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Original Research Article

A study to assess the efficacy of topical cyclosporine A 0.05% in the management of dry eye with meibomiam gland dysfunction

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ABSTRACT

Introduction: Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface. Meibomian Gland Dysfunction (MGD) is an abnormality of the meibomian gland that blocks the secretion of lipids. Without sufficient lipid production, tears evaporate quickly causing Dry Eye.

MGD is associated with multiple pathological mechanisms including inflammation, microbial factors and lipid deficiencies. Topical Cyclosporine A (CsA) 0.05% is a calcineurin inhibitor that reduces inflammation by specifically inhibiting T-cell activity, which reduces ocular surface inflammation and improves tear film dynamics.

Materials and Methods: This was a prospective observational study done on 100 patients at the Department of Ophthalmology Basaveshwar teaching and general hospital, on patients of dry eyes due to meibomian gland dysfunction. Patients who were diagnosed with dry eyes due to meibomian gland dysfunction were invited to take part in the study. Patients were divided randomly into two groups of 50 patients each. This study, was explained in detail to them. An informed consent was obtained. Patients fulfilling the inclusion criteria were listed.

Result: All OSDI scores (symptom intensity, frequency and aggravation) revealed decreasing patterns throughout the observation period in both the groups. In single analysis, the cyclosporine A 0.05% group showed a significant improvement for each score at 3 months ($p < 0.01$, $p = 0.01$, $p = 0.02$, respectively). The mean TBUT after treatment in the group A (cyclosporine A group) increased to 12.36± 3.58($p<0.001$) seconds, and in the group B (Control group) the TBUT score increased to 11.01±3.06 seconds. After 3 Months, there was statistically significant improvement in the mean Schirmer's scores in both the treatment groups, however improvement was significantly greater in Cyclosporine A group.

Prior to the treatment in group A (Cyclosporine A) mean Lissamine staining score was 2.73±0.15 and post treatment it reduced to 1.32±0.15 which was statistically significant ($P<0.001$). In group B (Control group) score before treatment was 2.46±0.15 and after treatment it reduced to 2.39±0.27 ($p=0.11$), not much difference was seen.

Conclusions: Findings from our study showed that there were significant improvements in the dry eye conditions due to defect in meibomian gland by treatment of topical Cyclosporine A 0.05% and sodium hyaluronate 0.1%.

1. Introduction

Dry eye is a multifactorial condition of the tears and ocular surface that causes symptoms such as pain, visual

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impairment, and tear film instability, as well as the possibility for ocular surface injury. It is accompanied by an increase in the osmolarity of the tear film as well as ocular surface irritation.[1,2] Tears are comprised of three layers. The fluid layer that nourishes the eye is known as the aqueous layer. The mucin layer contains mucus that aids in the adhesion of the aqueous layer to the eye's surface. Tears are made up of a lipid coating created by the meibomian glands in the eyelids, which serves to prevent evaporation and acts as a barrier to the environment. Meibomian gland dysfunction is an anomaly of the meibomian gland that prevents lipid release. Tears evaporate quickly if there is insufficient lipid production, resulting in dry eyes.[3]

Meibomian Gland Dysfunction occurs when the ductal epithelium of the meibomian glands becomes hyperkeratinized, resulting in increased intraductal pressure and stoppage of normal meibum flow. Meibomian ducts obstruction leads to accumulation and thickening of lipids and also colonisation of bacteria on the lid margins and inflammation of the lid margins. The secondary outcome may be defect of the tear film and related dry eye disease.[4]

1.1. Clinical signs and symptoms

Itching burning and a foreign body feel are among symptoms of dry eye.

Blurry vision on irregular basis.

Symptoms are frequently worse when first wake up, although heat and/or massage is effective to relieve symptoms.

Using an OSDI questionnaire (Ocular Surface Disease Index questionnaire): The OSDI questionnaire is a 12-item questionnaire that can be used to quickly assess symptoms of ocular irritation in dry eye and their influence on vision-related functions.

1. Tear volume assessment by Schirmer's test without topical anaesthesia using Whatmann filter paper 41measures reflex secretion. Normal range is >10mm in 5minutes.
2. Tear film stability is tested by Tear film breakup time (TBUT) : it is a practical method of measuring stability of pre-ocular tear film using moistened fluorescein strip. With the help of a slit light, the time between the last blink and the appearance of the first dry patch is recorded. The average TBUT is higher than 10 seconds.
3. Tear film composition by tear osmolarity.
4. Fluorescein Staining was used for Corneal evaluation
5. Lissamine green staining is helpful in staining of conjunctiva. Which is graded according to Oxford grading scale[5] as mild, moderate and severe.
6. Lid evaluation by slit lamp to see for lid morphology, expression of meibomian glands, and blink rate.

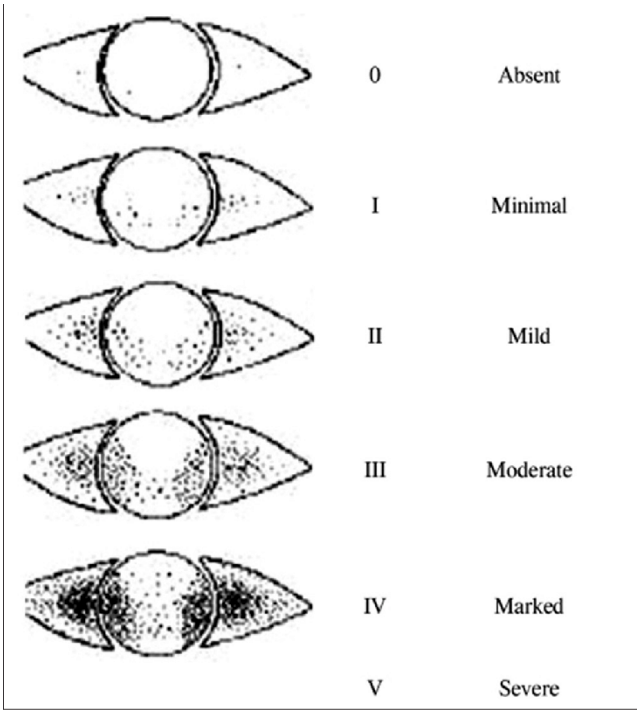

Fig. 1: Scale used to measure Lissamine Green 1% staining.[5]

Grading scale for meibomian gland secretion and expression[6]

1. Clear Normal
2. Cloudy Turbid
3. Granular Turbid with particulate matter
4. Inspissated Toothpaste like

1.2. Treatment

Various MGD treatments, like lid cleansing, eyelid warming massage, and artificial tears, are commonly employed. Systemic antibiotics, such as oral tetracycline, macrolides, or topical anti-inflammatory medications, such as topical steroid eye drops, may be administered if necessary. These treatments, however, are generally not effective. Anti-inflammatory drugs such as steroids, tetracycline, and cyclosporine A (CsA) have been used to treat inflammation in MGD and ameliorate the symptoms and signs of the disease.[7]

Cyclosporine A is a highly selective immunomodulator that mainly affects T cells and does not impair the phagocytic system as much as corticosteroids do. It has a favourable safety profile because it does not interfere with wound healing or cause lens alterations. Till now, topical cyclosporine A 0.05 percent is the only medication that has been demonstrated to boost the production of the patient's own natural tears in clinical trials. In addition to chronic dry eye, MGD, ocular rosacea, and contact lens sensitivity, it has been explored for the treatment of additional ophthalmic

disorders.[4]

This study is done to know the efficacy of topical cyclosporine A 0.05% in the treatment of dry eye caused due to meibomian gland dysfunction.

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2. Material and Methods

This study is a prospective observational type of study done at the Department of Ophthalmology in Basaveshwar teaching and general hospital, on patients of dry eyes due to meibomian gland dysfunction.

2.1. Inclusion criteria

1. > 18 years of age
2. Presence of conjunctival hyperaemia (tarsal and bulbar), lid margin (inflammation) vascular engorgement or thickening or irregularity of eyelid margins, and meibomian gland orifice inclusion (plugging).
3. Had a score > 12 on the OSDI questionairre

2.2. Exclusion criteria

Patient was excluded from the study if He/She:

1. History of contact lenses use (unless discontinued use for atleast 30 days)
2. Had any infectious disease excluding blepharitis
3. Had history of glaucoma.
4. Had undergone any ocular surgery within the past 3 months
5. Had active ocular allergies
6. Had been treated with isotretinoin within the past 6 months
7. Had autoimmune disease requiring systemic treatment
8. Had a history of hypersensitivity reaction to oral cyclosporine A
9. Was pregnant or nursing and using any oral contraceptives.

2.3. Methodology

Patients who were diagnosed with dry eyes due to meibomian gland dysfunction were invited to take part in the study. An informed consent was obtained from the patients after explaining the study. Patients fulfilling the inclusion criteria were listed. Patients were advised lid hygiene and lid warming massage for 10min before sleep, 0.1% sodium hyaluronate eye drops (preservative free) were instilled 4 times a day. Topical 0.05% CsA eyedrops was instilled twice a day in the experimental group. The group without cyclosporine eye drops use was defined as a control eye group. 50 study subjects were included in experimental group whereas 50 subjects were included in control group. All patients were evaluated at their first visit and followed up after 3month of treatment to determine the therapeutic effect. Institutional ethical clearance was obtained before the commencement of the study.

3. Results

In our study total 100 subjects were included, 50 subjects were included in experimental group and 50 subjects were in control group. The mean age was 50.40± 18.0 yrs in experimental group whereas 49.46±11.71 yrs in control group without any statistically significance with p value = 0.86.

Table 1: Sex distribution of cases studied (n=50)

Gender	Cyclosporine	Control group
Male	24	22
Female	26	28
Total	50	50

Of 50 cases studied, 24(48%) were males and 26 (52%) were females in experimental group whereas 22 (44%) male and 28 (56%) female were there in control group.

There was improvement in OSDI scores with respect to symptom intensity, frequency and aggravation in both groups. In single analysis, the cyclosporine A 0.05% group showed a significant improvement for each score at 3 months ($p < 0.01$, $p = 0.01$, $p = 0.02$, respectively).

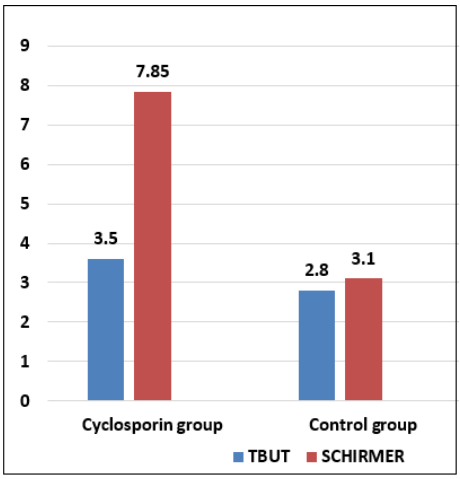

Fig. 2: Mean Tear Film Break Up Time (TBUT) and Schirmer's Test of both the groups.

The mean TBUT after treatment in the group A (cyclosporineA group) increased to 12.36±3.58sec (p value <0.001) and in the group B (Control group) the TBUT score increased to 11.01±3.06 sec. The mean change which was taken as difference of post treatment and pre- treatment in TBUT within the groups in group A (Cyclosporine A) and the group B (Control group) was 3.5 seconds and 2.8 seconds respectively.

The mean Schirmer's score in the cyclosporine group was 3.53±1.08mm at the first study visit, compared to 3.48±1.13mm in the control group. The mean Schirmer's scores improved statistically significantly in both therapy groups after 3 months (groupA =11.53±3.57, groupB=6.58±2.87). However there was an improvement in the Schirmer's score in the cyclosporine treatment group, 7.85mm(p<0.001), which was substantially greater than in the control group, i.e., 3.1mm. (p<0.001)

The mean of lissamine green staining before treatment was 2.73±0.15 in the Cyclosporine A group and 2.46±0.16 in control group and after 3months it was 1.32±0.15 (p<0.001) which was statistically significant in the Cyclosporine A group and 2.39±0.27 in control group (p=0.11) which was not statistically significant.

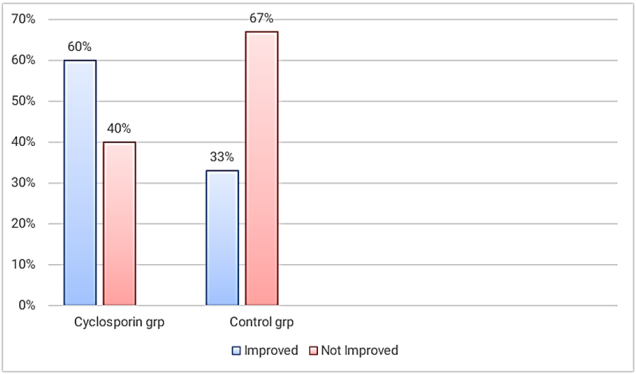

Fig. 3: Percentage of patients with improvement in vascular engorgement on lid

Percentage of patients with improvement in vascular engorgement on lid Vascular engorgement on lid was noted in total 76 patients, (40 in study group and 36 in control group) resolved in 60%(24 patients) of patients receiving cyclosporine and in 33% (11 patients) of patients receiving only 0.1% Sodium hyaluronate.

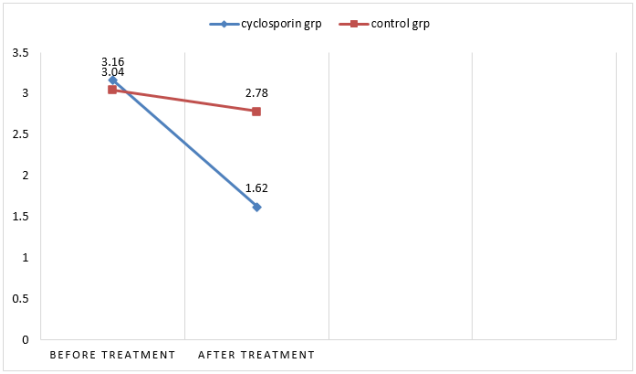

Fig. 4: Mean difference in secretion quality

The initial mean secretion quality score in cyclosporine group before treatment was 3.16± 0.75 and after treatment it reduced to 1.62± 0.67 (P< 0.01) whereas in control group before treatment was 3.04± 0.78 and after treatment it reduced to 2.78± 0.89 (P=0.12) which was not statistically significant.

4. Discussion

The objective of this study was to demonstrate the efficacy of cyclosporine A 0.05% in dry eyes caused by Meibomian Gland Dysfunction

In our study the mean age was found to be 50.4 years. Similar finding in a study by Henry D. Perry et al[4] where mean age was observed to be 57 years in patients with mild dry eyes and 66 years in patients with moderate dry eyes and 68 years in severe cases. Mean age of the patients was 44.2 years in a study by Jitender Phogat et al[8] and 47 years in a study by Tageldin M. Othman et al,[9] So we can say by this pattern that probability of dry eye disease increases after 40 years of age.

In the present study female outnumbered male. In a study done by Ho-Yun Kim et al[7] on 53 patients observed that 14 were male and 36 were females. The study by Jitender Phogat et al[8] included 18 women and 7 male patients. So these findings The patients were treated with cyclosporine 0.05% eye drops twice daily. Females are at a substantial risk factor for both DED and MGD development.[8,10,11] Because the androgen and oestrogen receptors are both present inside the meibomian glands, this could be related to the effect of hormonal changes on meibomian production.

In our study mean difference between pre-treatment and post-treatment ocular surface disease index score was 11.8. Mean OSDI score in a study by Pinnita Prabhasawat et al[12] was 43.32. In a study by Jitender Phogat et al[8] 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).

As per our present study findings TBUT increased to 12.36 ±3.58 seconds after cyclosporine treatment with mean change of 3.5 seconds (p<0.001). In a research by Henry D. Perry et colleague,[4] the mean TBUT in individuals with mild dry eyes was 1.21 seconds (range, 0-5 seconds), 0.27 seconds (range, 0-5 seconds) in moderate instances, and 0.00 seconds in severe instances. After treatment, mean TBUT in the mild group was 3.34 seconds (0-10 seconds) (P=0.015), 2.04 seconds (range, 0-10 seconds) in the moderate group (P=0.01), and 1.45 seconds (range, 0-5 seconds) in the severe group (P=0.001). In accordance similar results were observed in a study by Haitham Y et al.[13] BUT test showed early break-up of the tear film before the beginning of the treatment (5.57± 1.36 s), which improved after 1 month of treatment to 8.02 ±0.98 s, 7.28± 0.15 s after 2 months, and 9.9± 0.92 s, with a statistically significant difference after 3 months (P = 0.001). BUT test results in a study by Jitender Phogat et al[8] showed early tear

Table 2: Mean of Lissamine green staining in two groups

Group	Pre-treatment mean lissamine stain score	Post-treatment mean lissamine stain score	
Cyclosporine	2.73±0.15	1.32±0.15	p<0.001
Control group	2.46±0.15	2.39±0.27	p=0.11

film break-up before the start of treatment (5.49±0.91 s), which improved after 4 weeks of treatment to 7.91±0.88 s, 8.09±0.15 s after 8 weeks, and 9.86±0.84s improved statistically significant difference after 12weeks (p=0.001).

The mean Schirmer's score among patients was 3.53±1.08mm at first visit. After 3months, the average Schirmer's scores had improved by 7.85mm, which was statistically significant. According to a study by Henry D. Perry et al,[4] the mean Schirmer's test scores were 8.67 mm in mild cases of dry eyes, 6.33 mm in moderate instances, and 2.37 mm in severe instances at baseline. After therapy, mean Schirmer's test results in the mild group were 9.23 mm (P=0.109), 7.64 mm in the intermediate group (P=0.015), and 3.33 mm in the severe group (P=0.05). Similar results were seen in a study by Haitham Y. et al,[13] Schirmer's paper test, which showed a wetting of 1.15± 0.58 mm before treatment and improved to 2.2± 0.12 mm after 1 month, 4.82± 0.51 mm after 2 months, and 5.86 ±0.29 mm after 3 months with a statistically significant difference.

In our study, the mean of lissamine green staining in the Cyclosporine A group was 2.73±0.15 before treatment and 1.32±0.15 after 3 months (p< 0.001). In a study by Henry D. Perry et al[4] scores of lissamine green staining of the conjunctiva at baseline were 0.29 in the mild cases of dry eyes (range, 0-2), 0.55 in the moderate cases (range, 0- 2), and 2.46 in the severe cases (range, 1-4). Lissamine green staining after treatment was 0.18 in the mild group (P=0.001), 0.48 in the moderate group (P=.0078), and 1.62 in the severe group (P=0.001).

In our study, Lid telangiectasia improved in 60% of the 40 instances in the study. Mild lid telangiectasia was found in 38 eyes, moderate lid telangiectasia was found in 63 eyes, and severe lid telangiectasia was found in 5 eyes in a study by Ho-Yun Kim et al.[7] Mild telangiectasia was identified in 18 patients out of 36 getting cyclosporine in a research by Pinnita Prabhasawat et al,10] moderate telangiectasia in 10 cases, and severe telangiectasia in one instance.

5. Conclusion

In our study, patients treated with topical cyclosporine A 0.05% and 0.1% sodium hyaluronate showed significant improvement when compared to the patients treated with only 0.1% sodium hyaluronate.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare no conflict of interest.

References

1. Kabat AG. Meibomian Gland Dysfunction & Dry Eye : What Do the Experts Say; 2007. Available from: http://www.coavision.org/files/206-%20Kabat%20MGD%20%26%20Dry%20Eye.pdf.
2. Maurya R. Dry eye disease: An overview. *Indian J Clin Exp Ophthalmol*. 2019;4(4):433–4.
3. Lemp MA, Crews LA, Bron AJ, Foulks GN, Sullivan BD. Distribution of aqueous- deficient and evaporative dry eye in a clinic-based patient cohort: A retrospective study. *Cornea*. 2012;31(5):472–8.
4. Perry HD. Topical Cyclosporine Use in Meibomian Gland Dysfunction. *US Ophthalmic Rev*. 2006;17. doi:/10.17925/USOR.2006.00.00.17.
5. Bron A, Evan VE, Smith JA. Grading of corneal and conjunctival staining in the context of other dry eye tests. *Cornea*. 2003;22(7):640–50.
6. Wood SD, Mian SI. Diagnostic Tools for Dry Eye Disease. *Eur Ophthalmic Rev*. 2016;10(2):1001–7. doi:10.17925/EOR.2016.10.02.101.
7. Kim HY, Lee JE, Oh HN, Song JW, Han SY, Lee JS. Clinical efficacy of combined topical 0.05% cyclosporine a and 0.1% sodium hyaluronate in the dry eyes with meibomian gland dysfunction. *Int J Ophthalmol*. 2018;11(4):593–600.
8. Phogat J, Verma R, Rathi M, Sachdeva S, Pandey L. Efficacy of cyclosporine 0.05% in patients with dry eye syndrome. *Int J Community Med Public Heal*. 2019;6(8):3339.
9. Othman TM, Mousa A, Gikandi PW, Abdelmabod M, Abdelrahman AM. Efficacy and safety of using topical cyclosporine A for treatment of moderate to severe dry eye disease. *Saudi J Ophthal*. 2018;32(3):217–21. doi:10.1016/j.sjopt.2018.06.001.
10. Al-Nashar H. Efficacy of topical cyclosporine 0.05% eye drops in the treatment of dry eyes. *J Egypt Ophthalmol Soc*. 2015;108(4):233.
11. Dorenavar L, Maurya RP, Singh VP, Singh MK, Sharma K, Sharma R. The role of Rebampipde ophthalmic suspension in management of dry eye disease. *Indian J Clin Exp Ophthalmol*. 2015;1(4):191–6.
12. Prabhasawat P, Tesavibul N, Mahawong W. A randomized double-masked study of 0.05% cyclosporine ophthalmic emulsion in the treatment of meibomian gland dysfunction. *Cornea*. 2012;31(12):1386–93.
13. Al-Nashar HY. Efficacy of topical cyclosporine0.05% eye drops in the treatment of dry eyes. *J Egypt Ophthalmol Soc*. 2015;108(4):233–6.

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