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Original Research Article

Efficacy of cyclosporine 0.05% in patients with dry eye syndrome

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ABSTRACT

Background: An even and smooth ocular surface is vital for the functioning and comfort of the eyes. Dry eye is a group of disorders of the tear film which is due to either decreased production or increased evaporation and is associated with symptoms of ocular discomfort. Smoking and drugs have been suggested as risk factors in various studies. Cyclosporine has been shown to reduce the cell-mediated inflammatory reactions associated with the inflammatory ocular surface disease.
Methods: 50 eyes of 25 patients suffering from dry-eye syndrome were included in this study. Three major ocular symptoms of dry eye i.e., ocular pain, burning, and foreign body sensation were studied in this study. Each symptom was given a score from 0 to 1 so that the ocular symptoms were given a score from 0 to 3.
Results: There was a significant reduction in ocular symptoms score (OSS) 2.25 before treatment to 0.6 after 3 months of treatment (p=0.01). In addition, the Schirmer's paper test scores improved from 1.23 mm to 5.91 mm, which is significantly different (p=0.001). The tear film breakup time also improved from 5.49s to 9.86s.
Conclusions: Cyclosporine 0.05% has been established to be effective and safe in our study.

Keywords: Cyclosporine, Dry eye, Tear film

INTRODUCTION

A regular, even and smooth ocular surface is vital for the functioning and comfort of the eyes. Dry eye is a group of disorders of the tear film which is due to either decreased production or increased evaporation and is associated with symptoms of ocular discomfort. Smoking and drugs have been suggested as risk factors in various studies. The current concept in the pathophysiology of dry eye combines neurohormonal with immune factors that alter the lacrimal gland tear production. Qualitative and quantitative alterations in tears start an inflammatory cascade on the ocular surface, which is exacerbated by long-term changes in the local epithelium and goblet cells. The chronic inflammation is increased by molecules such as ICAM-1 which recruits more immune cells and induces apoptosis of the conjunctival epithelium. There is uneven distribution of tear film on the damaged ocular surface giving rise to a visious cycle of inflammation and altered tear film osmolarity which further causes the surface damage.[1,2] Inflammatory mediators play a major role in pathogenesis of dry eye syndrome as proven by many studies. Dry eye syndrome is essentially a clinical diagnosis, but various tests are available for diagnosis in certain cases.[3] Schirmer's test measures the amount of tear film production either basal or reflex based on the type of test used. Lysozyme concentrations associated with the tear film are also sometimes measured. Tear film cytology is used in cases with advance ocular surface damage to assess the goblet cell function.

Various clinical and pathological changes altering the tear film, lacrimal glands, and eyelids with resulting deficiency in the tear film whether caused by decreased lacrimation or excessive evaporation play a role in pathogenesis of dry eye syndrome.[4] An interplay of various factors including ocular surface cells, including epithelial, inflammatory, immune, and goblet cells, may play a role in pathogenesis.[5] This interplay between abnormal surface epithelium, abnormal tear film osmolarity and inflammation leads to surface toxicity mediated by T-cell lymphocytes.[6] Decreased tear volume, disorder of cytokine balance, and increased matrix metalloproteinases is also seen in dry-eye disease.[7]

Medical therapies are used in most cases to treat dry eyes. Inflammation is seen consistently in different forms of dry eye and dry-eye-associated complications, and many patients respond therapeutically to anti-inflammatory treatments. Cyclosporine decreases ocular surface inflammation and results in an improvement in Schirmer test results and punctuate corneal epithelial staining.[8] An increase in goblet cell numbers in both non-Sjögren's and Sjögren's syndrome dry eye, as well as a decrease in epithelial cell turnover has also being reported.[8,9] Therapeutic benefits of cyclosporine are typically achieved in about a month. Cyclosporine specifically blocks T-cell activation so it a better alternative as compared to corticosteroids because it is not associated with either significant systemic adverse events or the common steroid-related ocular side effects such as cataract and glaucoma.[9,10]

Cyclosporine also prevent the mitochondrial permeability transition pore from opening, with one of the effects of inhibiting cytochrome c release, resulting in an adverse effect on apoptosis.[10,11]

Its main complications are hypertension and nephrotoxicity, however, when used in low doses, the incidence of nephrotoxicity is much reduced.[10] Topical use of cyclosporine A avoid many side effects associated with systemic administration.[11,12] This study is being done to investigate and evaluate the safety and efficacy of topical cyclosporine A 0.05% for the treatment of moderate to severe dry eye disease.

METHODS

In this prospective study, 50 eyes of 25 patients with dry-eye disease were included.

Inclusion criteria

Patients included men and women aged ≥18 years, they must be able to understand and follow study related advice, their tear film break up time should be ≤10s and Schirmer tear test without anaesthesia ≤5mm in 5 minutes.

Exclusion criteria

Patients who were not willing to give consent, patients with active blepharitis, meibomian gland disease, lid margin inflammation or ocular allergy, Any structural abnormalities on external eye examination for e.g., entropion, trichiasis, lid scarring and many more, any systemic or topical medication other than artificial tears and contact lens wearer.

Non randomized controlled trial 3 months from February 2018 to April 2018 was done at PGIMS, Rohtak. All patients coming to the outpatient department with complaints of itching, watering, redness or foreign body sensation of eyes were evaluated for inclusion in study. The patients and the parents of minor patients were informed and written consent was taken regarding inclusion in the study. Their complete history, duration of illness, chief complaints and treatment taken were recorded. Three major ocular symptoms of dry eye i.e. ocular pain, burning, and foreign body sensation were studied in this study. Each symptom was given a score from 0 to 1 so that the ocular symptoms were given a score from 0 to 3. The BUT is the interval (s) between the last blink and the appearance of the first dry spot. Tear film break up time (BUT) was performed by instilling a fluorescein drop in the eye. The patient was asked to blink several times and the tear film was examined with a broad beam cobalt-blue filter in slit lamp. After few seconds, black spots or lines appeared in the fluorescein-stained film indicating the formation of dry areas. Schirmer's test was performed by placing a Schirmer's strip (Whatman filter paper no. 41) at the junction of the mid and the lateral third of lower eyelid. Schirmer's test was performed after the installation of a local anaesthetic agent. Then the filter paper was folded 5 mm from one end and inserted at the junction of middle and outer-third of the lower eyelid under aseptic conditions and the patient was asked to keep the eyes gently closed, and then after 5 min the filter paper was removed and the amount of wetting from the fold was measured in millimeters. Cyclosporine 0.05% eye drops were prescribed after informed consent was obtained. It was prescribed twice daily for 12 weeks. The patients were followed up after 4, 8, and 12 weeks. They were examined and scored for ocular symptoms, amount of wetting on Schirmer paper, and for the BUT. In addition, they were examined for any ocular complication and side effects.

Statistical analysis

The data was entered in Microsoft excel spreadsheet. The data was analysed using SPSS (Statistical Package for the Social Sciences) version 21.0. The descriptive statistics was used to express data in terms of frequency and percentage. Chi square test was applied for comparison. Point of statistical significance was considered if $p<0.05$.

RESULTS

50 eyes of 25 patients diagnosed with dry-eye syndrome were included in this study. The mean age of the patients was 44.2 years (Table 1). The study included 18 women and 7 male patients. The patients were treated with cyclosporine 0.05% eye drops twice daily. All patients were followed up for 12 weeks.

Table 1: Showing demographic data of the patients included in our study.

Age group (years)	Males	Females
35-40	2	8
41-45	2	6
46-50	1	1
51-55	1	2
56-60	1	1
Total	7	18

The patients were evaluated for ocular symptoms (burning, pain, and foreign body sensation), and the Schirmer's paper test and BUT test were conducted for all patients.

The score of ocular symptoms before the beginning of the treatment was 2.25±0.41 and this score improved after 4 weeks to 1.36±0.14, to 1.11±0.18 after 8 weeks, and to 0.6±0.44 after 12 weeks with a statistically significant difference (p=0.01).

Schirmer's paper test was carried out before the beginning of the treatment and showed a wetting of 1.23±0.55 mm of the paper, and improved after 4 weeks of treatment to 2.27±0.14 mm, to 4.66±0.44 mm after 8 weeks, and to 5.91±0.39 after 12 weeks with a statistically significant difference (p=0.001).

BUT test showed early break-up of the tear film before the beginning of the treatment (5.49±0.91 s), and improved after 4 weeks of treatment to 7.91±0.88 s, to 8.09±0.15 s after 8weeks, and to 9.86±0.84 s after 12 weeks with a statistically significant difference (p=0.001) (Table 2 and Figure 1).

Only two patients (8.0%) reported ocular side effects in the form of ocular irritation and pain.

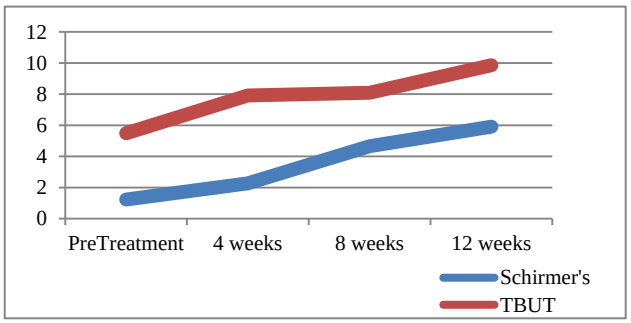

Figure 1: The pattern of change in Schirmer's and TBUT scores pre-treatment and 4, 8 and 12 weeks post-treatment.

Table 2: Showing pre-treatment and post-treatment (4, 8 and 12 weeks) scores for Ocular symptoms, Schirmer's and TBUT with respective p values.

Scoring	Pre-treatment	4 weeks	8 weeks	12 weeks	P value
Ocular symptoms	2.25±0.41	1.36±0.14	1.11±0.18	0.6±0.44	<0.05
Schirmer's test (mm)	1.23±0.55	2.27±0.14	4.66±0.44	5.91±0.39	<0.05
TBUT test (s)	5.49±0.91	7.91±0.88	8.09±0.15	9.86±0.84	<0.05

DISCUSSION

Dryness of eyes is a common problem worldwide and one of the frequent reasons for ophthalmic consultations. Although often considered as a minor problem, dry eye is a growing public health concern. Dry eye disease continues to be a challenging disease and its therapy depends on its severity. Initial treatment for mild dry eye disease is life style changes and use of artificial tears. As it is widely known that inflammation has main role in the etiopathogenesis of dry eye so a number of anti-inflammatory treatments are currently in use for its management. Anti-inflammatory medications are now being considered to be the first line approach in the treatment plethora of dry eye disease as they do not have side effects as with corticosteroids.

Observations from Stevenson et al study showed that treatment with cyclosporine 0.05–0.4% led to a significant improvement in the ocular manifestations of moderate to severe dry eye disease and these improvements resulted in a significant improvement of vision-related functioning. These finding support the results of our study that demonstrated a positive effect of topical cyclosporine.[7]

Perry et al evaluated a total of 158 patients with dry-eye disease using the Ocular Surface Disease Index for symptomatic improvement, tear BUT, fluorescein staining, lissamine green staining, and Schirmer's testing. Patients were observed for 3 to 16 months.13 They concluded that topical cyclosporine shows beneficial effects in all categories of dry-eye disease. Symptomatic improvement was greatest in the mild group, and the best

results in improvement of disease signs were seen in patients with severe dry-eye disease.[14]

In our study, Ocular Symptoms Score reduced from 2.25±0.41 before treatment to 0.6±0.44 after 3 months of treatment (p=0.01). In addition, the Schirmer's paper test scores improved from 1.23±0.55 mm to 5.91±0.39 mm, which is significantly different (p=0.001). The tear film breakup time also improved from 5.49±0.91 s to 9.86±0.84 s. These results are in accordance with the previous studies conducted by Salib et al and Guzey et al.[15,16]

CONCLUSION

Dry eye is a chronic condition and it has a significant personal, medical, and economic burden on the patient. Great efforts have been made to completely understand the pathogenesis of dry eye syndrome and more exciting therapies are in the horizon. Cyclosporine 0.05% has been demonstrated to be effective and safe in our study. It decreases signs and symptoms of dry eye disease. It is well-tolerated without ocular side effects as in our study only 2 patients complained of side effects. Its use is not associated with any systemic side effects. No microbial overgrowth or ocular infections happened during clinical studies. Cyclosporine eye drops also improve the BUT and Schirmer paper test.

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REFERENCES

1. The definition and classification of dry eye disease: report of the Definition and Classification Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf. 2007;5(2):75–92.
2. Javadi MA, Feizi S. Dry eye syndrome. J Ophthalmic Vis Res. 2011;6(3):192–8.
3. Methodologies to diagnose and monitor dry eye disease: report of the Diagnostic Methodology Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf. 2007;5(2):108–52.
4. Gayton JL. Etiology, prevalence, and treatment of dry eye disease. Clin Ophthalmol. 2009; 3 :405-12.
5. Johnson ME, Murphy PJ. Changes in the tear film and ocular surface from dry eye syndrome. Prog Retin Eye Res 2004;23:449-74.
6. Chen Q, Li X, He W, Zhang H, Gao A, Cheng Y, et al. The epitope study of alpha-fodrin autoantibody in primary Sjögren's syndrome. Clin Exp Immunol. 2007;149:497-503.
7. Pflugfelder SC. Anti-inflammatory therapy for dry eye. Am J Ophthalmol. 2004;137:337-42.
8. Behrens A, Doyle JJ, Stern L. Dysfunctional tear syndrome: a Delphi approach to treatment recommendations. Cornea. 2006;25:900-7.
9. Rajpal RK, Digby D, D'Aversa G, Mah F, Hollander DA, Conway T. Intraocular pressure elevations with loteprednol etabonate: a retrospective chart review. J Ocul Pharmacol Ther. 2011;27:305-8.
10. Strong B, Farley W, Stern ME, Pflugfelder SC. Topical cyclosporine inhibits conjunctival epithelial apoptosis in experimental murine kerato-conjunctivitis sicca. Cornea. 2005;24:80–5.
11. Lallemand F, Felt-Baeyens O, Besseghir K, Behar-Cohen F, Gurny R. Cyclosporine A delivery to the eye: a pharmaceutical challenge. Eur J Pharm Biopharm. 2003;56:307–18.
12. Power WJ, Mullaney P, Farrell M, Collum LM. Effect of topical cyclosporin A on conjunctival T cells in patients with secondary Sjogren's syndrome. Cornea. 1993;12:507–11.
13. Perry HD, Solomon R, Donnenfeld ED, Perry AR, Wittpenn JR, Greenman HE, et al. Evaluation of topical cyclosporine for the treatment of dry eye disease. Arch Ophthalmol. 2008;126:1046-50.
14. Byun YS, Rho CR, Cho K, Choi JA, Na KS, Joo CK. Cyclosporine 0.05% ophthalmic emulsion for dry eye in Korea: a prospective, multicenter, open-label, surveillance study. Korean J Ophthalmol. 2011;25(6):369–74.
15. Salib GM, McDonald MB, Smolek M. Safety and efficacy of cyclosporine 0.05% drops versus unpreserved artificial tears in dry-eye patients having laser in situ keratomileusis. J Cataract Refract Surg. 2006;32:772-8.
16. Guzey M, Karaman SK, Satici A, Ozardali I, Sezer S, Bozkurt O. Efficacy of topical cyclosporine A in the treatment of severe trachomatous dry eye. Clin Experiment Ophthalmol. 2009;37:541-9.

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