ORIGINAL ARTICLE

Comparison of Topical Steroid Drops with Cyclosporin Eye Drops in the Treatment of Corneal Subepithelial Infiltrates in Epidemic Keratoconjunctivitis

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ABSTRACT

Aim: To assess and compare the incidence of recurrence of sub epithelial corneal infiltrates in epidemic keratoconjunctivitis after cessation of topical steroid Vs cyclosporin eye drops.
Method: This study was conducted at CMH Kharian from Jan 2017 to June 2018. The patients were divided into two groups using nonprobability lottery method. Group A included those who received topical steroid drops and group B received topical Cyclosporine eye drops. A total of 88 patients fulfilling inclusion and exclusion criteria were enrolled in the study. Patients in group A were started with topical Loteprednol eye drops eight hourly and those of group B were started with topical Cyclosporine 0.05% eye drops eight hourly. The patients were followed up at two, four, eight and 12 weeks.
Results: The SEIs resolved in both the groups by week 12, however the resolution was slightly quicker in group A. The SEIs resolved in about 84.1% of cases in group A and in 70.4% cases in group B at the end of 4 weeks. The incidence of recurrence was higher in group A being 11.3%(5 patients) while it was 2(4.5%) in group B
Conclusion: Cyclosporine eye drops are a safe and effective treatment of epidemic keratoconjunctivitis related SEIs, with an added advantage of reducing incidence of recurrence.
Keywords: Epidemic Keratoconjunctivitis (EKC), Corneal Subepithelial Infiltrates (SEIs), Cyclosporin eye drops.

INTRODUCTION

Epidemic keratoconjunctivitis (EKC) is caused mostly by adenovirus, especially its strains eight, 19 and 37[4,5,6]. Adenovirus is a ubiquitous virus which predominantly affects the mucoepithelium. It is the most common cause of infectious conjunctivitis worldwide accounting for about 75% of all cases[1]. Its morbidity is high in children and immunocompromised patients[2]. Its mode of transmission is direct i.e., by hands, fomites etc. and indirect i.e., by tonometer, eye dropper bottle, slit lamp etc.[3]. The incubation period is usually 2 to 14 days [7] and the person remains infectious for up to 10 to 14 days after the onset of symptoms[8]. The corneal involvement typically appears after 7 to 10 days of initial presentation in the form of Sub Epithelial Infiltrates (SEIs) in the anterior stroma[9]. These opacities are pathognomonic of EKC and may persists for several weeks to years causing visual deterioration, glare, photophobia and irregular astigmatism[10]. These SEIs represents cellular immune reaction comprising of lymphocytes, macrophages and antigen presenting Langerhans cells[11,14]. Although it is a self-limiting disease, but treatment is frequently needed to shorten the duration and relieve the symptoms[12]. A few Ophthalmologists have used topical steroid eye drops to resolve these lesions with encouraging results, however these drops are associated with increased incidence of recurrence of these lesions[13]. Cyclosporin eye drops have also shown promising results in resolution of these SEIs with an added advantage of reduced incidence of recurrence[13,18]. This study was done to compare the recurrence of SEIs after stopping topical Cyclosporin eye drops Vs steroid eye drops

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METHODOLOGY

This study was conducted at CMH Kharian from Jan 2017 to June 2018, after taking clearance from the hospital ethical committee. It was a single blinded, prospective study. The patients were divided into two groups using nonprobability lottery method. Group A included those who received topical steroid drops and group B received topical Cyclosporine A eye drops. The inclusion criteria comprise of fresh cases of SEIs, between the ages of 20 to 50 years, having a vision of 6/6 before the illness. The exclusion criteria included patients suffering from allergic conjunctivitis, ocular surface disease like Sjogren syndrome, corneal ulcer, blepharitis, old corneal opacity, glaucoma and those who had been using steroids in the past e.g., uveitis. The diagnosis of epidemic keratoconjunctivitis related SEIs was made clinically based on symptoms of glare, photophobia and blurred vision after recent episode of epidemic keratoconjunctivitis. On Slit lamp examination SEIs were confirmed as greyish white granular sub epithelial lesion with fuzzy borders.

A total of 88 patients fulfilling the above criteria were included in the study. After taking the informed consent the patients were divided into group A and group B. All patients underwent complete ophthalmic examination including visual acuity, tear film assessment, corneal examination and anterior chamber assessment. Intra ocular pressure was measured using air puff tonometer. The corneal sub epithelial opacities were examined under high magnification of slit lamp and counted, and the patients were divided in two groups depending upon the number of SEIs in each cornea, i.e., less than eight SEIs or more than eight SEIs. Patients in group A were started with topical Loteprednoleye drops eight hourly and those of group B were started with topical Cyclosporine 0.05% eye drops

eight hourly. The patients were followed up at two, four, eight and 12 weeks. Resolution of SEIs were defined as complete disappearance of these opacities leaving behind clear cornea. On resolution both cyclosporine and loteprednol eye drops were tapered off in next two weeks. The patients were advised to continue monthly follow up for next two months, during which they were assessed for any recurrence of corneal SEIs. Those who remained clear at the end of two months were discharged from the outpatient department. Data was recorded in predesigned proforma and SPSS version 21 was used for data analysis. Frequency and percentages were calculated and presented for qualitative data. Studentt-test was applied for numerical variables. P value ≤0.05 was considered as significant.

RESULTS

A total of 88 patients were included in this study which were divided in two equal groups. Group A were treated with topical Loteprednol and group B with cyclosporin eye drops. The demographic details are shown in table 1 which shows the mean age of patients in group A was 30.47 years (20 to 49 years) while it was 29.54 years for group B

Table 1: Demographic characteristics

AGE	Group A	Group B
20 – 30	23	25
31 – 40	15	14
41 – 50	6	5
Range	20 - 49 years	20 – 46 years
Mean	30.48±7.53	29.55±7.17
Male	29	26
Female	15	18

In group A there were 30 (68.2%) patients with less than 8 SEIs and 14 (34.1%) with more than 8 SEIs, while in group B 26 (59.1%) patients had less than 8 SEIs and 18 (40.9%) had more than 8 SEIs.

Table 2: Resolution of Corneal SEIs

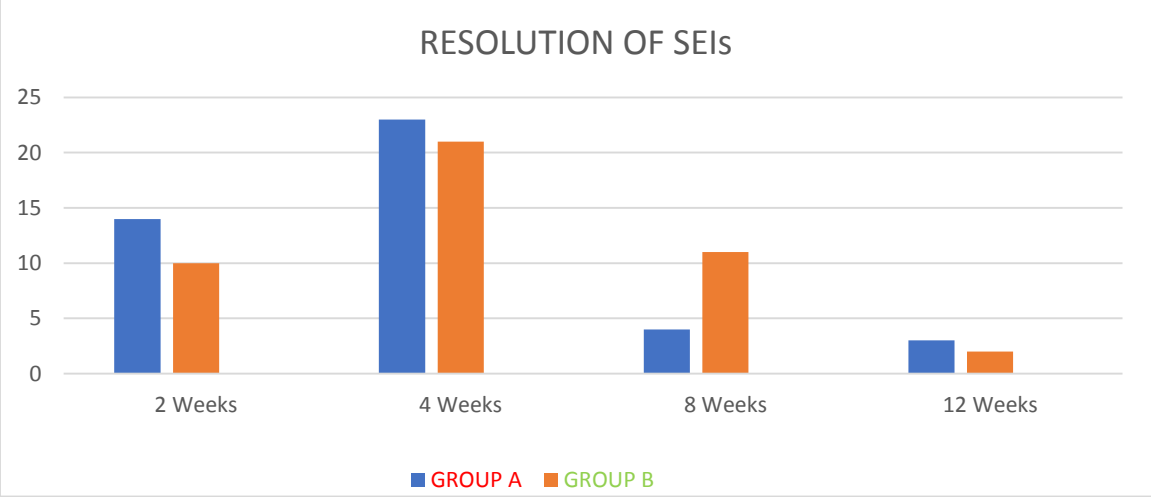
Corneal Involvement	Group A	Group B
Less than 8 SEIs	30 (68.18%)	26 (59.09%)
More than 8 SEIs	14 (31.81%)	18 (40.90%)
Resolution in 2 weeks	14 (31.8%)	10 (22.7%)
Resolution in 4 weeks	23 (52.2%)	21 (47.7%)
Resolution in 8 weeks	4 (9.1%)	11 (25%)
Resolution in 12 weeks	3 (6.8%)	2 (4.5%)

As is clear from table 2 these SEIs resolved in both the groups by week 12, however the resolution was slightly quicker in group A. In group A 31.8% of SEIs resolved at the end of second week and another 52.3 % by the end of fourth week(total 84.1%) whereas 22.7% resolved at second week and another 47.7% at the end of fourth week (total 70.4%) in group B at the end of same interval.
The incidence of recurrence was higher in group A than Group B with a significant p-value 0.017 (Table 3)

Table 3: Recurrence

Drug Used	n	Recurrence
Topical steroids (Group A)	44	5 (11.3%)
Topical Cyclosporin (Group B)	44	2 (4.5%)

P value 0.017



DISCUSSION

Viral Keratoconjunctivitis is a condition that frequently affects the population as an epidemic especially in summers. The human Adenovirus accounts for about 65% to 90% of these [15]. In addition to its morbidity it also cost in the form of lost productivity and cost of medicines etc. which amounts to approx. US$ 430million[16]. Epidemic Keratoconjunctivitis involves both the conjunctiva and cornea and can cause long lasting morbidity in the form of Development of corneal SEIs. Traditionally it had been treated symptomatically with artificial tears, topical antihistamine drops and cold compresses, however the patients demand some treatment to shorten the course of illness and relieve symptoms. In a study conducted by Butt AL, the corneal subepithelial infiltrates lasts for about 45 days causing photophobia, blurring of vision and astigmatism[10], a fact also observed in our study where about 70% to 80% of SEIs lasted for about 30 days. A few ophthalmologists use topical steroids with the aim to shorten the duration and decrease patients discomfort[17-21].These drops do make the patients comfortable however they are associated with higher incidence of recurrence of these SEIs and it also increases virus shedding there by

prolonging the infectivity periods[17,18,19]. Our study also shows that those patients who have used topical steroids showed relatively early resolution as compared to those who used cyclosporine drops, however it was observed that ultimately the corneal lesions resolved in both the groups[20]. Okumus in his study also showed complete resolution of SEIs in patients who used cyclosporin eye drops [20]. Our study also showed that the incidence of recurrence of SEIs was lower in patients who used cyclosporine drops being only 4.5% as compared to 11.7% in steroid group. It has also been learnt that cyclosporine is also effecting in treating the recurrences that occur after using topical steroids, as has been showed by Levinger et al in their study, that compared the efficacy of cyclosporin eye drops and showed improvement in SEIs in 9 out of 12 patients who had previously used topical steroid drops and were resistant to it[22]. Similar results were seen in a study by Jeng et al on twelve eyes which have developed SEIs and were responsive to steroids drops but were resistant to tapering. After the initiation of cyclosporin drops steroids could be successfully tapered without any recurrence[23]. Romanowisky et al showed in their study that use of topical steroids only improves patients' comfort, however it does not shorten the course of illness, rather their prolonged use is associated with serious side effects like glaucoma, cataract and corneal thinning[13].We have also found in our study that cyclosporine eye drops are comparable to topical steroid drops in resolving the SEIs but has an added advantage of reduce recurrence rate moreover they are safe and effective in treatment with the added advantage that there is a statistically significant reduction in recurrence**.**

CONCLUSION

Cyclosporine eye drops are a safe and effective treatment of epidemic keratoconjunctivitis related SEIs, with an added advantage of reduced incidence of recurrence.

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REFERENCES

1. Jhanji V, Chan TC, Li EY, Agarwal K, Vajpayee RB. Adenoviral Keratoconjunctivitis. Surv. Ophthalmol 2015; 60(5):435-443
2. Ghebremedhin B. Human Adenovirus: Viral pathogen with increasing importance. Eur J of Microbial Immuno l(BP). 2014;4(!): 26-33
3. Lion T. Adenovirus infection in immunocompetent and immunocompromised patients. Clinical Microbiol Rev. 2014; 27(#):441-462
4. Zhang L, Zhao N, Sha J et al. Virology and epidemiology analysis of global Adeno Virus associated conjunctivitis outbreak 1953-1013. Epidemiol Infect 2016; 144(8): 1661-1672
5. Lee YC, Chan N, Hnng IT et al. Human Adenovirus type 8 epidemic keratoconjunctivitis with large corneal epithelial full layer detachment. An endemic outbreak with uncommon manifestations. Clin. Ophthalmol. 2015;9: 953-957
6. Melendez CP, Florentino MM, Martinez IL. Outbreak of epidemic keratoconjunctivitis caused by adenovirus in medical students. Mol Vis 2009; 15: 557-562
7. Kaufman HE. Adenovirus advances. New diagnostic and therapeutic options. Current Opin in Ophthalmol. 2011; 22: 290-293
8. Ford E, Nelson KE, Warren D. Epidemiology of epidemic keratoconjunctivitis. Epidemiol Review. 1987;9: 244-261
9. Rajaiya J, Chodosh J. New paradigms in infectious eye disease; adenoviral keratoconjunctivitis. Arch soc Esp Oftalmol 2006; 81: 493-498
10. Butt Al, Chodosh J. Adenoviral keratoconjunctivitis in a tertiary care eye clinic. Cornea 2006;25: 199-202
11. Kurna SA, Altun A, Oflaz A, Arsan AK. Evaluation of impact of persistent subepithelial corneal infiltrates on the visual performance and corneal optical quality after epidemic keratoconjunctivitis. Acta Ophthalmol 2015;93(4):377-382
12. Leanerts L, Naesens L. Antiviral therapy for adenovirus infection. Antiviral res2006;17:172-180
13. Romanowisky EG, Yates KA, Gordon YJ. Short term treatment with a potent topical corticosteroid of an acute ocular adenoviral infection in the New Zealand white rabbit. Cornea; 20: 657-660
14. Lund E, Stefani FH. Cornealhistology after epidemic keratoconjunctivitis. Arch Ophthalmol 1978; 96: 2085-88
15. O' Brien TP, Jeng BH, Mc Donald M, Raizman MB. Acute conjunctivitis truth and misconceptions. Curr Med Res Opin 2009; 25(8): 1953-61
16. Udeh BL, Schneider JE, Obsfeldt RL. Cost effectiveness of a point of care test for adenoviral conjunctivitis. Am J Med Sci 2008; 336(3): 254-64
17. Wilkins MR, Khan S, Bunce C, Khawaja A, Siriwardena D, Larkin DF. A randomized placebo-controlled trial of topical steroids in presumed viral conjunctivitis. Br. J Ophthalmol 2011;95: 1299-1303
18. Clement C, Capriotti JA, Kumar M et al.Clinical and antiviral efficacy of an ophthalmic formulation of dexamethasone povidone-iodine in a rabbit model of adenoviral keratoconjunctivitis. Inves Sci 2011; 52(1):845-850
19. Ghanem RC, Vargas JF, Ghanem VC. Tacrolimus for the treatment of subepithelial infiltrates resistant to topical steroids after adenoviral keratoconjunctivitis. Cornea 2014;33: 1210-13.
20. Clement C, Coskun E, Jatar MG, Kaydu E, Yayuspayi R, Comez A et al. Cyclosporin A0.5% eye drops for the treatment of subepithelial infiltrates after epidemic keratoconjunctivitis. BMC Ophthalmol2012;12: 42
21. Aydin Kurna S, Altun S, Olfaz A, Karatay Arsan A. Evaluation of the impact of persistent subepithelial corneal infiltration on the visual performance and optical quality after epidemic keratoconjunctivitis. Acta Ophthalmol 2015;93: 77-82
22. Levinger E, Slomovic A, Sansanayndh W, Bahar I, Stomovic AR. Topical treatment with 1% cyclosporin eye drops for subepithelial infiltrates secondary to adenoviral keratoconjunctivitis. Cornea 2010;29: 638-640.
23. Jeng BH, Holsclaw DS. Cyclosporin A 1% eye drops for the treatment of subepithelial infiltrates after adenoviral keratoconjunctivitis. Cornea 2011; 30(9): 958-61