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Original Article

Comparison of Clinical Efficacy of Topical Cyclosporine A 0.05% With Loteprednol 0.5% In The Treatment of Chronic Blepharitis

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ABSTRACT

Objective: To compare efficacy of topical Cyclosporine A 0.05% and Loteprednol 0.5% in treatment of Chronic Blepharitis.
Study Design: Quasi-Experimental study
Place and Duration of Study: Department of Ophthalmology Combined Military Hospital Quetta, Pakistan from Jul to Dec 2020.
Methodology: Thirty two patients with chronic blepharitis, Tear Film Breakup time of less than 10 seconds and Ocular Surface Disease Index Score of more than 22 in both eyes were included. Patients were randomly assigned in a 1:1 ratio to receive either topical Cyclosporine A 0.05% eye drops (Group-A) or topical Loteprednol 0.5% (Group-B) twice daily. In addition to this warm compresses, lid hygiene, topical artificial tears and antibiotic ointment were given. Follow-up appointments were scheduled at baseline, 4 weeks, 8 weeks, and 12 weeks to monitor patient progress. Data was analyzed using SPSS.
Results: A total of thirty two patients (64 eyes) were enrolled in the study, with 26 patients (52 eyes) completing the full study period. OSDI scores improved over time in both groups, indicating disease resolution. However, significant improvements were observed in Group-A compared to Group-B at 3 months in OSDI scores (10.79±1.25 vs 18.23±0.65, $p<0.05$), TBUT (9.86±0.71 vs 8.77±0.65, $p<0.05$), MGSS (0.43±0.50 vs 0.81±0.63, $p=0.02$), LMTS (0.11±0.32 vs 0.83±0.47, $p=0.05$) and LSCS (0.18±0.39 vs 0.67±0.56, $p=0.05$). These findings suggest that Cyclosporine (Group-A) was more effective than Loteprednol (Group-B) in improving ocular surface parameters and reducing symptoms at 3 months.
Conclusion: This study demonstrates that both Cyclosporine and Loteprednol are effective in alleviating signs and symptoms of chronic blepharitis, but Cyclosporine shows significantly better outcomes after 12 weeks.

Keywords: Blepharitis, Clinical Efficacy, Cyclosporine, Loteprednol

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INTRODUCTION

Blepharitis, first identified by Elsching in 1908.[1] is an ocular surface disease commonly encountered in clinical practice. It is characterized by an abnormal balance of lid margin flora, meibomian gland dysfunction, and a dysfunctional pre-corneal tear film, leading to inflammation, corneal and conjunctival changes, and symptoms of ocular discomfort. Blepharitis is associated with various conditions, including seborrheic dermatitis, rosacea, eczema, and type 2 diabetes mellitus.[2,3] The disease is classified into two main categories based on anatomical location: anterior blepharitis, which includes both staphylococcal and seborrheic blepharitis, and posterior blepharitis, which affects the meibomian glands located posterior to the grey line on the lid margin.[4] The Demodex mite is involved in both anterior (Demodex folliculorum) and posterior (Demodex brevis) blepharitis.[5]

Blepharitis can also be categorized as acute or chronic, depending on the duration of the disease. The inflammatory changes associated with blepharitis include erythema, hyper keratinization, vascularization, and notching of the lids, as well as abnormalities in the meibomian glands. This leads to altered secretions, which appear turbid, foamy, or granular in appearance. The resulting meibomian gland dysfunction ultimately leads to symptoms of dry eye disease.

Blepharitis can affect anyone, but its prevalence increases with age. A large epidemiological study across eleven countries reported a significant prevalence of meibomian gland disease, affecting approximately 54.3% of the population.[6] A study in South Korea found that the prevalence of blepharitis was around 8.1% among individuals aged 40 and older.[7] Interestingly, studies have shown that Asian populations have a higher prevalence of meibomian gland dysfunction, exceeding 60%, whereas in Caucasian populations, it ranges from 3.5% to 19.9%.[8]

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The American Academy of Ophthalmology's 2018 guidelines outline various treatment options for managing chronic blepharitis, including warm compresses, eyelid cleansing, topical and systemic antibiotics, and topical anti-inflammatory agents.[9] Loteprednol etabonate (LE) is a corticosteroid that binds with high affinity to the glucocorticoid receptor, minimizing side effects such as elevated intraocular pressure (IOP) and cataract formation, as unbound LE is metabolized to an inactive form.[10] Cyclosporine A, on the other hand, works by inhibiting calcineurin, an activator of T-cells, thereby reducing inflammation associated with blepharitis through its immunomodulatory activity.

While various studies have shown the efficacy of topical Cyclosporine and Loteprednol in treating chronic blepharitis, there is a lack of local studies comparing their clinical efficacy in treating this condition. Therefore, the purpose of this study was to compare the clinical efficacy of Loteprednol with Cyclosporine in the treatment of chronic blepharitis, aiming to provide valuable insights into their relative effectiveness.

METHODOLOGY

The Quasi-experimental study was conducted at Department of Ophthalmology at Combined Military Hospital Quetta, Pakistan from July 2020 to December 2020. Written informed consent was obtained for each patient and study protocols were approved by Institutional Review Board and Ethical Committee (EXT-23-05/READ/IRB/2020). Thirty two patients (sixty four eyes) were enrolled in the study with clinical features of chronic blepharitis in both eyes on slit lamp examination. The sample size was calculated by using G*Power; effect size: 0.5, alpha: 0.05, power: 0.8, SD: 2.5 (values estimated from a previous study).[11] The calculated total sample size was 64 and sample size per group was 32.

Inclusion Criteria: Patients of either gender with age ranging from 21 to 70 years, presenting in Outpatient Department with clinical features of burning, irritation, itching, photophobia foreign body sensation, epiphora, tear film breakup time of <10s, and ocular surface disease index score of >22 were included in the study.

Exclusion Criteria: Patients with history of ocular trauma, surgery, herpes keratitis, glaucoma or uveitis, pregnancy or lactating women and previous use of cyclosporine or Loteprednol eye drops within 3 months were excluded from the study.

All patients received standard treatment, including topical artificial tears applied three times daily, topical Bacitracin/Tobramycin eye ointment applied twice daily to the lid margin and lid hygiene instructions, including lid cleansing with baby shampoo twice daily and lid warming massage for 10 minutes before bedtime. Patients were then randomly assigned in a 1:1 ratio to receive either topical Cyclosporine A 0.05% eye drops (Group-A), instilled twice daily or topical Loteprednol 0.5% (Group-B), instilled twice daily. Follow-up appointments were scheduled at baseline, 4 weeks, 8 weeks, and 12 weeks to monitor patient progress. (Figure)

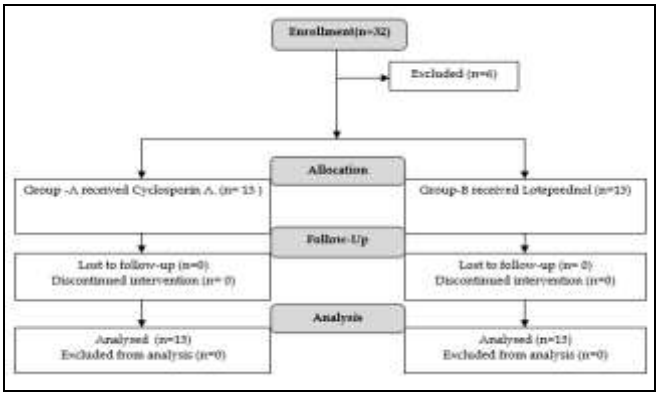

Figure: Patient Flow diagram

A standardized proforma was utilized for the clinical assessment of each patient, capturing essential information, including demographic data, visual acuity assessment, Ocular Surface Disease Index (OSDI) score, Tear Film Break-Up Time (TBUT), Meibomian Gland Secretion Score (MGS), Lid Margin Telangiectasia Score (LMT), Conjunctival Injection Score (CIS) and Lid Scaling/Crusting Score (LSCS). All examinations were conducted by the authors at the same study site, ensuring consistency and accuracy in the data collection process.

The Ocular Surface Disease Index (OSDI) is a questionnaire designed to rapidly assess ocular symptoms related to dry eye disease. The OSDI consists of three subscales; ocular symptom, vision-related function and environmental triggers. Patients rate their responses on a scale of 0 to 4. The final score is calculated, with the following classifications; 0-12 representing normal.[13-22] representing mild dry eye disease, 23-32 representing moderate dry eye disease and greater than 33 representing severe dry eye disease.[11-14] This questionnaire provides a valuable tool for evaluating the severity of dry eye disease and monitoring treatment effectiveness.

The tear film breakup time (TBUT) is a clinical test used to evaluate the stability of the tear film.[15] During the test, fluorescein is instilled into the patient's eye, and the time between the last blink and the appearance of the first dry spot on the cornea is recorded. A TBUT value of over 10 seconds is typically considered normal, indicating a stable tear film. This test provides a valuable assessment of the eye's ability to maintain a healthy, intact tear film.

The Meibomian gland secretion score was evaluated by gently pressing on the center of the upper eyelid margin to express secretions from the meibomian gland orifices. The secretions were then scored based on their appearance, using the following scale.16 0: Clear secretion, 1: Turbid (cloudy) secretion, 2: Granular secretion, 3: Solid or thick secretion. This scoring system assesses the quality and consistency of the meibomian gland secretions, providing insight into the gland's functionality.

Telangiectasia is more easily observable in the upper lid due to the wider vascular zone. The degree of telangiectasia on the upper lid margin was assessed and scored as follows; 0: No capillary dilatation (absence of telangiectasia), 1: Mild capillary dilatation (slight telangiectasia), 2: Moderate capillary dilatation (moderate telangiectasia), 3: Severe capillary dilatation (prominent telangiectasia).[17] This scoring system evaluates the extent of telangiectasia on the upper lid margin, providing a quantitative measure of the condition's severity.

Conjunctival injection was evaluated and scored based on the degree of vasodilation in the bulbar conjunctiva, using the following scale; 0: Normal (no injection), 1: Mild congestion (slight vasodilation), 2: Moderate congestion (moderate vasodilation), 3: Severe congestion (prominent vasodilation). Additionally, the presence of scaling and crusting around the lashes was assessed, which is a characteristic feature of seborrheic and staphylococcal blepharitis.

Seborrheic blepharitis is distinguished by the presence of greasy scales and crusting on the lashes, whereas Staphylococcal blepharitis is characterized by brittle scales on the eyelashes, which may form collarettes as they grow around the lashes.[18] The severity of lid scaling and crusting was evaluated and scored using the following scale; 0: Normal (no scaling or crusting), 1: Mild scaling/crusting (slight deposits on lashes), 2: Moderate scaling/crusting (noticeable deposits on lashes), 3: Severe scaling/crusting (extensive deposits on lashes, potentially causing lash matting or tangling). This scoring system assesses the extent of scaling and crusting on the lashes, providing a quantitative measure of the condition's severity.

Statistical analysis was performed using IBM SPSS (Statistical Package for Social Sciences) software version 20 for Windows. The Independent sample t-test was employed to compare the effects between the two groups at different time points and to evaluate the mean changes from baseline between the two groups at each time point. The *p*-value of less than 0.05 was considered statistically significant, indicating a significant difference between the groups. This statistical approach enabled the comparison of the treatment outcomes between the two groups and the evaluation of the significance of the changes observed over time.

RESULTS

A total of thirty-two patients (64 eyes) were enrolled in the study, with 26 patients completing the full study period. Six patients (12 eyes) were lost to follow-up during the study. Baseline characteristics and test results were comparable between the two groups. The mean age of patients in Group-A was 53.9±1.23 years (range: 24-71 years) and Group-B was 54.1 years (range: 22-77 years). No significant differences were observed between the two groups in terms of age (p=0.97), OSDI scores (p=0.23), p=0.29, MGS (p=0.12), LMTS (p=0.91) and CIS (p=0.83). However, a trend towards significance was observed in LSCS, with Group-A showing a lower score compared to Group-B (p=0.08).These findings indicate that both groups were well-matched at baseline, with no significant differences in demographic and ocular surface parameters, except for a possible difference in lid scaling/crusting score, thereby allowing for a valid comparison of treatment outcomes. (Table-I)

OSDI scores improved over time in both groups, indicating disease resolution. No significant difference in OSDI scores was observed between the two groups at the 1st visit (p>0.05). However, significant improvements were observed in Group-A compared to Group-B at 3 months in OSDI scores (10.79±1.25 vs 18.23±0.65, p<0.05), TBUT (9.86±0.71 vs 8.77±0.65, p<0.05), MGSS (0.43±0.50 vs 0.81±0.63, p=0.02), LMTS (0.11±0.32 vs 0.83±0.47, p=0.05) and LSCS (0.18±0.39 vs 0.67±0.56, p=0.05). No significant differences were observed in CIS at 3 months (0.21±0.42 vs 0.22±0.42, p=0.94). These findings suggest that Cyclosporine (Group-A) was more effective than Loteprednol

(Group-B) in improving ocular surface parameters and reducing symptoms at 3 months. (Table-II)

Table-I: The baseline Variable(s) of patients in both Group-A (Cyclosporine) and Group-B (Loteprednol). (n=26)

Variable(s)	Group-A (n=13) (Cyclosporine)	Group-B (n=13) (Loteprednol)	*p*-value
Age(years)	53.94±1.42	54.06±1.49	0.97
OSDI (ocular surface disease index)	33.09±1.12	29.63±1.61	0.23
TBUT (tear film breakup time)	7.06±1.16	7.38±1.18	0.29
MGS (Meibomian gland score)	1.78±0.75	1.66±0.97	0.12
LMTS (Lid margin telangiectasia score)	1.53±0.62	1.55±0.62	0.91
CIS (conjunctival injection score)	1.84±0.68	1.81±0.70	0.83
LSCS (lid scaling/crusting score)	1.53±0.62	1.84±0.73	0.08

Table-II: Comparison of Outcomes Between Group-A (Cyclosporine) and Group-B (Loteprednol) at 3 Months. (n=26)

Parameters	Group-A (n=13)	Group-B (n=13)	*p*-value
OSDI 1st visit	26.0±0.37	25.13±0.15	0.67
OSDI 3rd visit	10.79±1.25	18.23±0.65	0.02
TBUT 1st visit	7.06±1.17	7.38±1.19	0.29
TBUT 2ndvisit	9.86±0.71	8.77±0.65	0.03
MGSS 1st visit	1.44±0.76	1.28±0.89	0.45
MGSS 3rd visit	0.43±0.50	0.81±0.63	0.02
LMTS 1st visit	1.22±0.66	1.35±0.66	0.42
LMTS 3rd visit	0.11±0.32	0.83±0.47	0.05
CIS 1st visit	1.25±0.51	1.29±0.53	0.76
CIS 3rd visit	0.21±0.42	0.22±0.42	0.94
LSCS 1st visit	1.31±0.69	1.48±0.63	0.31
LSCS 3rd visit	0.18±0.39	0.67±0.56	0.05

OSDI (ocular surface disease index), TBUT (tear film breakup time), TBUT (tear film breakup time), MGS (Meibomian gland score), LMTS (Lid margin telangiectasia score), CIS (conjunctival injection score), LSCS (lid scaling/crusting score).

DISCUSSION

In this study, both Cyclosporine and Loteprednol were effective in treatment of chronic blepharitis. However, the cyclosporine group had statistically significant improvement in OSDI, TBUT, MGS and LMTS and LSCS compared to Loteprednol group.

Meibomian glands produce the outer layer of tear film, known as meibum, which helps prevent evaporation and contamination.[12] However, in patients with meibomian gland disease, the tears evaporate rapidly, leading to inflammation and an increase in pro-inflammatory cytokines resulting in conjunctival redness, tear film instability, angiogenesis and ocular discomfort.[13-14] To combat these symptoms, anti-inflammatory agents are used to counteract the effects of these cytokines in the treatment of blepharitis. Cyclosporine has additional benefits, including improving tear film stability and volume 11 by reducing inflammation in the lacrimal and meibomian glands and increasing mucin production through enhanced conjunctival goblet cells density.[15-17] This results in better tear film stability, reduced ocular discomfort and improved ocular surface disease index in the cyclosporine group. [18-20]

Our findings align with existing research. Rubin *et al.*[21] who reported superior improvement in posterior blepharitis with cyclosporine compared to dexamethasone at three months, indicating a delayed but more effective response. Good eyelid hygiene is a crucial aspect of managing chronic blepharitis, and all patients in both groups were advised to follow this regimen. This included applying warm compresses to loosen eyelid debris and reduce meibum buildup, as well as gently scrubbing the lids with diluted baby shampoo to remove scales and debris. As a result, both groups showed significant improvement in lid scaling and crusting scores over time. Similarly, Kim HY *et al.*[22] reported that cyclosporine improves tear film stability, ocular discomfort, and lid margin inflammation in dry eyes with meibomian gland disease, with better outcomes seen after two months of treatment. Our findings showed that both groups had similar improvements in conjunctival hyperemia/injection, which was unexpected since cyclosporine reduces inflammatory cytokines like IL-1, IL-6, and IL-8, which should lead to less conjunctival hyperemia. However, cyclosporine's common side effect of causing a stinging sensation in the eye and hyperemia offset its anti-inflammatory benefits, resulting in no significant difference between the two groups. Studies by Ames P *et al.*[23] and Tageldin M *et al.*[24] showed results that are in harmony with the results of our study. They concluded that cyclosporine 0.05% ophthalmic emulsion is a definitive treatment that targets the underlying immune-mediated inflammation in chronic dry eye, with continued improvement even after treatment cessation. These studies support the efficacy and prolonged benefits of cyclosporine in managing dry eye and blepharitis. The study found that both cyclosporin and Loteprednol

groups showed similar results at the first two visits, with no significant differences in ocular surface disease index (OSDI), tear break-up time (TBUT), lid margin thickness (LMT) and meibomian gland score (MGS). However, at the third visit, the cyclosporine group demonstrated marked improvement, suggesting that cyclosporine has a slower onset of action but ultimately leads to better outcomes. Therefore, long-term treatment with cyclosporine (at least 2 months) is recommended, which is feasible due to its minimal systemic absorption and side effects. In contrast, Loteprednol, a low potency steroid, reduces ocular inflammation and inflammatory cytokines but has limitations for long-term use due to potential side effects like increased intraocular pressure and cataract formation

This study has several limitations. Firstly, the absence of a control group makes it difficult to fully assess the efficacy of Cyclosporine and Loteprednol. Additionally, the small sample size and short follow-up period of 4 weeks may not be sufficient to capture the full benefits of the treatments, considering the chronic nature of the disease.

CONCLUSION

This study demonstrates that both Cyclosporine and Loteprednol are effective in alleviating signs and symptoms of chronic blepharitis, but cyclosporine shows significantly better outcomes after 12 weeks. These findings suggest that adding cyclosporine to the treatment regimen of patients who are non-responsive to conservative management and those at risk of steroid-related side effects may help reduce ocular surface inflammation and improve tear film stability.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SNM & HM: Data acquisition, data analysis, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Mathers WD, Shields WJ, Sachdev MS, Petroll WM, Jester JV. Meibomian gland dysfunction in chronic blepharitis. Cornea 1991; 10(4): 277-285. https://doi.org/10.1097/00003226-199107000-00001
2. Lemp MA, Nichols KK. Blepharitis in the United States 2009: a survey-based perspective on prevalence and treatment. Ocular Surf 2009; 7(2): S1-S14. https://doi.org/10.1016/s1542-0124(12)70620-1
3. Sandra Johanna GP, Antonio LA, Andrés GS. Correlation between type 2 diabetes, dry eye and Meibomian glands dysfunction. J Optom 2019; 12(4): 256-262. https://doi.org/10.1016/j.optom.2019.02.003
4. Putnam CM. Diagnosis and management of blepharitis: an optometrist's perspective. Clin Optom 2016; 8: 71-78.
5. Fromstein SR, Harthan JS, Patel J, Opitz DL.Demodex blepharitis: clinical perspectives. Clin Optom 2018; 10: 57-63 https://doi.org/10.2147/opto.s142708
6. Doan S, Zagórski Z, Palmares J, Yağmur M, Kaercher T, Benítez-Del-Castillo JM,et al. Eyelid Disorders in Ophthalmology Practice: Results from a Large International Epidemiological Study in Eleven Countries. Ophthalmol Ther 2020; 9(3): 597-608. https://doi.org/10.1007/s40123-020-00268-4
7. Rim TH, Kang MJ, Choi M, Seo KY, Kim SS. Ten-year incidence and prevalence of clinically diagnosed blepharitis in South Korea: a nationwide population-based cohort study. Clin Exp Ophthalmol 2017 ; 45(5): 448-454. https://doi.org/10.1111/ceo.12929
8. Schaumberg DA, Nichols JJ, Papas EB, Tong L, Uchino M, Nichols KK. The international workshop on meibomian gland dysfunction: report of the subcommittee on the epidemiology of, and associated risk factors for, MGD. Invest Ophthalmol Vis Sci 2011; 52(4): 1994-2005.https://doi.org/10.1167/iovs.10-6997e
9. Amescua G, Akpek EK, Farid M, Garcia-Ferrer FJ, Lin A, Rhee MK, et al ; American Academy of Ophthalmology Preferred Practice Pattern Cornea and External Disease Panel. Blepharitis Preferred Practice Pattern®. Ophthalmology 2019; 126(1): P56-P93. https://doi.org/10.1016/j.ophtha.2018.10.019
10. Comstock TL, Sheppard JD. Loteprednol etabonate for inflammatory conditions of the anterior segment of the eye: twenty years of clinical experience with a retrometabolically designed corticosteroid. Expert Opin Pharmacother 2018; 19(4): 337-353. https://doi.org/10.1080/14656566.2018.1439920
11. Moon I, Kang HG, Yeo A, Noh H, Kim HC, Song JS, et al. Comparison of Ocular Surface Mucin Expression After Topical Ophthalmic Drug Administration in Dry Eye-Induced Mouse Model. J Ocul Pharmacol Ther 2018; 34(9): 612-620. https://doi.org/10.1089/jop.2018.0005
12. Periman LM, Mah FS, Karpecki PM. A Review of the Mechanism of Action of Cyclosporine A: The Role of Cyclosporine A in Dry Eye Disease and Recent Formulation Developments.Clin Ophthalmol 2020; 14: 4187-4200. https://doi.org/10.2147/opth.s279051
13. Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. Arch Ophthalmol 2000; 118(5): 615-621. https://doi.org/10.1001/archopht.118.5.615
14. Lu F, Tao A, Hu Y, Tao W, Lu P. Evaluation of Reliability and Validity of Three Common Dry Eye Questionnaires in Chinese. J Ophthalmol 2018; 2018: 2401213. https://doi.org/10.1155/2018/2401213
15. Kanski JJ, Bowling B. Clinical Ophthalmology: A Systemic Approach (Ninth Edition). New York: Elsevier Saunders; 2020, 159-160
16. Turgut B, Çatak O, Demir T. Meibomian gland dysfunction: an overlooked eyelid disease. Adv Ophthalmol Vis Sys 2018; 8(3): 168-172.
17. Chhadva P, Goldhardt R, Galor A. Meibomian gland disease: the role of gland dysfunction in dry eye disease. Ophthalmol 2017; 124(11): S20-06. https://doi.org/10.1016/j.ophtha.2017.05.031

18. Baudouin C, Messmer EM, Aragona P, Geerling G, Akova YA, Benítez-del-Castillo J et al. Revisiting the vicious circle of dry eye disease: a focus on the pathophysiology of meibomian gland dysfunction. Br J Ophthalmol 2016; 100(3): 300-306. https://doi.org/10.1136/bjophthalmol-2015-307415
19. Opitz DL, Harthan JS, Fromstein SR, Hauswirth S. Diagnosis and management of meibomian gland dysfunction: optometrists' perspective. Clini Optometry 2015; 7(1): 59–69.
20. Thode AR, Latkany RA. Current and emerging therapeutic strategies for the treatment of meibomian gland dysfunction (MGD). Drugs 2015; 75(11): 1177-1185. https://doi.org/10.1007/s40265-015-0432-8
21. Rubin M, Rao SN. Efficacy of topical cyclosporine 0.05% in the treatment of posterior blepharitis. J Ocul Pharmacol Ther 2006; 22(1): 47-53.https://doi.org/10.1089/jop.2006.22.47
22. 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. Intl J Ophthalmol 2018; 11(4): 593-596. https://doi.org/10.18240/ijo.2018.04.09
23. Ames P, Galor A. Cyclosporin ophthalmic emulsions for the treatment of dry eye: a review of the clinical evidence. Clin Investig 2015; 5(3): 267-285. https://doi.org/10.4155/cli.14.135
24. 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 Ophthalmol 2018; 32(3): 217-221. https://doi.org/10.1016/j.sjopt.2018.06.001