ORIGINAL ARTICLE
KLİNİK ARAŞTIRMA

The efficacy of topical vitamin A in allergic conjunctivitis - case control research

Allerjik konjonktivitte topikal A vitaminin etkinliği- olgu kontrol araştırması

Hakika Erdogan[1], Ziya Akingöl[2], Kardelen Taş[1],

[1]Çanakkale Onsekiz Mart University, Faculty of Medicine, Department of Ophtalmology, Çanakkale, Turkey
[2]Marmara University, Faculty of Medicine, Department of Ophtalmology Istanbul, Turkey

Correspondence: Kardelen Taş
Çanakkale Onsekiz Mart University, Faculty of Medicine, Department of Ophtalmology, Çanakkale, Turkey
e-mail: kardelentas05@gmail.com

ORCID ID: HE 0000-0001-7749-2814
ZA 0000-0002-2107-4370
KT 0009-0003-3847-1887

Submitted Date: 06 December 2024**, Accepted Date:** 27 December 2024

SUMMARY

Aim: The aim of this study is to evaluate the efficacy of topical vitamin A ointment (retinol palmitate, 250 IU/g) on the comfort of for the patients with symptomatic allergic conjunctivitis and dry eye.

Material and Methods: 93 patients with seasonal and perennial allergic conjunctivitis were enrolled in this study. We prescribed topical vitamin A ointment and the classic ocular allergy treatment to 47 and classic ocular allergy treatment only to 46 (control group) patients, respectively. Patients' ocular allergy and dry eye signs and symptoms were compared before and after the treatment in each group.

Results: The topical vitamin A treatment and control groups led to significant improvement in the ocular examination in terms of ocular surface disease index (OSDI) scores and breakup time (BUT) values, but the results were comparatively better in the vitamin A group. We observed the results of the Oxford scheme for the corneal surface condition, and the main symptoms and the other findings of ocular allergy had improved in both the groups after the treatment, without significant differences between the groups.

Conclusion: Our findings suggest that the adjunct treatment with topical vitamin A is effective for allergic conjunctivitis accompanied by dry eye symptoms.

Keywords: Allergic conjunctivitis, topical vitamin A, dry eye, OSDI, BUT, Oxford

ÖZET

Amaç: Bu çalışmanın amacı semptomatik alerjik konjonktivit ve kuru göz hastalarının konforu üzerine topikal A vitamini merheminin (retinol palmitat, 250 IU/g) etkinliğini değerlendirmektir.

Materyal ve Metodlar: Bu çalışmaya mevsimsel ve perennial alerjik konjonktivitli 93 hasta dahil edildi. 47 hastaya topikal A vitamini merhemi ve klasik oküler alerji tedavisi, 46 hastaya ise sadece klasik oküler alerji tedavisi (kontrol grubu) reçete edildi. Hastaların oküler alerji ve kuru göz belirtileri ve semptomları her grupta tedavi öncesi ve sonrası karşılaştırıldı.

Bulgular: Topikal A vitamini tedavisi ve kontrol grupları, oküler yüzey hastalığı indeksi (OSDI) skorları ve parçalanma zamanı (BUT) değerleri açısından oküler muayenede anlamlı iyileşmeye yol açtı, ancak sonuçlar A vitamini grubunda karşılaştırmalı olarak daha iyiydi. Kornea yüzey durumu için Oxford şemasının sonuçlarını gözlemledik ve oküler alerjinin ana semptomları ve diğer bulguları, gruplar arasında anlamlı bir fark olmaksızın, tedaviden sonra her iki grupta da düzeldi.

Sonuç: Bulgularımız, topikal A vitamini ile yapılan ek tedavinin kuru göz semptomlarının eşlik ettiği alerjik konjonktivit için etkili olduğunu göstermektedir

Anahtar kelimeler: Allerjik konjonktivit, topikal A vitamini, Kuru göz, OSDI, BUT, Oxford

Maltepe tıp derg. Cilt:16 Sayı:3/2024
https://doi.org/10.35514/mtd.2024.115

INTRODUCTION

Dry eye disease (DED) is one of the most common diagnoses in outpatient ophthalmology clinics. DED is caused by many different reasons, but especially the malfunction of the glands causing imbalance between three lacrimal layers is the main reason in many patients (1-3).

Allergic conjunctivitis (AC), a prevalent condition in 6%–30% of the general population, has a negative impact on the quality of life (4). The ocular surface is constantly exposed to irritants and allergens that trigger a constant immune response (5). T cell activation leads to the destruction of conjunctival epithelial and goblet cells with an increase in inflammatory cytokine levels such as IL1, IL8, IFNɤ, and TNFα (6). The reduction in the number of goblet cells, in turn, decreases the amount of mucin and disrupts tear stability. Therefore, this condition leads to an evaporative-type DED (7,8).

Thus, AC may cause true DED secondary to decreased conjunctival goblet cells and mucin secretion and chronic allergens may produce a DED effect by disrupting the ocular surface (7, 9, 10). In addition, antihistamines used for allergy can make DED worse (1). Similar symptoms and findings such as redness, itchiness, and foreign body sensation can be observed in AC and DED, irrespective of whether they are separately or simultaneously present (11, 12)

Topical vitamin A is a physiological mediator in the proliferation and differentiation of topical surface epithelial cells and inhibits epithelial distortion (13, 14). In addition, the deficiency of vitamin A leads to the loss of conjunctival goblet cells, and it has been used for dry eye treatment (15, 16)

The aim of our study was to investigate the effects of topical vitamin A (tv A) on patients' comfort after AC treatment by comparing the severity of the symptoms and findings during the healing process of patients receiving tv A treatment and those receiving the classical allergy treatment.

MATERIAL AND METHODS

Staging

This is a retrospective study conducted between April 2017 and June 2017. We collected data from the medical record files of the patients who were examined for itching, photophobia, irritation, and ocular pain and who were diagnosed as seasonal and perennial AC at the Maltepe University Medical Faculty Hospital. Our institutional review board (the Ethics Committee of Maltepe University) approved the study protocol that adhered to the tenets of the Declaration of Helsinki.

Technique

All of the 93 patients were examined and received the same treatment with exception of the tv A ointment, which was administered only to 47 patients in the test group . We decided to include in the study only the data from the eye with most severe symptoms during the diagnosis. We found no significant differences in terms of severity of dry eye disease and ocular allergy (signs or symptoms) among the study patients.Dry eye severity grading scheme according to International Dry Eye Work Shop (2007) in first group and second group is 2,71±0,72 and 2,78±0,8 respectively, it is not statistically significant.

We divided the patients with ocular allergy into two groups according to their treatment. The first group (control group) received a topical steroid (dexamethasone sodium phosphate, Lotemax®) four times daily and topical antihistamine (ketotifen hydrogen fumarate, Zaditen®) twice daily. On the other hand, the second group received topical steroid (dexamethasone sodium phosphate, Lotemax®) four times daily, topical antihistamine (ketotifen hydrogen fumarate, Zaditen®) twice daily, and topical vitamin A ointment (retinol palmitate 250 IU/g, Vitamin A Pos®) once daily.

There was no standardization in terms of the active content of the tear drop in patients using tear drops. Since the effect of tear drops would affect the outcome of the study and no comparison could be made in terms of the active substance, patients using tear drops were excluded from the study.

The data for ocular surface disease index (OSDI) scores, breakup time (BUT) values, Oxford scheme scores, symptoms and physical findings were recorded before and after the treatment for the patients. We excluded the patients with other concomitant ocular surface eye diseases, those with an ophthalmic surgery history, those with systemic disease, and those using any systemic medication.

The OSDI test is a 12-question questionnaire that evaluates the symptoms of ocular irritation and its visual-related functions to assess DED severity with scores ranging from 0 to 100 (17).

The Schirmer test I measures the tear amounts on the eye surface by placing filter papers (SNO* Strips, Lab Chauvin, Aubenas, France) in the inferior fornix without topical anesthesia.

The amount of wetting on the filter paper after 5 min is recorded as the test result. For our study, we defined the results < 10 mm in the Schirmer test as positive for DED (17).

In the tear BUT test, the inferior fornix is touched using saline-soaked fluorescein sticks (Fluorescein, Haagen–

Streit International, Koeniz, Switzerland). The patients are asked to blink and then abstain from blinking until told to do so. The time from the first blink to the detection of dry area formation on the cornea is recorded as the BUT value. We used the BUT values < 8 s to detect DED (18).

The Oxford scheme is a test to assess the state of the ocular surface using a fluorescein stick to stain the cornea, and the results are graded from 0 (no staining) to 5 (severe staining) (19).

Relevant symptoms and findings were extracted and scored from the patients' record files. Papillary hypertrophy, redness, chemosis, and lid edema were the main physical findings, whereas pruritus, irritation, foreign body sensation (discomfort), and photophobia were the main symptoms. We adopted the symptom and sign score measurements from the publication by Ozcan et al. (20).

Statistical Analysis

The distribution of the variables was measured by the Kolmogorov–Smirnov test. We used the Mann–Whitney U-test,Wilcoxon test, chi-square test for the analysis of quantitative data.We used the SPSS 22.0 software for all statistical analyses. P-value (p) < 0,05 is statistically signicant.

RESULTS

Ninety-three eyes of 93 patients were included in the study. The test group that used tv A comprised 47 participants (21 women and 26 men), and the control group comprised 46 participants (22 women and 24 men). The mean age was 18,9 ± 12,6 y in the vitamin A group and 16,6 ± 10,01 y in the control group. We found no differences in terms of age of the patients (p > 0,05) or gender distributions (p > 0,05) between the groups. (Table 1)

Table 1. Demographic characteristics of the study population

		Case Group		Control Group		
		Means s.d / n - %	median	Means s.d / n - %	median	*p*
Age		18,9 ± 12,6	15	16,6 ± 10,1	13	0,32
Sex	Female	21	44,7	22		0,76
	Male	26	55,3	24		

m: Mann Whitney u test, x2: Chi-square test

In our study there was a negative correlation between OSDI and BUT values before the treatment for all patient with ocular allergy. There was a positive correlation between schirmer test values and BUT values before the treatment for all patient with ocular allergy. There was a negative correlation oxford score, and schirmer values before treatment for all patient with ocular allergy. There was a positive correlation between oxford score and OSDI before treatment for all patient with ocular allergy.

The OSDI, BUT, and Schirmer test results of the patients were examined, and we found no significant differences in terms of the results of these tests before the treatment between the two groups (Table 2).

Table 2. Changes in BUT, OSDI and Schirmer values before and after the treatment

	Case Group		Control Group		
	Mean±s.d.	Median	Mean±s.d.	Median	p
OSDI					
Before Treatment	50,2 ± 12,1	54,6	50,2 ± 12,1	54,6	1,000 [m]
First Control	20,8 ± 6,7	20,5	23,7 ± 7,1	20,5	***0,008*** [m]
Difference With Before Treatment p	***0,000*** [w]		***0,000*** [w]		
Second Control	10,1 ± 6,5	11,4	15,0 ± 6,2	18,2	***0,000*** [m]
Difference With Before Treatment p	***0,000*** [w]		***0,000*** [w]		
Schirmer (mm)					
Before Treatment	9,9 ± 2,2	10,0	9,9 ± 2,2	10,0	1,000 [m]
First Control	14,3 ± 1,4	14,0	14,3 ± 1,4	14,0	1,000 [m]
Difference With Before Treatment p	***0,000*** [w]		***0,000*** [w]		
Second Control	17,2 ± 2,9	16,0	16,3 ± 2,9	16,0	***0,020*** [m]
Difference With Before Treatment p	***0,000*** [w]		***0,000*** [w]		
BUT (second)					
Before Treatment	6,7 ± 2,9	5,0	6,7 ± 2,9	5,0	1,000 [m]
First Control	13,6 ± 1,6	14,0	12,7 ± 1,6	13,0	***0,008*** [m]
Difference With Before Treatment p	***0,000*** [w]		***0,000*** [w]		
Second Control	16,9 ± 3,0	16,0	16,1 ± 3,1	16,0	***0,038*** [m]
Difference With Before Treatment p	***0,000*** [w]		***0,000*** [w]		

[m] Mann-whitney u test / [w] Wilcoxon test

However, the OSDI scores and BUT values at the first and second controls after the treatment were better in the tvA group than in the control group (p< 0,001). And, in the first and second controls, these values were better than those before the treatment in each group (p< 0,001). While the Schirmer values were higher in the tvA and control group after the treatment than that prior to it, we found no significant difference between the control and tvA groups in first control. But ın second control schirmer valuesbetervtAgrup than control (p< 0,05).

In addition, we found no significant difference in the Oxford scheme scores between the patients in the tvA group and those in the control group after the treatment(p< 0,05) (Table 3). Lastly, we found no significant differences among the main signs (itching, photophobia, tearing, discomfort-foreign body sensation) and symptoms (hyperemia, papilla size, chemosis, and lid edema) between the groups after the treatment (p< 0,05) (Table 3-4).

DISCUSSION

The association between AC with DED has been investigated in many studies, reporting that DED symptoms and findings are commonly seen in ocular allergies (7,9,21,22). Moreover, there was a study showing that DED symptoms (irritation, pain, blurred vision, and photophobia) were more frequent in the months when the allergens are abundantly present (2).

In fact, allergic symptoms and finding are often intertwined.

Maltepe tıp derg. Cilt:16 Sayı:3/2024 https://doi.org/10.35514/mtd.2024.115

Table 3. Changes in Oxford scor and ocular symptoms before and after the treatment

		Case Group		Control Group		
		n	%	n	%	*p**
Itching						
Before Treatment	Modarete	27	57,4	27	57,4	1,00
	Severe	20	42,6	20	42,6	
First Control	No Symptom	30	63,8	30	63,8	1,00
	Light	17	36,2	17	36,2	
Second Control	No Symptom	30	63,8	29	61,7	0,83
	Light	17	36,2	18	38,3	
Tearing						
Before Treatment	light	7	14,9	7	14,9	1,00
	Modarete	28	59,6	28	59,6	
	Severe	12	25,5	12	25,5	
First Control	No Symptom	38	80,4	38	80,4	1,00
	Light	9	19,1	9	19,1	
Second Control	No Symptom	38	80,9	38	80,9	1,00
	Light	9	19,1	9	19,1	
Discomfort						
Before Treatment	light	3	6,4	3	6,4	1,00
	Modarete	26	55,3	26	55,3	
	Severe	18	38,3	18	38,3	
First Control	No Symptom	33	70,2	33	70,2	1,00
	Light	14	29,8	14	29,8	
Second Control	No Symptom	33	70,2	33	70,2	1,00
	Light	14	29,8	14	29,8	
Photophobia						
Before Treatment	light	18	38,3	18	38,3	1,00
	Modarete	24	51,1	24	51,1	
	Severe	5	10,6	5	10,6	
First Control	No Symptom	26	55,3	26	55,3	1,00
	Light	20	42,6	20	42,6	
	Modarete	1	2,1	1	2,1	
Second Control	No Symptom	26	55,3	26	55,3	1,00
	Light	20	42,6	20	42,6	
	Modarete	1	2,1	1	2,1	

** x^2 Chi-square test*

Hence, it is difficult to distinguish between the two conditions and antihistamines may cause deterioration of DED findings when used for a long time leading to treatment failure considering that AC treatment is mainly directed at alleviating the classic finding and symptoms of allergies (7, 9, 21, 23, 24).

Table 4. Changes in ocular signs before and after the treatment

		Case Group		Control Group		
		n	%	n	%	*p**
Hyperemia						
Before Treatment	Light	7	14,9	7	14,9	1,00
	Modarete	35	74,5	35	74,5	
	Severe	5	10,6	5	10,6	
First Control	No Symptom	5	95,7	5	95,7	1,00
	Light	45	4,3	45	4,3	
Second Control	No Symptom	2	95,7	2	95,7	1,00
	Light	45	4,3	45	4,3	
Papillae						
Before Treatment	Light	1	2,1	1	2,1	1,00
	Modarete	30	63,8	30	63,8	
	Severe	16	34,0	16	34,0	
First Control	No Symptom	24	51,1	24	51,1	1,00
	Light	23	48,9	23	48,9	
Second Control	No Symptom	24	51,1	24	51,1	1,00
	Light	23	48,9	23	48,9	
Chemosis						
Before Treatment	No Symptom	28	59,6	28	59,6	1,00
	Light	17	36,2	17	36,2	
	Modarete	2	4,3	2	4,3	
First Control	No Symptom	47	100,0	47	100,0	-
Second Control	No Symptom	47	100,0	47	100,0	-
Lıd Edema						
Before Treatment	No Symptom	43	91,5	43	91,5	1,00
	Light	4	8,5	4	8,5	
First Control	No Symptom	47	100,0	47	100,0	-
Second Control	No Symptom	47	100,0	47	100,0	-

**x^2 Chi-square test*

Our study was performed retrospectively. More than one doctor is involved in the treatment of the patients. Some doctors preferred to use vitamin A for dry eye symptoms in patients with allergic conjunctivitis, while the others preferred to observe dry eye symptoms by treating allergic conjunctivitis. During the follow-up period, a tear drop was started to the patients had severe dry eye symptoms. These patients were excluded from study And also patients using long-term anti-histaminic drops to minimize the

direct effect on DED findings were also excluded. They are limitations for the present study because we did not effect tvA in patient had severe symptoms and signs. Vitamin A

ointment was used in some of our patients considering that ocular allergy-caused inflammation can lead to the loss of goblet cells, leading to a decrease in MUC5AC secretion, which in particular provides tear stability (25). Vitamin A has been directly related to tear quality (26).

In studies comparing AC and DED associations, BUT values were found to be lower in ocular allergy cases compared with those in non-ocular allergy cases (2,8,21,23). However, other studies found no such difference. In our study, we found the BUT values to be lower than the normally accepted value in patients with AC (18). The differences between the results of the studies may depend on the duration of the ocular condition and the degree of destruction in goblet cells in different patient populations. Therefore, the comparison of cytological analyses may be important for proper patient evaluation.

The results of the Schirmer test in AC cases differ among studies (2,23). Higher values may be linked to ocular surface irritation and eye wetness in an acute phase of AC. In our study, we found the Schirmer test values to be close to the normal limits in the pretreatment period. Our patients had normal or lower Schirmer test values and lower BUT values in the pretreatment phase; therefore, it is possible that this reflects chronic AC stages with some goblet cell loss before the treatment. This may explain the greater increase in BUT and Schirmer values in the group using tvA compared to the results of the tests in the control group.

Our study results are supported by another study wherein a group of patients with DED using 0,005% retinyl palmitate showed higher BUT and Schirmer test values than those in the control patients (27). In another study, topical retinoic acid has been shown to improve ocular symptoms and BUT and Schirmer test values (28). Lastly, in another study using topical vitamin A palmitate (50 IU/ml), blurred vision and symptoms did not improve and BUT scores increased, but no changes were detected in terms of the Schirmer test values (29). The differences among the different studies may be due to the differences in the underlying causes among the different patients with DED.

The OSDI and Oxford scheme scoring, which we used to evaluate the severity of DED, has been shown to be higher in patients with AC (3,23). In addition, a negative correlation has been reported between BUT and OSDI (23). In our study, we also found a negative correlation between the BUT values and OSDI before treatment in ocular allergy cases. Particularly, we found a significant increase in the OSDİ values in the tvA group compared to those in the control group after the treatment. In a group of patients with glaucoma wherein prostaglandin agonist and topical vitamin A were used, the treatment improved the OSDI index and prevented the decrease in BUT values like the present study (30).

Topical vitamin A derivatives are used in various ocular surface anomalies in epithelial healing after refractive surgery after the distortion and death of epithelial cells, after glaucoma and for the corneal–scleral incision site healing to promote faster healing of the epithelium (14-16, 21, 31, 32, 33). In our study, we found no difference between the groups in terms of the Oxford scheme test after the treatment. This can be attributed to the fact that the pretreatment Oxford scheme results in our study were not severe to begin with.

In AC cases, papillary hypertrophy, redness, irritation, and lid edema are common findings and pruritus, foreign body sensation, and photophobia are common symptoms. The papillary formation has been associated with low Schirmer test and BUT scores and high IG count and papillary hypertrophy is common in ocular surface allergy cases (7, 23). The most common symptoms in AC are itching, photophobia, and foreign body sensation (24). In a group of patients with AC and DED, pruritus and redness were more frequently seen than in patients who had only AC or DED. In our study, the most prominent AC symptoms were itching and foreign body sensation, and the most obvious findings included hyperemia and papillary formation. In the post-treatment period, we found that the patients in both the groups had symptom improvement, and we could not find any significant differences between them. This can be attributed to the use of topical antihistamine and topical steroid use in both the groups. Therefore, this is a limitation of our study; we could not assess the effects of only tvA.

As seen from the results of the study, significant improvement was observed in both groups. This may indicate that the most important step in the treatment of allergy is the use of antihistamines and steroids. However, topical tv A treatment showed a better improvement especially in OSDI scores. This may suggest that the use of tv A affects patient comfort more than the clinic.

Other limitations of our study include the inability to perform cytological studies or to assess the serum and tear vitamin A levels, blood eosinophilia, and serum IgE levels. In addition, the group we followed did not have severe allergic signs and symptoms, and almost all of our patients responded to the topical treatment. Therefore, further studies that test tvA for severe ocular allergy patients are warranted. Lastly, we could not collect the data about long-term topical vitamin A effects because of the short follow-ups in our study.

CONCLUSION

The symptoms and findings in AC are similar to those in DED, and in many cases, both conditions coexist in the

Maltepe tıp derg. Cilt:16 Sayı:3/2024
https://doi.org/10.35514/mtd.2024.115

same patient. The main deficiency in patients presenting the evaporative-type DED is the decrease in mucin secretion, and vitamin A is essential for goblet cells and has been proven helpful in these instances (8).

As shown in our study, topical vitamin A may be an adjunct to treatment when DED findings such as BUT and Schirmer test abnormalities suggest its presence in ocular allergy.

Author Contributions: Working Concept/Design: HE, Data Collection: KT, Data Analysis / Interpretation: ZA, Text Draft: HE, ZA, Critical Review of Content: ZA, KT, Final Approval and Responsibility: HE, Technical Support: ZA, KT, Supervisor: HE.
Conflict of Interest: The authors state that there is no conflict of interest regarding this manuscript.
Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1.Golden MI, Fries PL. Dry Eye Syndrome. StatPearls. Treasure Island (FL): StatPearls Publishing StatPearls Publishing LLC.; 2017.
2.Ayaki M, Kawashima M, Uchino M, Tsubota K, Negishi K. Possible association between subtypes of dry eye disease and seasonal variation. Clinical ophthalmology. (Auckland, NZ) 2017; 11: 1769-75.
3.Chen L, Pi L, Fang J, Chen X, Ke N, Liu Q. High incidence of dry eye in young children with allergic conjunctivitis in Southwest China. Acta ophthalmologica 2016; 94(8): e727-e30.
4.Thong BY. Allergic conjunctivitis in Asia. Asia Pacific allergy. 2017; 7(2): 57-64.
5.Galletti JG, Guzman M, Giordano MN. Mucosal immune tolerance at the ocular surface in health and disease. Immunology. 2017; 150(4): 397-407.
6.Dartt DA, Masli S. Conjunctival epithelial and goblet cell function in chronic inflammation and ocular allergic inflammation. Current opinion in allergy and clinical immunology. 2014; 14(5): 464-70.
7.Toda I, Shimazaki J, Tsubota K. Dry eye with only decreased tear break-up time is sometimes associated with allergic conjunctivitis. Ophthalmology. 1995; 102(2): 302-9.
8.Dogru M, Okada N ,Asano-Kato N,Tanaka M.,Igarashi A,Takano Y, et al. Atopic ocular surface disease: implications on tear function and ocular surface mucins. Cornea. 2005; 24(8 Suppl): S18-s23.
9.Hom MM, Nguyen AL, Bielory L. Allergic conjunctivitis and dry eye syndrome. Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology. 2012; 108(3): 163-6.
10.Lobefalo L,.D'Antonio E,Colangelo L,Della Loggia G ,Di Gioacchino M, Angelucci D, et al. Dry eye in allergic conjunctivitis: role of inflammatory infiltrate. International journal of immunopathology and pharmacology. 1999; 12(3): 133-7.
11.Fujishima H, Toda I, Shimazaki J, Tsubota K. Allergic conjunctivitis and dry eye. The British journal of ophthalmology.1996; 80(11): 994-7.
12.Bielory L. Role of antihistamines in ocular allergy. The American journal of medicine. 2002; 113 Suppl 9A: 34s-7s.
13.Kruse FE, Tseng SC. Retinoic acid regulates clonal growth and differentiation of cultured limbal and peripheral corneal epithelium. Investigative ophthalmology & visual science. 1994; 35(5): 2405-20.
14.Cho HK, Park MH, Moon JI. The effect of additional topical cyclosporine or vitamin A on the ocular surface during antiglaucoma medication administration. Ophthalmic research. 2012; 48(3): 139-45.
15.Chelala E, Dirani A, Fadlallah A, Fahd S. The role of topical vitamin A in promoting healing in surface refractive procedures: a prospective randomized controlled study. Clinical ophthalmology. (Auckland, NZ) 2013; 7: 1913-8.
16.Ubels JL, Edelhauser HF, Foley KM, Liao JC, Gressel P. The efficacy of retinoic acid ointment for treatment of xerophthalmia and corneal epithelial wounds. Current eye research. 1985; 4(10): 1049-57.
17.Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. Archives of ophthalmology. (Chicago, Ill : 1960) 2000; 118(5): 615-21.
18.McCarty CA, Bansal AK, Livingston PM, Stanislavsky YL, Taylor HR. The epidemiology of dry eye in Melbourne, Australia. Ophthalmology. 1998; 105(6): 1114-9.
19.Bron AJ, Evans VE, Smith JA. Grading of corneal and conjunctival staining in the context of other dry eye tests. Cornea. 2003; 22(7): 640-50.
20.Ozcan AA, Ersoz TR, Dulger E. Management of severe allergic conjunctivitis with topical cyclosporin a 0.05% eyedrops. Cornea. 2007; 26(9): 1035-8.
21.Villani E, Strologo M. D, Pichi F, Luccarelli S. V, De Cilla S, et al. Dry Eye in Vernal Keratoconjunctivitis: A Cross-Sectional Comparative Study. Medicine. 2015; 94(42): e1648.
22.Kim TH, Moon NJ. Clinical correlations of dry eye syndrome and allergic conjunctivitis in Korean children. Journal of pediatric ophthalmology and strabismus. 2013; 50(2): 124-7.
23.Akil H, Celik F, Ulas F, Kara IS. Dry Eye Syndrome and Allergic Conjunctivitis in the Pediatric Population. Middle East African journal of ophthalmology. 2015; 22(4): 467-71.
24.Geraldini M, Chong Neto HJ, Riedi CA, Rosario NA. Epidemiology of ocular allergy and co-morbidities in adolescents. Jornal de pediatria. 2013; 89(4): 354-60.
25.Hu Y, Matsumoto Y, Dogru M, Okada N, Igarashi A, Fukagawa K., et al. The differences of tear function and ocular surface findings in patients with atopic keratoconjunctivitis and vernal keratoconjunctivitis. Allergy. 2007; 62(8): 917-25.
26.Kobayashi TK, Tsubota K, Takamura E, Sawa M, Ohashi Y, Usui M. Effect of retinol palmitate as a treatment for dry eye: a cytological evaluation. Ophthalmologica Journal

international d'ophtalmologie International journal of ophthalmology Zeitschrift fur Augenheilkunde. 1997; 211(6): 358-61.
27.Kim EC, Choi JS, Joo CK. A comparison of vitamin and cyclosporine a 0.05% eye drops for treatment of dry eye syndrome. Am J Ophthalmol. 2009; 147(2): 206-13.e3.
28.Selek H, Unlu N, Orhan M, Irkec M. Evaluation of retinoic acid ophthalmic emulsion in dry eye. European journal of ophthalmology. 2000; 10(2): 121-7.
29.Toshida H, Funaki T, Ono K, Tabuchi N, Watanabe S, Seki T, et al. Efficacy and safety of retinol palmitate ophthalmic solution in the treatment of dry eye: a Japanese Phase II clinical trial. Drug design, development and therapy. 2017; 11: 1871-9.
30.Cui X, Xiang J, Zhu W, Wei A, Le Q , Xu J , et al. Vitamin A Palmitate and Carbomer Gel Protects the Conjunctiva of Patients With Long-term Prostaglandin Analogs Application. Journal of glaucoma. 2016; 25(6): 487-92.
31.Johansen S, Heegaard S, Prause JU, Rask-Pedersen E. The healing effect of all-trans retinoic acid on epithelial corneal abrasions in rabbits. Acta ophthalmologica Scandinavica. 1998; 76(4): 401-4.
32.Soker S, Nergiz Y, Cakmak S, Bahceci S, Soker M. Conjunctival impression cytology and correlation with vitamin a levels in children with Down Syndrome. The Medical Journal of Goztepe Training and Research Hospital. 2010; 25(3): 121-5.
33.Kastl PR, Rosenthal WN, Batlle I, Karcioglu Z. Topical vitamin A ointment increases healing of cataract incisions. Annals of ophthalmology. 1987; 19(5): 175-7, 80.

Maltepe tıp derg. Cilt:16 Sayı:3/2024
https://doi.org/10.35514/mtd.2024.115