy of 0.05% Cyclosporine-A in the treatment of allergic conjunctivitis.

MATERIAL & METHOD: A case series study of seven months duration was done at the Department of Ophthalmology, Khyber Teaching Hospital, Peshawar between July, 2016 to January, 2017. In this study a total of 259 patients were observed. The sample size was calculated by using WHO software in which the efficacy of 0.05% Cyclosporine-A eye drops was 78.6% with 95% confidence level and 5% margin of error.

RESULTS: In our study the mean age was 17 years ± 3.38. 59% patients were male while 41% patients were female. Efficacy of 0.05% Cyclosporine-A eye drops was analyzed in terms of itching score. It was effective in 228 (88%) patients and was not effective in 31 (12%) patients.

CONCLUSION: Our study concludes that the efficacy of 0.05% Cyclosporine-A eye drops was found to be 88% in treating allergic conjunctivitis in terms of improvement in ocular itching score.

Key words: Allergic conjunctivitis, Cyclosporine A, ocular itching score.

INTRODUCTION

Allergic conjunctivitis is type I hypersensitivity reaction, which occurs due to degranulation of Mast cells in response to the action of IgE. Ocular allergy is one of the most common hypersensitivity disorder affecting 15-20% of population in developed countries. It usually affects children in spring and summer season. One survey found that 14% of children in Hong Kong between 6 to 7 years of age and 24% of 13 to 14 years old people were affected by rhino-conjunctivitis. According to another epidemiological surveys, up to 35% of the US population suffers from ocular allergies, though the true prevalence may be higher.

Little data is available about Allergic conjunctivitis in the Asian population, however some understanding of prevalence of the condition has been obtained from the International Study of Asthma and Allergies in Childhood (ISAAC). 13-14 year age group revealed prevalence rates of 4.8% in Indonesia, 17.6% in Japan, 22.6% in Hong Kong and 23.9% in Bangkok. A cross sectional study conducted in Karachi by Baig et al. determined the prevalence of Allergic conjunctivitis among school going children age between 5-19 years. A total of 818 children were examined; 19.2% had Allergic conjunctivitis. Boys were more affected and increasing age was significantly associated with the diagnosis.

Allergic conjunctivitis can be divided into seasonal, perennial allergic conjunctivitis, vernal kerato-conjunctivitis, atopic kerato-conjunctivitis and giant papillary conjunctivitis. Patients with allergic and vernal kerato-conjunctivitis may develop corneal ulcers and extensive corneal vascularization that can lead to loss of vision. First line treatment includes avoidance of the allergens, cold compressions, artificial tears, lubricants, topical antihistamines and mast cell stabilizers. Topical steroids are used in more severe cases. Because of the side effects and complications related to long term use of steroids immuno modulators like Cyclosporine have been used in ocular allergies as an alternative anti-inflammatory with fewer side effects.

Cyclosporine-A (CsA) is a newer and safer steroid sparing alternative drug which is approved by the United States Food and Drug Administration.

In a meta-analysis, Wan and associates have concluded that though CsA is effective treatment for most forms of allergic conjunctivitis, most of the reported improvements by clinicians are subjective in nature and lack objectivity from a
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research point of view. However, it is also stated that clinical improvement is more effectively measured by taking into consideration the improvement in subjective symptoms as reported by patients. This shows the importance of utilizing a uniform grading score for reporting the discomfort of allergic conjunctivitis. The results of this study will give us new insight to the local efficacy of 0.05% Cyclosporine-A for allergic conjunctivitis and open future research recommendations in the treatment of allergic conjunctivitis.

The present study is designed to determine the efficacy of 0.05% Cyclosporine-A in the treatment of allergic conjunctivitis. 0.05% Cyclosporine-A is a novel drug and research studies are not yet conducted vastly on this drug regarding its role in allergic conjunctivitis. The results of this study will give us new insight to the local efficacy of 0.05% Cyclosporine-A for allergic conjunctivitis and open future research recommendations in the treatment of allergic conjunctivitis.

MATERIAL AND METHODS

A case series study was done at the Department of Ophthalmology, Khyber Teaching Hospital, Peshawar between July, 2016 to January, 2017. The study was conducted after approval from hospital ethical and research committee. Patients of either gender, between 6 to 26 years of age with history of perennial allergic-conjunctivitis, vernal kerato-conjunctivitis or atopic kerato-conjunctivitis were selected by Consecutive (non-probability) sampling technique and included in the study. While cases undergone eye surgery in last 3 months, experienced any adverse reaction to ocular drug, used any ocular or systemic medications like anti-histamines, mast cell stabilizers, non-steroidal anti-inflammatory drugs or steroids within 14 days prior to start of study, history of dry eye syndrome and bronchial asthma were excluded from study to avoid confounders.

All the patients were worked up with detailed history and clinical examination and diagnosis were confirmed using slit lamp examination. Ocular Itching Score was used to assess the severity of itching of the eye and has 4 grades. Grade 4 means an incapacitating itch which would require significant eye rubbing. 3 means a definite itch, you would like to rub the eye. 2 means mild continuous itch (can be localized) not requiring rubbing. 1 means an intermittent tickle sensation while 0 means absence of any discomfort. All the selected subjects had ocular itching score range 1-4. A pre-treatment OIS was recorded in the proforma. After confirmation of diagnosis, the patients were started on 0.05% Cyclosporine-A eye drops (one drop 12 hourly) in the affected eye(s). The patients were evaluated at Weeks 4, 8 and 12 after the initiation of therapy. Outcome was marked as either effective itch relief or no effective itch relief. The OIS was recorded at the end of follow-up (3-months) with total score on OIS as well as outcome group as whether the patient has achieved an effective itch relief or not. An improvement of ocular itching score 0-2 was considered as effective.

Complications were recorded in terms of increase in ocular itching, dryness, redness and severe burning at the time of instillation of drops.

The data was analyzed using the SPSS (version 16). Mean ± standard deviation were calculated for quantitative variables like age, pre-treatment and post-treatment ocular itching score. Frequency and Percentages were calculated for categorical variables like gender and efficacy. Efficacy was stratified with age and gender to see the effect modifiers. Post stratification chi square test was applied in which P value =0.05 was considered as significant. All results were presented in the form of tables.

RESULTS

In this study, a total of 259 patients were observed to determine the efficacy of 0.05% Cyclosporine-A eye drops for allergic conjunctivitis in terms of improvement in ocular itching score and the results were analyzed.

93(36%) patients were in age range of 6-15 years while 166(64%) patients were in age range of 16-26 years. Mean age was 17 year with SD ± 3.38.153(59%) patients were male while 106(41%) patients were female.

Pre-treatment and post treatment Ocular itching scores are analyzed in Table 1. All the patients had an ocular itching score range 1-4. After treatment, 228(88%) patients had ocular itching score range 0-2 and 31(12%) patients had ocular itching score range 3-4.

Stratification of efficacy with respect to age and gender are mentioned in Table 2 while stratification of frequency and efficacy with respect to type of allergic conjunctivitis are given in Table 3. As far as the efficacy of 0.05% Cyclosporine-A eye drops was concern, results showed that it was effective in 228(88%) patients and was not effective in 31(12%) patients.
Efficacy of 0.05% cyclosporine a eye drops in allergic conjunctivitis in terms of improvement in ocular itching score

### TABLE NO. 1
PRE & POST TREATMENT OCULAR ITCHING SCORE
(n=259)

<table>
<thead>
<tr>
<th>OCULAR ITCHING SCORE</th>
<th>FREQUENCY</th>
<th>PERCENTAGE</th>
<th>MEAN ITCHING SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PRE TREATMENT OIS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-2</td>
<td>0</td>
<td>0%</td>
<td>3 (SD ± 2.67)</td>
</tr>
<tr>
<td>3-4</td>
<td>259</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>259</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>POST TREATMENT OIS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-2</td>
<td>228</td>
<td>88%</td>
<td>1 (SD ± 1.03)</td>
</tr>
<tr>
<td>3-4</td>
<td>31</td>
<td>12%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>259</td>
<td>100%</td>
<td></td>
</tr>
</tbody>
</table>

### TABLE NO. 2
STRATIFICATION OF EFFICACY W.R.T AGE & GENDER DISTRIBUTION
(n=259)

#### STRATIFICATION OF EFFICACY W.R.T AGE DISTRIBUTION

<table>
<thead>
<tr>
<th>EFFICACY</th>
<th>6-15 years</th>
<th>16-26 years</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective</td>
<td>82 (35.96%)</td>
<td>146 (64.03%)</td>
<td>228</td>
<td>0.9582</td>
</tr>
<tr>
<td>Not effective</td>
<td>11 (35.48%)</td>
<td>20 (64.51%)</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>93 (35.90%)</td>
<td>166 (64.09%)</td>
<td>259</td>
<td></td>
</tr>
</tbody>
</table>

#### STRATIFICATION OF EFFICACY W.R.T GENDER DISTRIBUTION

<table>
<thead>
<tr>
<th>EFFICACY</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective</td>
<td>135 (59.21%)</td>
<td>93 (40.78%)</td>
<td>228 (99.99%)</td>
<td>0.9030</td>
</tr>
<tr>
<td>Not effective</td>
<td>18 (58.06%)</td>
<td>13 (41.09%)</td>
<td>31 (99.99%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>153 (59.04%)</td>
<td>106 (40.92%)</td>
<td>259 (99.99%)</td>
<td></td>
</tr>
</tbody>
</table>

### TABLE NO. 3
STRATIFICATION OF FREQUENCY AND EFFICACY W.R.T TYPE OF ALLERGIC CONJUNCTIVITIS
(n=259)

<table>
<thead>
<tr>
<th>Type of Allergic Conjunctivitis</th>
<th>Frequency</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perennial</td>
<td>117 (45.17%)</td>
<td>101 (44.29%)</td>
</tr>
<tr>
<td>Vernal</td>
<td>63 (24.32%)</td>
<td>53 (23.24%)</td>
</tr>
<tr>
<td>Atopic</td>
<td>79 (30.50%)</td>
<td>74 (32.45%)</td>
</tr>
<tr>
<td>Total</td>
<td>259 (99.99%)</td>
<td>228 (99.99%)</td>
</tr>
</tbody>
</table>

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DISCUSSION
Allergic conjunctivitis, a common ophthalmic condition targeting mostly children and young adults is a bilateral interstitial inflammation of the conjunctiva. The immuno-pathogenic mechanism is complicated but considered to be mediated by IgE. Itching is a consistent and most common symptom of seasonal and perennial allergic conjunctivitis. The diagnosis of allergic conjunctivitis is usually clinical. Milder cases are mostly managed with topical anti-histamines with or without tear substitutes while advanced cases need long term steroid therapy, which is associated with list of known complications. Our study is designed to determine the efficacy of 0.05% Cyclosporine-A in the treatment of allergic conjunctivitis. In our study, mean age was 17 years with SD ± 3.38. Male patients constitute 59% while 41% patients were female. Efficacy of 0.05% Cyclosporine-A eye drops was analyzed and found to be effective in 228(88%) patients and was not effective in 31(12%) patients. In addition, it has been observed that among different types, CsA was more effective in perennial conjunctivitis (44.29%) followed by Atopic (32.45%) and Vernal (23.24%) conjunctivitis, but proper clinical trial need to be conducted to confirm it.

In a retrospective review by Wu M and co-workers, it was found that after 3-month treatment with topical 0.05% CsA drops, there was reduction in the itch severity score compared with baseline. Itch severity score (out of 10) at baseline was 7.9 ± 0.7 and after 3-months treatment with topical 0.05% CsA drops were 4.5±1.0 (P-value <0.0001) and 78.6% of subjects were able to be tapered off steroid eye drops. In another study conducted by Jameel et al, ocular itching score was not the variable, but certain other variables were analysed and topical use of cyclosporine-A proved to be effective. In this study there were 32 males and 5 females. Patients had mean age of 9.8 years (ranged 5 to 18 years). There was a statistically significant improvement in the conjunctival and cornel signs after using topical cyclosporine. Bulbar conjunctival hyperemia improved in 36(97.3%) patients (p<0.01) while punctate keratitis improved in 34(91.9%) patients (p<0.02). Trantas dots showed decrease in number in 31(83.8%) patients (p<0.01). Limbal edema improved in 33(89.2%) patients (p>0.05). Palpebral conjunctival papillae showed improvement in 19(51.4%) patients (p>0.05). Results near to our study were shown in another study conducted by Ozcan AA in which mean age was 20 years with SD ± 4.11. Fifty five percent patients were male while 45% patients were female. Efficacy of 0.05% Cyclosporine-A eye drops was analyzed and found to be effective in 85% patients but not in 15% patients.

CONCLUSION
Our study concludes that 0.05% Cyclosporine-A eye drops was found to be effective in the treatment of allergic conjunctivitis in terms of improvement in ocular itching score.

REFERENCES
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