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Use of Topical Cyclosporine A 0.05% in Treatment of Adenoviral Keratoconjunctivitis-Related Subepithelial Infiltrates

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Abstract
Aim : *To evaluate the treatment with topical cyclosporine A (CsA) in patients with subepithelial infiltrates (SEI).*
Material & Methods: *Hospital-based study was conducted over a period of one year. A total of 25 patients, 36 eyes with supepithelial infiltrates following adenoviral keratoconjunctivitis were included in the study. All patients had been previously treated with topical corticosteroids without any improvement. Data was recorded in form of best corrected visual acuity (BCVA), evaluation of corneal subepithelial infiltrate score (CSIS) prior to treatemt and after the last follow up visit.*
Results:*10 females(40 %) and 15 males (60 %) were included in the study, best corrected visual acuity (BCVA) was in range 6/6-6/60 pre-treatement and 6/6-6/18 after treatment.The average followup in patients was after 4-6 months. After treatment with 0.05 % topical CsA, 28 eyes (77 %) improved to 0 score on CSIS and BCVA of 6/6 in 27 eyes while recurrence occurred in 6 eyes (16.6 %).*
Conclusion*: Topical Cyclosporine A 0.05% is a safe and effective alternative treatment in patients with adenoviral keratoconjunctivitis -related subepithelial infiltrates.*
Keywords: *Epidemic keratoconjunctivitis, subepithelial infiltrates, cyclosporine A*

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I. Introduction

Adenoviridae are icosahedral, nonenveloped, double stranded DNA viruses that can cause an array of diseases including conjunctivitis, gastroenteritis, hepatitis, myocarditis and pneumonia. This family of viruses is the most common cause of acute viral infection of the conjunctiva, accounting for up to 75% of all conjunctivitis cases. The most frequent manifestation of ocular adenoviral infection is epidemic keratoconjunctivitis (EKC) [1]. The incubation period of EKC varies between 4 and 24 days, and the symptoms tend to last for 7–21 days. The patient may remain infectious for 10–14 days. The most common symptoms are red eyes, excessive tearing, foreign body sensation, and photophobia. In more severe cases, patients can present with ocular or periorbital pain and decreased visual acuity. Decreased visual acuity is generally seen as a result of multifocal subepithelial infiltrates (SEIs) which are observed in up to 50% of the cases. These SEIs represent a cellular immune reaction against viral antigens deposited in the corneal stroma under the Bowman's membrane and can persist for weeks to years and cause blurred vision, halos, glare, and photophobia. Topical steroids are effective in the treatment of SEI; however, after stopping steroid eye drops, recurrences may develop, and the patient may become steroid dependent. With long-term treatment, side effects of steroids such as intraocular pressure (IOP) increase, and cataract can develop. Therefore, topical cyclosporine A (CsA) has been proposed as a means of longterm treatment of SEIs [2, 3]. This study is focused to evaluate the treatment with topical cyclosporine A (CsA) in patients with subepithelial infiltrates (SEI).

II. Material & Methods

Hospital-based study was conducted over a period of one year. A total of 25 patients, 36 eyes with supepithelial infiltrates following adenoviral keratoconjunctivitis were included in the study. Written informed consent was taken from all the study patients. A detailed history and ocular examination of each patient were recorded. All patients had been previously treated with topical corticosteroids without any improvement and in whom SEIs had persisted for more than 3 months. Data was recorded in form of best corrected visual acuity (BCVA) and detailed biomicrocopic anterior segment examination. The corneal subepithelial infiltrate score (CSIS) prior to treatment and after the last follow up visit was recorded. CSIS varied between 0-4 was constituted according to SEI seen on biomicrocopic anterior segment examination (0= no infiltrates, 1=1-5 ,2 =6-10,3=11-15 and 4 constituted more than 16 infiltrates).All patients were treated with topical cyclosporine

0.05 % four times daily along with topical steroids that patient was using previously for one month followed by only topical cyclosporine 0.05 % twice daily and follow-up period was between 4-6 months. BCVA and CSIS score were recorded for each patient at the last follow-up visit.

Figure 1: Subepithelial infiltrates CSIS = 2

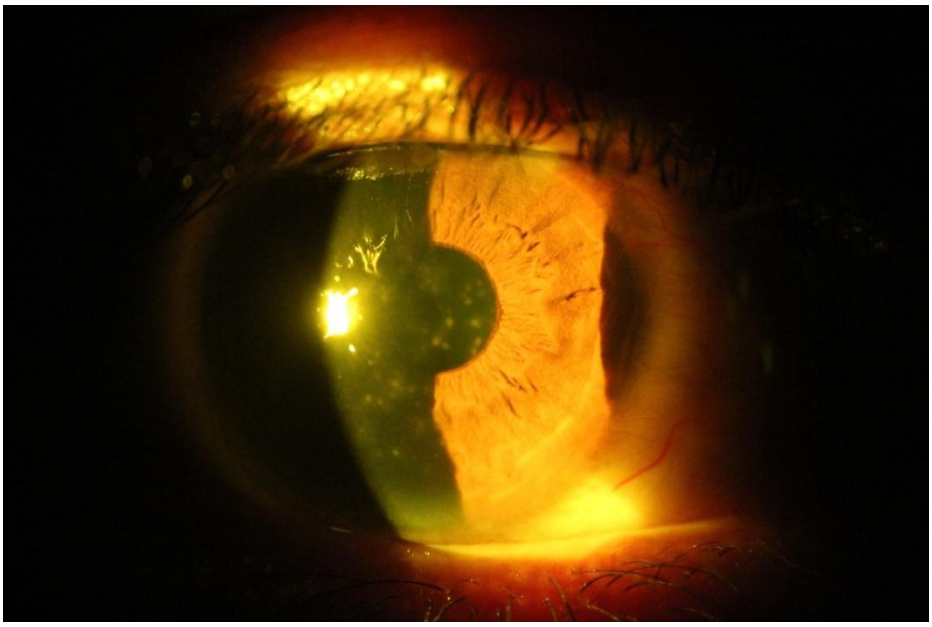

Figure 2: CSIS =4

III. Results

A total of 25 patients, 36 eyes with supepithelial infiltrates following adenoviral keratoconjunctivitis were included in the study , of these 10 were females(40 %) and 15 were males (60 %).SEI were located in both eyes of 11 patients and affected one eye of 14 patients. Prior to treatment, BCVA was 6/6 in 19 eyes and there were varying degrees of visual loss with values 6/9 to 6/60.Prior to therapy, 1 patient had CSIS of 4 while majority had score of 1.Therapy with topical CsA 0.05 % was started in all the patients. After treatment, 28 eyes (77 %) improved to 0 score on CSIS and BCVA of 6/6 in 27 eyes while recurrence occurred in 6 eyes (16.6 %).Treatment was discontinued in patients with no SEIs left.

IV. Discussion

Adenoviridae cause EKC, which can have profound effects on patients' quality of life for weeks. Subepithelial inflitrates are seen in 50% of these patients and cause decreased visual acuity, blurred vision, halos, glare, and photophobia [1]. Immune response against viral replication in subepithelial keratocytes is responsible for SEIs. Histologically, these infiltrates are composed of lymphocytes, histiocytes, and antigen-presenting Langerhans cells[4]. Hence, topical corticosteroids and topical CsA are considered effective treatment

regimens [2, 3, 5].But many patients suffer from long term side effects of topical steroids including raised intraocular pressure, cataract formation and recurrence of infiltrates after discontinuation of steroids. The main reason cyclosporine is a beneficial is because it allows the clinician to use an agent that is a powerful T-cell immunomodulator without the inherent complications associated with chronic corticosteroid usage .Thus topical Cyclosporine A 0.05 % as evaluated in this study is an effective alternative. Jeng and colleagues have reported that a single dose per day or every other day of 1% or 0.05% topical CsA treatment following an initial therapy of topical 1% CsA and steroids for a month was effective in SEI treatment [2]. Reinhart and colleagues have reported that there were amelioration and decrease in SEI number in the 48 eyes out of 70 which had SEIs after EKC infection after a therapy with 2% topical CsA, and there were no recurrences after therapy was discontinued[6]. Romanowski and colleagues reported that in their trials 0.5% and 2% topical CsA treatments were effective in decreasing the number of SEI formations, however it was claimed that this agent could facilitate the risk of endemics by increasing viral replication[7].

Table 1: Clinical course of patients in whom SEI developed after EKC,that were treated with topical CsA 0.05% eye drops

Patient	Age/Sex	Affected eye	Initial BCVA	Initial CSIS	BCVA at last follow-up	CSIS at last follow-up	Recurrence
1	22/F	R/E	6/6	1	6/6	0	NO
2	36/M	R/E,L/E	6/6,6/9	1,1	6/6,6/6	0,0	NO
3	16/M	R/E	6/6	1	6/6	0	NO
4	50/F	L/E	6/60	4	6/12	1	YES
5	30/F	R/E,L/E	6/9,6/12	1,2	6/9,6/6	1,0	NO
6	18/M	R/E,L/E	6/12,6/12	1,1	6/6,6/6	0,0	NO
7	40/F	L/E	6/9	1	6/6	0	NO
8	75/M	R/E,L/E	6/9,6/60	1,3	6/9,6/18	1,2	YES
9	27/M	R/E	6/6	1	6/6	0	NO
10	30/M	L/E	6/6	1	6/6	0	NO
11	17/F	R/E,L/E	6/6,6/6	1,1	6/6,6/6	0,0	NO
12	22/M	R/E	6/18	2	6/6	0	NO
13	26/M	R/E	6/6	1	6/6	0	NO
14	27/F	R/E,L/E	6/6,6/9	1,1	6/6,6/6	0,0	NO
15	52/M	L/E	6/12	1	6/9	1	NO
16	56/M	R/E	6/9	1	6/9	1	YES
17	28/F	R/E,L/E	6/6,6/6	1,1	6/6,6/6	0,0	NO
18	22/M	R/E	6/6	1	6/6	0	NO
19	21/M	R/E,L/E	6/6,6/6	1,1	6/6,6/6	0,0	NO
20	43/M	L/E	6/12	2	6/6	0	NO
21	36/F	R/E,L/E	6/6,6/6	1,1	6/6,6/6	0,0	NO
22	33/M	R/E	6/9	1	6/9	1	NO
23	37/F	L/E	6/6	1	6/6	0	NO
24	66/M	R/E,L/E	6/9,6/18	1,2	6/9,6/9	0,1	YES
25	16/F	R/E,L/E	6/6,6/6	1,1	6/6,6/6	0,0	NO

V. Conclusion

Topical Cyclosporine A 0.05% is a safe and effective alternative treatment in patients with adenoviral keratoconjunctivitis -related subepithelial infiltrates in patients previously treated with topical corticosteroids without any improvement.

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