Efficacy of Topical Cyclosporine 0.05% in the Treatment of Meibomian Gland Dysfunction: A Hospital Based Prospective Study

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ABSTRACT

Purpose: To compare the efficacy of topical cyclosporine 0.05% with tobramycin 0.3% and dexamethasone 0.1% eye drop in reducing signs and symptoms of Meibomian gland dysfunction.

Design: A hospital based randomized prospective study conducted at Manipal Teaching Hospital, Department of Ophthalmology, Pokhara, over a period of 18 months, from January 2012 to June 2013.

Methods: 30 patients who were diagnosed as Meibomian gland dysfunction were recruited and randomly assigned into two groups i.e. Group- A received Cyclosporine 0.05% and Group-B received Tobramycin/dexamethasone. Before starting treatment ocular symptoms were recorded with help of Ocular Surface Disease Index (OSDI) score. All patients underwent examinations including visual acuity, intraocular pressure, Schirmer's test, Tear break up time, Lissamine staining, slit lamp examination for lid telangiectasia, open and clogged meibomian glands, inclusions and meibomian secretion quality.

Result: OSDI score significantly improved in cyclosporine group than in tobramycin/dexamethasone group. Other objective measurements like Schirmer value, Lissamine staining, meibomian secretion quality, number of lid telangiectasia and clogged glands improved in Cyclosporine group.

Conclusion: The present hospital based study noted that Meibomian gland dysfunction can be more effectively treated with cyclosporine than tobramycin/dexamethasone.

Keywords: *Meibomian gland disease, Topical cyclosporine A, Topical tobramycin/dexamethasone.*

INTRODUCTION

Meibomian gland dysfunction describes variety of changes in the tarsal glands that need not necessarily be inflammatory.[1] Altered or reduced lipid excreta in MGD leads to disruption of the tear film with resultant irritation to the cornea, conjunctiva, and lids. MGD is believed to be the most common cause of evaporative dry eye syndrome, so dry eye and MGD are closely associated.[2] The treatment of meibomian gland dysfunction (MGD) consists of warm compresses, eyelid massage and eyelid scrubs, systemic antibiotics, topical antibiotics. Topical antibiotics such as bacitracin, erythromycin, fusidic acid or chloramphenicol are the commonly used agents.[3] The use of topical steroids is reserved only for cases with significant inflammation.[4] Cyclosporine, a calcineurine inhibitors is used in the treatment of many inflammatory ocular conditions, such as uveitis, atopic keratoconjunctivitis, and vernal keratoconjunctivitis. Several published reports provide support for the treatment of MGD in conjunction with rosacea and/or aqueous-deficient dry eye with cyclosporine.[5]

METHODS

This was a prospective randomized study of consecutive patients diagnosed as Meibomian gland dysfunction who presented at Manipal College of medical sciences in Ophthalmology department during a period of eighteen months (January 2012 to June 2013). The symptoms of meibomian gland dysfunction were recorded on the 12-item Ocular Surface Disease Index (OSDI) questionnaire developed by the Outcomes Research Group at Allergan. Symptoms score was recorded before undergoing the objective tests of ocular surface changes. OSDI questionnaire included 12 questions divided into three groups. The first group contained questions about the ocular symptoms of dry eye syndrome, the second about ocular symptoms while watching television or reading book and the third group contained the questions about ocular symptoms induced by environmental factors. Patient's eligibility criteria and exclusion criteria are listed in Tables 1 and 2. All the subjects underwent comprehensive eye examination consisting of visual acuity and refractive assessment, slit lamp examination, intraocular pressure measurement, Schirmer's test, Tear break up time (TBUT), Lissamine green staining.

Table 1: Study Inclusion Criteria

A Patient Was Eligible to Be Included in This Study if He/She:

- Was ≥18 years of age
- Had a slit-lamp diagnosis of meibomian gland dysfunction based on the presence of all of the following: lid margin or tarsal erythema, bulbar conjunctival hyperemia, telangiectasia or thickening or irregularity of the eyelid margins, and meibomian gland orifice inclusions (plugging)
- Had a score ≥12 on the patient Ocular Symptoms Scale
- Had the ability to understand and give signed informed consent
- Was willing and able to cooperate with study requirements
- Agreed to use a reliable form of contraception if of childbearing potential

Table 2: Study exclusion criteria

A Patient Was Excluded From the Study if He/She:

- Wore contact lenses (unless discontinued use ≥30 days before randomization)
- Had active ocular diseases, excluding glaucoma, or infections other than blepharitis
- Had ocular surgery within the past 3 months
- Had active ocular allergies
- Used isotretinoin (Accutane) within the past 6 months
- Had autoimmune disease requiring systemic treatment
- Had a history of hypersensitivity to oral cyclosporine A
- Was pregnant or nursing or not using a reliable form of contraception

Following the initial study visit, patients was randomized to receive either topical cyclosporine 0.05% or tobramycin 0.3%/dexamethasone 0.1% suspension and instructed to use 1 drop in the affected eye every 12 hour. Patient evaluations were administered at the initial evaluation and every 2 weeks for 3 months. Measures of eyelid health, including lid erythema and lid telangiectasia, were evaluated, and their presence or absence was noted. Presence of lid erythema was defined as a red discoloration, compared to the surrounding eyelid skin. Lid telangiectasia was defined as the presence of at least two blood vessels along the eyelid margin. Meibomian gland secretion quality was graded on a scale of 0–3 in which 0 = clear excreta with small particles; 1 = opaque excreta with normal viscosity; 2 = opaque excreta with increased viscosity; and 3 = secreta that retained shape after digital expression. Evaluation of patient was performed by comparing the response at the initial visit with the response given at month 3 for each evaluated eye.

STATISTICAL ANALYSIS

Student t test on mean difference were used to detect differences between the cyclosporine and tobramycin/dexamethasone group in mean OSDI scores, tear break up time, Schirmer scores, lissamine green staining, lid telangiectasia, open and clogged glands and inclusions. The values taken were mean of the both eyes for the analysis. The presumptive level of significance for all tests was P<0.05 CI<95%. Data were analyzed using commercially available statistical software package (SPSS for Windows, version 16).

RESULTS

A total of 30 patients who were diagnosed as Meibomian gland dysfunction were recruited in this study as per the inclusion criteria. They were randomized into two groups, where Group- A received treatment with topical Cyclosporine 0.05% and the Group-B received treatment with topical Tobramycine 0.3%/Dexamethasone 0.1%. Both the groups included 15 patients each. There was no statistically significant P>0.005% difference in between two groups in demographic variable (Table 3)

Table 3: Demographics N = 15

Age/Sex	Cyclosporine	Tobramycin/ Dexamethasone	P-value
Mean Age	50.40± 18.0	49.46± 11.71	0.86
Gender			
Male	7	8	0.77
Female	6	9	

Prior to the treatment there was no statistically significant difference in OSDI score between both the groups. Mean difference between pre-treatment and post-treatment was 11.8 in cyclosporine group and 6.4 in Tobramycin/ Dexamethasone group respectively, as the difference is more in cyclosporine group so this drug was better to reduce symptoms in Meibomian gland dysfunction.

The TBUT after treatment in the group A (cyclosporine group) increased to 12.40± 3.54 seconds, and in the group B (tobramycine/ dexamethasone group) the TBUT score increased to 11.6± 3.01sec (p=0.002). The mean change which was taken as difference of post treatment and pre- treatment in TBUT within the groups- in group A (Cyclosporine) and the group B (tobramycine and dexamethasone group) was 2.66 seconds and 3.4 seconds respectively (Figure 1). The mean difference showed more improvement in tobramycin/dexamethasone group. At the, initial study visit the mean Schirmer's score in cyclosporine group was 11.53±3.48mm, compared with 11.60± 2.64mm in the tobramycin/dexamethasone group. After 12 weeks, there was statistically significant improvement in the mean Schirmer scores in both the treatment groups (P< 0.005). The mean improvement in Schirmer score was significantly greater in cyclosporine treatment group (4.8mm) than in tobramycin/ dexamethasone group (3.7mm) Figure 1.

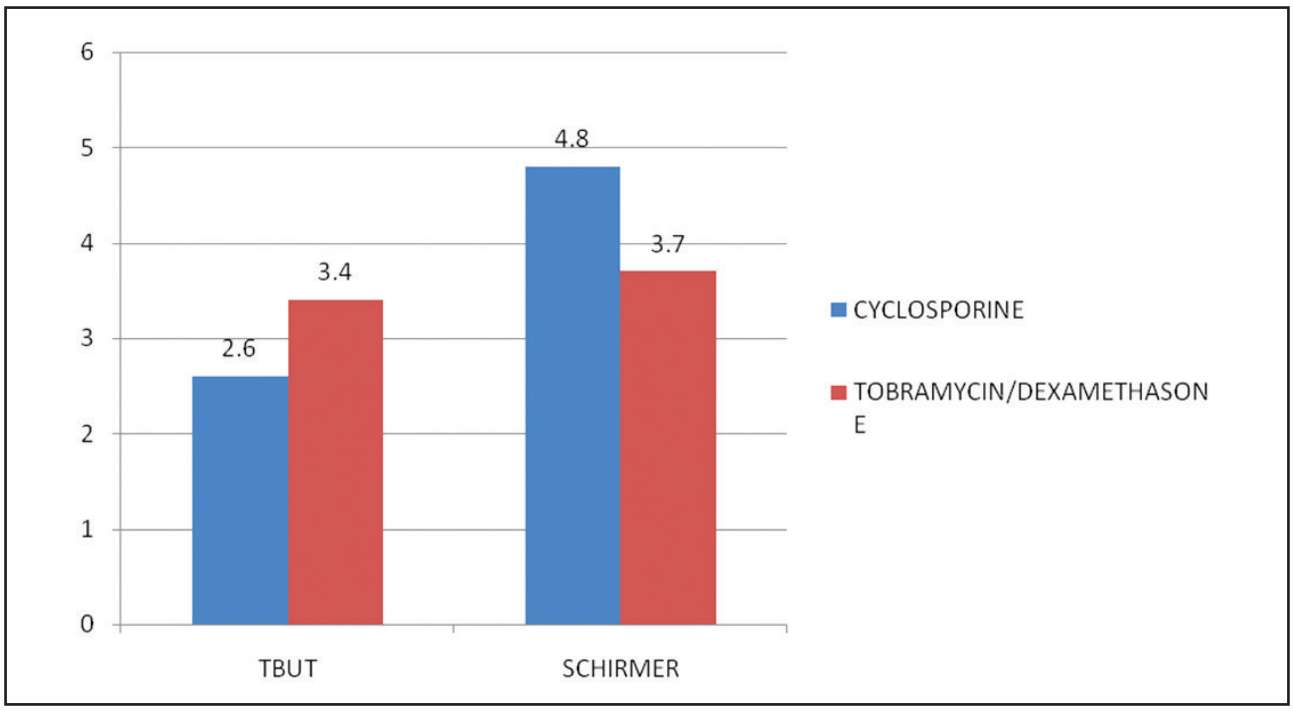

Figure 1: Mean difference of TBUT and Schirmer's test

The mean score of table 4 shows prior to the treatment in group A (Cyclosporine) Lissamine staining score 17.53± 11.82 and post treatment it reduced to 8.53± 6.4 which was statistically significant (P= 0.015). In group B (Tobramycin/Dexamethasone) score before treatment was 12.27± 9.93 and after treatment it reduced to 11.73± 10.93, not much difference was seen.

Table 4: Mean of Lissamine staining in two groups

Groups	Pre-Treatment Lissamine score	Post-Treatment Lissamine score	P value
Group A (cyclosporine)	17.53±11.82	8.53±6.4	0.015
Group B (tobramycin/ dexamethasone)	12.27±9.93	11.73±10.93	0.89

Figure 2 shows lid telangiectasia resolved in 60% of patients receiving cyclosporine and in 33% of patients receiving tobramycin/dexamethasone

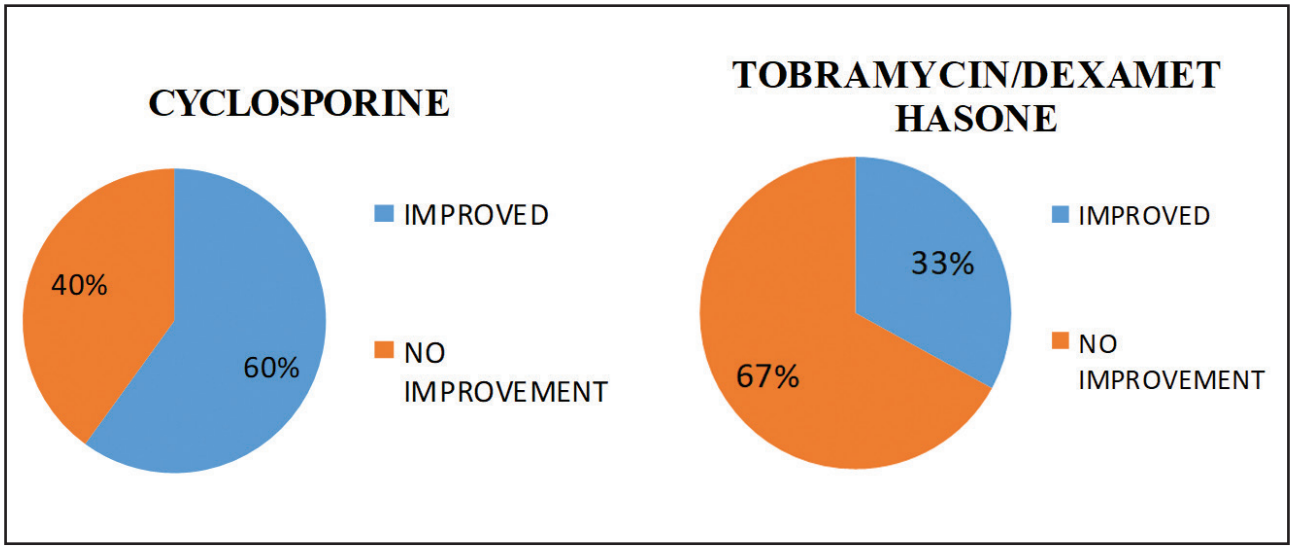

Figure 2: Percentage of patients with improvement in lid telangiectasia

The initial mean secretion quality score in cyclosporine group before treatment was 0.80± 0.86 and after treatment it reduced to 0.20± 0.41 (P= 0.02) whereas in tobramycine/dexamethasone group before treatment was 0.86± 0.74 and after treatment it reduced to 0.40± 0.63 (P=0.07) which was not statistically significant (Figure 3).

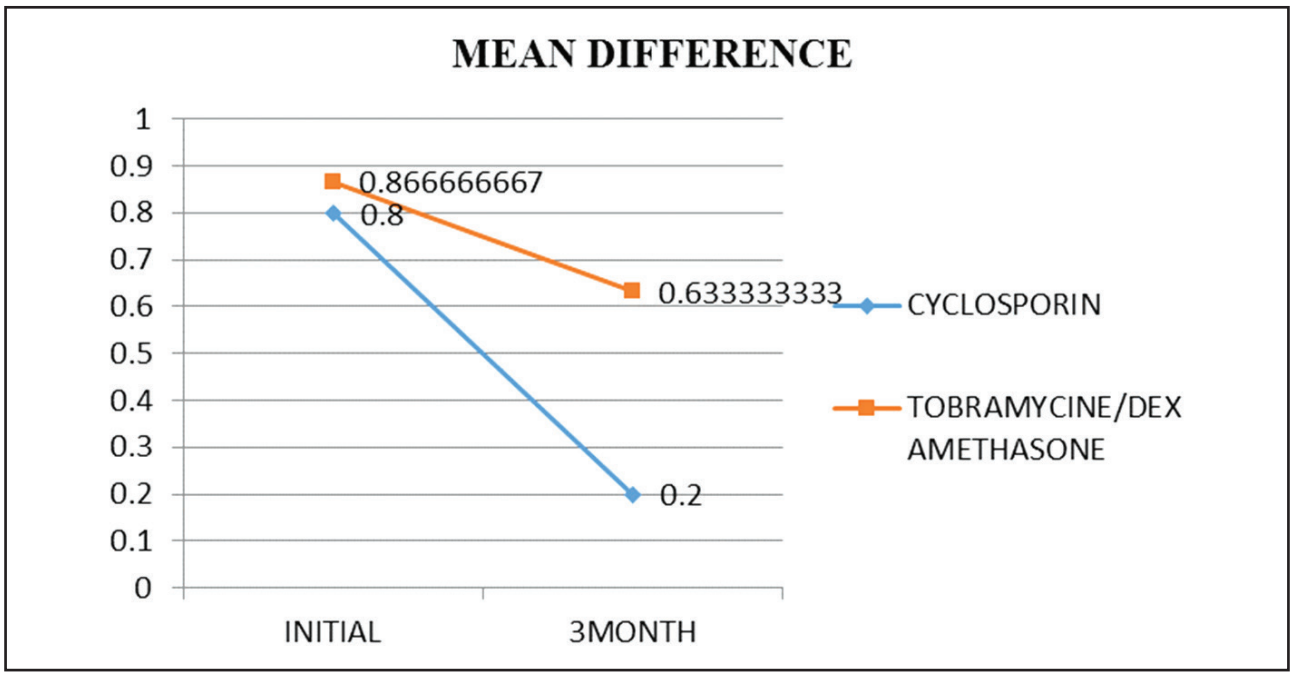

Figure 3: Mean difference in secretion quality

No significant adverse events associated with topical cyclosporine or tobramycin/dexamethasone were noted in the study. There were no elevations in intraocular pressure greater than 3mmHg, and no patients developed secondary ocular infections.

DISCUSSION

The result of this study suggests that cyclosporine 0.05% is an effective treatment for signs and symptoms of meibomian gland dysfunction. At the three month visit, symptoms and many objective clinical findings were significantly better in the cyclosporine group than in tobramycin/dexamethasone group. Three months of cyclosporine therapy provided statistically significant improvements in OSDI score, Schirmer value, lid telangiectasia, mean secretion quality compared to other group.

Topical cyclosporine has been shown to improve the ocular signs and symptoms of moderate to severe dry eye disease. Previous studies have shown that concentrations of topical cyclosporine above 0.05% and 0.1% did not yield an additional therapeutic benefit.[6,7] Therefore, in this study topical cyclosporine 0.05% was used. In dry eye disease, cyclosporine is thought to work by modulating the immune cell populations of both the conjunctiva and lacrimal gland.[8] It is because meibomian gland dysfunction and dry eye disease often coexist, topical cyclosporine may have been effective in part by alleviating dry eye. However topical cyclosporine may have another mechanism in ameliorating meibomian gland dysfunction by affecting primarily T lymphocytes which may decrease the inflammation of the meibomian glands and thus reduce plugging and dysfunction.

Kenneth Shall et.al[7] demonstrated with use of cyclosporine statistically significant changes from baseline were observed within all treatment groups at all time points in dryness (P≤ 0.001), sandy/gritty feeling (P≤ 0.001) and itching (P≤ 0.038) and also in Schirmer value, Lissamine green staining. Gunduj and Ozden[9] found improvement in tear break up time in cyclosporine group in treatment of Sjogren syndrome. However, in this study improvement in tear break up time is seen in both, but it was more in tobramycin/

dexamethasone group. This difference in the results between our study and previous studies might be due to personal variation in recording time and small sample size. Study by Rubin[10] had also showed statistically significant improvement in mean Schirmer's score in the cyclosporine treatment group (2.33mm) than in tobramycin/dexamethasone treatment group (P< 0.001). Another study done by Henry[5] to compare efficacy of cyclosporine with placebo in meibomian gland dysfunction showed significant increase in Schirmer score after treatment with cyclosporine. Perry[5] and Rao[10] observed more improvement in lid telangiectasia, decrease in clogged meibomian gland and inclusions in cyclosporine group than in tobramycin/dexamethasone group. Whereas in this study no statistically significant difference was seen in number of open glands and inclusions in both the group. The difference in the result between our study and previous studies might be because of other factors i.e. irregularity in lid hygiene. Arati observed meibomian secretion quality score was significantly higher for obstructive meibomian gland dysfunction. The correlation of meibomian secretion score was positively significant with the lid margin abnormality[11]. In this study also we find significant difference in meibomian secretion quality in cyclosporine group than in tobramycin/dexamethasone group which is consistent with other studies.[5, 10]

In addition to effectively targeting the mechanism of inflammation, cyclosporine may present several clinical advantages over corticosteroids and antibiotics. For instance, the use of corticosteroids, both topically and systemically, can predispose the host to severe ocular herpes simplex keratitis infection.[12,13] Steroids are also associated with the exacerbation and spread of active viral infection by suppression of the normal host immune response and stimulation of viral replication, enhancement of collagenolytic enzyme production with subsequent corneal thinning, creation of a steroid-dependent ocular tissue by allowing for the buildup of viral antigens, and increased risk of opportunistic super added infections, and steroid-induced glaucoma and cataracts.[14] Also, extended use of antibiotics may result in increased microbial resistance. The strengths of this study is it is a prospective study and both subjective and multiple objective parameters were assessed including ocular symptoms, lid margin vascularity, telangiectasia, meibomian gland inclusions, tear breakup time, and fluorescein staining. The limitations of this study include a small sample size.

CONCLUSIONS

In conclusion, the findings of this study suggest that meibomian gland dysfunction can be more effectively treated with cyclosporine than with tobramycin/dexamethasone. These findings should be further evaluated in large-scale, controlled, clinical trials.

REFERENCES

1. Bron AJ, Benjamin L Sibson GR. Meibomian gland disease. Classification and grading of lid changes. Eye 1991;5:395-411.
2. Lemp MA, Nichols KK. Blepharitis in the United States 2009: a survey-based perspective on prevalence and treatment. Ocular Surface 2009;7:1–14.
3. Ayliffe W. Blepharitis and meibomian gland dysfunction. In: Foster CS, Azar DT, Dohlman CS, eds. The cornea (Scientific foundations and clinical practice). Philadelphia: Lippincott Williams & Wilkins 2005;647-56.
4. Driver PJ, Lemp MA. Meibomian gland dysfunction. Surv Ophthalmol 1996; 40:343–67.
5. Perry HD, Doshi-Carnevale S, Donnenfeld ED, Solomon R, Biser SA, Bloom AH. Efficacy of commercially available topical cyclosporine A 0.05% in the treatment of meibomian gland dysfunction. Cornea 2006; 25:171–175.
6. Stevenson D, Tauber J, Reis BL. Efficacy and safety of cyclosporin A ophthalmic emulsion in the treatment of moderate-to-severe dry eye disease: a dose-ranging, randomized trial. The Cyclosporin A Phase 2 Study Group. Ophthalmology 2000;107:967–974.
7. Sall K, Stevenson OD, Mundorf TK. Two multicenter, randomized studies of the efficacy and safety of cyclosporine ophthalmic emulsion

in moderate to severe dry eye disease. Phase 3 Study Group. Ophthalmology 2000;107: 631–639.

8. Kunert KS, Tisdale AS, Stern ME, Smith JA, Gipson IK. Analysis of topical cyclosporine treatment of patients with dry eye syndrome: effect on conjunctival lymphocytes. Arch Ophthalmol 2000;118:1489–1496.

9. Gundu¨z K, Ozdemir O. Topical cyclosporine treatment of keratoconjunctivitis sicca in secondary Sjo¨gren's syndrome. Acta Ophthalmol (Copenh) 1994;72:438-42.

10. Rubin M, Rao SN. Efficacy of topical cyclosporine 0.05 % in the treatment of posterior blepharitis. J Ocul Pharmacol Ther 2006; 32:47-53.

11. AritaR, Ioth K, Maeda K, Furuta A, Fukuoka S, Tomidokoro A, Amano S. Proposed Diagnostic Criteria for ObstructiveMeibomian Gland Dysfunction. Ophthalmology 2009; 116:2058–63.

12. Marquart M, Bhattacharjee P, Zheng X, Kaufman H, Thompson H, Varnel E, Hill J. Ocular reactivation phenotype of HSV-1 strain a corticosteroid-sensitive strain. Curr. Eye Res 2003;26:205–209.

13. Wilhelmus KR, Dawson CR., Barron BA, Bacchetti P, Gee L, Jones DB, Kaufman HE. Risk factors for herpes simplex virus epithelial keratitis recurring during treatment of stromal keratitis or iridocyclitis. Herpetic Eye Disease Study Group. Br. J. Ophthalmol 1996;80:969–972

14. Carnahan MC, Goldstein DA. Ocular complications of topical, periocular, and systemic corticosteroids.Curr. Opin. Ophthalmol 2000;11:478–483.

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