Comparison of the clinical effects of two different doses (0.05% and 0.1%) of topical cyclosporine A in dry eyes with meibomian gland dysfunction

Comparação de efeitos clínicos de duas doses diferentes (0,05% e 0,1%) de ciclosporina A tópica em olhos secos com disfunção da glândula tarsal

Kemal Bayrakceken[1], **Adem Ugurlu**[1]

[1] Department of Ophthalmology, Erzincan Binali Yildirim University Faculty of Medicine, Erzincan, Turkey.

How to cite:
Bayrakceken K, Ugurlu A. Comparison of the clinical effects of two different doses (0.05% and 0.1%) of topical cyclosporine A in dry eyes with meibomian gland dysfunction. Rev Bras Oftalmol. 2022;81:e0044.

doi:
https://doi.org/10.37039/1982.8551.20220044

Keywords:
Cyclosporine; Dry eye syndrome; Tear function test

Descritores:
Ciclosporina; Síndromes do olho seco; Teste de função lacrimogênea

Received on:
Feb 17,2022

Accepted on:
Apr 13,2022

Corresponding author:
Adem Ugurlu
Erzincan Binali Yildirim University Faculty of Medicine, Erzincan, Turkey
E-mail : ademugurlu88@hotmail.com

Institution:
Erzincan Binali Yildirim University Faculty of Medicine, Erzincan, Turkey.

Conflict of interest:
no conflict of interest.

Financial support:
the authors received no financial support for this work.

ABSTRACT

Objective: To compare the clinical efficacy of two different doses of topical cyclosporine A used in addition to artificial tears in the treatment of patients with meibomian dysfunction and secondary dry eye.

Methods: Fifty patients aged 18 to 40 years, who presented to our clinic between June 2020 and June 2021 were included in our study. Patients were divided into two groups as Group A (topical cyclosporine A 0.05%) and Group B (topical cyclosporine A 0.1%). All the patients underwent a detailed ophthalmological examination, basal Ocular Surface Disease Index measurement, and Schirmer 1 and tear break-up time tests at all visits.

Results: The mean age was 32±7.1 years in Group A and 30.7±8.5 years in Group B. In Group A, there were 15 women and ten men, and Group B consisted of 14 women and 11 men. There was no difference between the groups in terms of age and gender distribution (p>0.05). Schirmer 1 and tear break-up time results and Ocular Surface Disease Index score also did not significantly differ between the groups (p>0.05).

Conclusion: Cyclosporine A 0.05% and 0.1% eye drops were both seen to be effective in managing dry eye disease in patients with meibomian gland dysfunction.

RESUMO

Objetivo: Comparar a eficácia clínica de duas doses diferentes de ciclosporina A tópica utilizada além da lágrima artificial no tratamento de pacientes com disfunção da glândula tarsal e olho seco secundário.

Métodos: No estudo, foram incluídos 50 pacientes com idades entre 18 e 40 anos, que se apresentaram em nossa clínica entre junho de 2020 e junho de 2021. Os pacientes foram divididos em dois grupos: Grupo A (ciclosporina A 0,05% tópica) e Grupo B (ciclosporina A 0,1% tópica). Todos os pacientes foram submetidos a um exame oftalmológico detalhado, medição basal do Índice de Doença da Superfície Ocular, e testes de Schirmer 1 e de tempo de ruptura em todas as visitas.

Resultados: A idade média foi de 32±7,1 anos no Grupo A e 30,7±8,5 anos no Grupo B. No Grupo A, havia 15 mulheres e dez homens, e o Grupo B consistia de 14 mulheres e 11 homens. Não havia diferença significativa entre os grupos em termos de distribuição por idade e gênero (p>0,05). Os resultados do Schirmer 1 e do tempo de ruptura e do Índice de Doenças da Superfície Ocular também não apresentaram diferença significativa entre os grupos (p>0,05).

Conclusão: Observou-se que os colírios de ciclosporina A 0,05% e 0,1% são eficazes no tratamento da síndrome do olho seco em pacientes com disfunção da glândula tarsal.

INTRODUCTION

Dry eye is becoming more and more common around the world due to the rapid evaporation of tears from increased exposure to digital screens and other causes. Dry eye syndrome, a multifactorial disease of the ocular surface that can cause eye discomfort and visual impairment, may occur as a result of lack of aqueous tears or impaired evaporation of tears.[1,2] The most common cause of tear evaporation disorder is meibomian gland dysfunction (MGD), which results in the instability of the tear film layer, increased tear evaporation, and dry eye disease. The meibomian glands, located in the tarsal plate of the upper and lower eyelids, are responsible for the formation of the lipid component of the tear film layer.[3,4] The diagnosis of MGD is made by determining the symptoms of patients with questionnaires, biomicroscopic examination of lid morphology and ocular surface, measurement of tear osmolarity, measurement of tear secretion, staining of the ocular surface, and determination of tear film stability using tear break-up time (TBUT).[5] In the treatment of MGD, hot compress, lid cleaning, and drop therapy are recommended. Artificial tears are primarily used in the treatment of dry eye,[6] but this is not sufficient in most patients; therefore, topical cyclosporine A is additionally applied. Topical cyclosporin A reduces T-cell mediated inflammation of the lacrimal tissue, resulting in an increase in the number of goblet cells and reversal of the squamous metaplasia of the conjunctiva. Currently, two different topical doses of cyclosporine A are used in therapy: 0.05% and 0.1%.[7]

In this study, we aimed to compare the clinical efficacy of two different doses of topical cyclosporine A used in addition to artificial tears in the treatment of patients with MGD and secondary dry eye based on the Ocular Surface Disease Index (OSDI) and TBUT test results.

METHODS

The study was designed as observational at the Department of Ophthalmology of Erzincan Binali Yildirim University Faculty of Medicine. Ethical approval was obtained from the local ethics committee, and the principles of the Declaration of Helsinki were adhered to throughout the study (decision no: 10/05). Signed consent was not required for participation because the study involved only observation of clinical practice, and no patient identifying data were collected.

Fifty patients aged 18 to 40 years, who presented to our clinic between June 2020 and June 2021 with chronic blepharitis and related MGD and had no ocular or systemic disease other than meibomitis were included in our study. At the time of admission, all the patients underwent a detailed ophthalmological examination and basal OSDI and TBUT tests.

Ocular Surface Disease Index, a 12-item questionnaire, was used to determine the patient's complaints about dry eye within the last two weeks. The results were evaluated on a scale of zero to one hundred, and a higher score was interpreted to indicate greater severity of dry eye.[8] Tear break-up time was measured in seconds by applying fluorescein paper to the lower fornix without anesthesia.

In addition to artificial tears, 25 patients were started on topical cyclosporine A 0.05% (Depores, DEVA, Turkey) twice a day and constituted Group A. Other 25 patients who were given topical cyclosporine A 0.1% (Depores X, DEVA, Turkey) once a day and were evaluated as Group B. Routine ophthalmological examinations were performed at the first- and third-month controls in both groups, and the OSDI and tear break-up time tests were repeated.

The Statistical Package for the Social Sciences (SPSS, IBM), version 23, was used for the statistical analyses. The normality of the distribution of continuous variables was determined with the Kolmogorov-Smirnov test. Descriptive statistics for continuous variables were expressed as mean ± standard deviation values with ranges or medians (25^{th}-75^{th} percentile), where applicable. Categorical data were expressed as the number and percentage of cases. The independent *t*-test and analysis of variance (ANOVA) were used as parametric tests to compare normally distributed data. Post-hoc multiple comparisons were adjusted using the Bonferroni correction. The Mann Whitney-U test was used as a non-parametric method. The repeated-measures ANOVA was used to analyze the repeating data, and the Friedman variance analysis was conducted when the data were not normally distributed. Differences were considered significant at $p \leq 0.05$.

RESULTS

The mean age was 32±7.1 years in Group A and 30.7±8.5 years in Group B. There were 15 women and 10 men in Group A and 14 women and 11 men in Group B. No significant difference was observed between the two groups in terms of age and gender distribution ($p>0.05$). Table 1 presents the comparison of the groups in terms of the TBUT results and OSDI scores.

The results of the Schirmer 1 test were 4.9±1.8 [1-9] mm in Group A and 4.85±2.2 [1-9] mm in Group B at admission

Table 1. Comparison of the study groups in terms of the tear function tests and Ocular Surface Disease Index score

	Group A	Group B	p-value
Schirmer V0	4.9±1.8	4.85±2.2	0.742
Schirmer V1	8.5±3.3	8.7±3.8	0.123
Schirmer V2	11.92±4.34	12.2±4.15	0.099
TBUT V0	3.4±0.75	3.4±0.63	0.998
TBUT V1	9.1±5.3	9.25±5.9	0.587
TBUT V2	12.2±4.9	11.96±5.1	0.232
OSDI V0	58.2±21.3	59.1±19.6	0.427
OSDI V1	35.1±14.4	36.1±16.5	0.145
OSDI V2	15.9±7.4	16.2±6.9	0.278

Group A: cyclosporine A 0.05%; Group B: cyclosporine-A 0.1.
V0: first visit (admission); V1: visit at the first month; V2: visit at the third month; TBUT: tear break-up time; OSDI: Ocular Surface Disease Index.

(V0) (p=0.742), 8.5±3.3 [5-12] mm and 8.7±3.8 [5-13] mm, respectively at the first-month visit (V1) (p=0.123), and 11.92±4.34 [8-18] mm and 12.2±4.15 [8-17] mm, respectively at the second-month visit (V2) (p=0.099). There was no significant difference between the two groups in terms of the Schirmer 1 test results. The mean TBUT was 3.4±0.75 [1-5] sec in Group A and 3.4±0.63 [1-5] sec in group B at V0 (p=0.998), 9.1±5.3 [4-15] sec and 9.25±5.9 [3-15] sec, respectively at V2 (p=0.587), and 12.2±4.9 [7-17] sec and 11.96±5.1 [7-17] sec, respectively at V2 (p=0.232), indicating no significant difference between the two groups. Lastly, the mean OSDI score was 58.2±21.3 [36-80] in Group A and 59.1±19.6 [39-79] in group B at V0 (p=0.427), 35.1±14.4 [20-50] and 36.1±16.5 [19-53], respectively at V1 (p=0.145), and 15.9±7.4 [8-23] and 16.2±6.9 [9-23], respectively at V2 (p=0.278), and these values did not significantly differ between the two groups.

DISCUSSION

The aim of the study was to evaluate the effects of two doses of cyclosporine A eye drops in patients with dry eye, which has an increasing incidence across the world. Many studies have shown that dry eye is an inflammatory disease that has many features in common with autoimmune disorders.[9]

In recent studies, treatment with cyclosporine A 0.05% eyedrops twice a day have been shown to improve dry eye symptoms and reduce the use of artificial tears.[10-13] In our study, we compared cyclosporine A 0.05% and 0.1% eyedrops and found that dry eye symptoms improved in both groups, with no significant difference between the two doses.

In the current study, improvement in the tear function tests and OSDI score was observed with the use of both 0.05% and 0.1% cyclosporine A eye drops in patients with dry eye. Similarly, Boboridis et al. suggested that topical cyclosporine A 0.1% presented as a novel promising medication for the management of dry eye disease and MGD.[14]

The short follow-up time and low number of patients can be considered as a limitation of our study.

CONCLUSION

Cyclosporine A 0.05% and 0.1% eye drops were determined to be effective in managing dry eye disease in our study. There was no significant difference between the two different doses of topical cyclosporine A over the three-month use. Currently, there are limited published clinical data concerning the efficacy of these two different doses of topical cyclosporine A, and further studies with a higher number of patients and longer follow-up are needed.

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. The epidemiology of dry eye disease: report of the Epidemiology Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf. 2007;5(2):93-107.
3. Chhadva P, Goldhardt R, Galor A. Meibomian gland disease: the role of gland dysfunction in dry eye disease. Ophthalmol. 2017; 124(11): S20-S26.
4. Sullivan BD, Evans JE, Dana MR, Sullivan DA. Influence of aging on the polar and neutral lipid profiles in human meibo-mian gland secretions. Arch Ophthalmol. 2006;124(9):1286-92.
5. Tomlinson A, Bron AJ, Korb DR, Amano S, Paugh JR, Pearce EI, et al. The international workshop on meibomian gland dysfunction: report of the diagnosis subcommittee. Invest Ophthalmol Vis Sci. 2011;52(4):2006-49.
6. Geerling G, Tauber J, Baudouin C, Goto E, Matsumoto Y, O'Brien T, et al. The international workshop on meibomian gland dysfunction: report of the subcommittee on management and treatment of meibomian gland dysfunction. Investigative Ophthalmol Visual Sci. 2011;52(4):2050-64.
7. Thode AR, Latkany RA. Current and emerging therapeutic strategies for the treatment of meibomian gland dysfunction (MGD). Drugs. 2015;75(11):1177-85.
8. Cömez AT, Tufan HA, Kocabıyık O, Gencer B. Effects of lubricating agents with different osmolalities on tear osmolarity and other tear function tests in patients with dry eye. Curr Eye Res. 2013;38(11):1095-103.
9. Stern ME, Schaumburg CS, Pflugfelder SC. Dry eye as a mucosal autoimmune disease. Int Rev Immunol. 2013;32:19-41.
10. Stevenson W, Chauhan SK, Dana R. Dry eye disease: an immunemediated ocular surface disorder. Arch Ophthalmol. 2012;130:90-100.
11. Sall K, Stevenson OD, Mundorf TK, Reis BL. Two multicenter, ran domized studies of the efficacy and safety of cyclosporine ophthalmic emulsion in moderate to severe dry eye disease. CsA Phase 3 Study Group. Ophthalmology. 2000;107:631-9.
12. Baiza-Duran L, Medrano-Palafox J, Hernandez-Quintela E, Lozano-Alcazar J, Alaniz-de la OJ. A comparative clinical trial of the efficacy of two different aqueous solutions of cyclosporine for the treatment of moderate-to-severe dry eye syndrome. Br J Ophthalmol. 2010;94:1312-5.
13. Demiryay E, Yaylali V, Cetin EN, Yildirim C. Effects of topical cyclosporine a plus artificial tears versus artificial tears treatment on conjunctival goblet cell density in dysfunctional tear syndrome. Eye Contact Lens. 2011;37:312-5.
14. Boboridis KG, Konstas AG. Evaluating the novel application of cyclosporine 0.1% in ocular surface disease. Expert Opin Pharmacother. 2018;19(9):1027-39.