ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

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Efficacy of Dexpanthenol/Sodium Hyaluronate Fixed Combination Versus Sodium Hyaluronate Eye Drops for the Treatment of Dry Eye Disease and Ocular Surface Inflammation Following Cataract Surgery: A Comparative Study

Katarakt Cerrahisi Sonrası Oküler Yüzey İnflamasyonu ve Kuru Göz Hastalığı Tedavisinde Dekspantenol/Sodyum Hyaluronat Fiks Kombinasyonuna Karşı Sodyum Hyaluronat Damla Etkinliği: Karşılaştırmalı Çalışma

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ABSTRACT Objective: To compare the efficacy of dexpanthenol/ sodium hyaluronate fixed combination with sodium hyaluronate eye drops in the treatment of dry eye disease (DED) and ocular surface inflammation (OSI) following cataract surgery. **Material and Methods:** Sixty-three patients who underwent cataract surgery were included in this study. In addition to the standard postoperative treatment, one group (study group, n=30 eyes) received dexpanthenol/sodium hyaluronate fixed combination eye drops, while the other group was given sodium hyaluronate eye drops (control group, n=33 eyes). The 2 groups were compared in terms of best-corrected visual acuity, tear break-up time (TBUT), corneal flourescein staining, ocular surface disease index (OSDI) and in vivo confocal microscopy (IVCM) findings. **Results:** While TBUT was significantly greater in the study group than the control group (11.2, 8.9, respectively), corneal floresein staining (0.13, 0.48, respectively) and OSDI (10.8, 17.1, respectively) were significantly lower in the study group compared to the control group at postoperative 4 months. In IVCM, the number of dendritic cells and activated keratocytes were significantly lower in the study group (40.8, 13.9 respectively) compared to the control group (51.2, 18.0, respectively). In addition, while the total number of nerves in the study group (4.57) was higher than that of the control group (3.91), the nerve tortuosity was lower in the study group (1.57, 2.18, respectively). **Conclusion:** Dexpanthenol/sodium hyaluronate fixed combination eye drops could be preferred as an adjuvant for the treatment of DED and OSI following cataract surgery.

Keywords: Cataract surgery; dry eye disease; dexpanthenol/sodium hyaluronate fixed combination; in vivo confocal microscopy; ocular surface inflammation

ÖZET Amaç: Katarakt cerrahisi sonrası kuru göz hastalığı (KGH) ve oküler yüzey inflamasyonu (OYİ) tedavisinde dekspantenol/sodyum hyaluronat fiks kombinasyon etkinliğini, sodyum hyaluronat göz damlası ile karşılaştırmaktır. **Gereç ve Yöntemler:** Çalışmaya, katarakt cerrahisi uygulanan 63 hasta dâhil edildi. Standart postoperatif tedaviye ek olarak, bir gruba (çalışma grubu, n=30 göz) dekspantenol/sodyum hyaluronat fiks kombinasyon göz damlası, diğer gruba ise sodyum hyaluronat göz damlası (kontrol grubu, n=33 göz) verildi. İki grup, en iyi düzeltilmiş görme keskinliği (EİDGK), gözyaşı kırılma zamanı (GKZ), fluoresein ile korneal boyanma, oküler yüzey hastalığı indeksi (OYHİ) ve in vivo konfokal mikroskopi (IVKM) bulguları açısından karşılaştırıldı. **Bulgular:** Ameliyat sonrası 4. ayda GKZ çalışma grubunda kontrol grubuna göre (11,2-8,9, sırasıyla) anlamlı olarak daha yüksek iken, fluoresein ile korneal boyanma (0,13-0,48, sırasıyla) ve OYHİ (10,8-17,1, sırasıyla) çalışma grubunda kontrol grubuna göre anlamlı derecede düşüktü. IVKM'de dendritik hücre ve aktive keratosit sayısı, çalışma grubunda (40,8-13,9, sırasıyla) kontrol grubuna göre (51,2-18,0, sırasıyla) daha düşük saptandı. Ayrıca çalışma grubunda sinir sayısı (4,57) kontrol grubuna göre (3,91) daha yüksek iken, sinir kıvrımlanması çalışma grubunda (1,57-2,18, sırasıyla) daha azdı. **Sonuç:** Dekspantenol/sodyum hyaluronat fiks kombinasyon göz damlası, katarakt cerrahisi sonrası KGH ve OYİ tedavisinde yardımcı ajan olarak tercih edilebilir.

Anahtar Kelimeler: Katarakt cerrahisi; kuru göz hastalığı; dekspantenol/sodyum hyaluronat fiks kombinasyonu; in vivo konfokal mikroskopi; oküler yüzey inflamasyonu

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Cataract surgery is the most performed eye surgery and one of the leading causes of iatrogenic dry eye disease (DED).[1] Several factors contribute to the development of DED after cataract surgery, including the use of anesthetic drops and povidone-iodine before surgery, corneal incisions, microscope light toxicity, and goblet cell damage during surgery, and the use of eye drops containing preservatives following surgery.[1,2] Many patients are dissatisfied with the surgical outcome due to postoperative DED symptoms, despite an uncomplicated surgery and achieving the target refraction.

Various treatments are recommended for the management of DED after cataract surgery, including lid hygiene, artificial tear substitutes, and topical cyclosporine 0.05%.[1,2] It has been demonstrated that using sodium hyaluronate eye drops after cataract surgery reduces postoperative DED symptoms and ocular surface staining while increasing tear break-up time (TBUT).[3]

Dexpanthenol is the alcohol form of pantothenic acid (vitamin B5) and has been used for epithelial healing in the form of an ointment and as an adjuvant in the antiseptic eye drops for contact lens users in ophthalmology.[4,5] Eye drops containing 2% dexpanthenol and 0.15% sodium hyaluronate have recently been introduced to the market, but no clinical study has been conducted to determine this product's effectiveness on iatrogenic DED management following cataract surgery.

The purpose of this study is to compare the efficacy of dexpanthenol/sodium hyaluronate fixed combination eye drops with sodium hyaluronate eye drops in the treatment of DED and ocular surface inflammation (OSI) following cataract surgery.

MATERIAL AND METHODS

STUDY DESIGN AND SUBJECTS

This retrospective comparative study included patients who underwent cataract surgery and were treated for iatrogenic DED between January-May 2022.

Diagnosis of iatrogenic DED was made using the TFOS DEWS II guidelines and the following criteria were used: patients with an ocular surface disease index (OSDI) score ≥13, TBUT<10 seconds, and/or positive corneal flourescein staining (CFS) after cataract surgery.[1,6,7] As specular microscopy is unavailable in our clinic, corneal endothelium is evaluated with in vivo confocal microscopy (IVCM) prior to cataract surgery. Furthermore, a comprehensive evaluation including eyelid examination, nasolacrimal canal lavage, DED tests were routinely performed when a patient decided to have cataract operation. In addition, IVCM has been used to evaluate postoperative OSI in patients with DED. Thus, patients who underwent preoperative and postoperative these measurements and used tear film substitutes including dexpanthenol/sodium hyaluronate fixed combination or sodium hyaluronate eye drops were included in this study.

The patients with the following exclusion criteria were excluded from the study: patients aged 18 years or younger; use of systemic medications such as antihistamines, antihypertensives, antidepressants, or any medication that may cause DED; having moderate to severe DED before surgery; contact lens wearers; use of any topical eye drops such as antiglaucoma medications, cyclosporine, tear film substitutes, corticosteroids; the presence of an eye disease other than cataract such as eyelid disease, ocular surface problem, glaucoma, allergic conjunctivitis; history of previous ocular surgery and trauma; patients operated for mature or morgagnien cataracts; the presence of any complications during cataract surgery; files with missing data.

The study was performed according to the guidelines listed in the Declaration of Helsinki and Health Sciences University Dışkapı Yıldırım Beyazıt Training and Research Hospital local ethics committee approval (date: Jun 06, 2022, no: 139/10) was obtained. Each patient provided written informed consent.

SURGICAL PROCEDURE AND POSTOPERATIVE CARE

All surgeries were performed by the same surgeons under topical anesthesia (proparacaine, Alcaine, Alcon Lab. Inc., Fort Worth, USA). After draping the eye under sterile conditions, 5% povidone-iodine so-

lution was applied to the conjunctival sac for 3 minutes. Then, a 2.2-mm main incision and 2 side port incisions of 90-degree away from the main incision were created. Phacoemulsification was performed using the Centurion Vision System (Alcon Lab. Inc., Fort Worth, USA) with gravity-based fluidics, continuous phacoemulsification mode, and a maximum of 60% torsional power.

All patients were instilled moxifloxacin (Vigamox, Alcon Lab. Inc., Fort Worth, USA) and dexamethasone (Maxidex, Alcon Lab. Inc., Fort Worth, USA) eye drops every 2 hours for the first week and 4 times a day for the following 3 weeks for postoperative standard care. In addition to this treatment, tear film substitutes were also given 4 times a day for 4 months.

Two groups were created according to the eye drops used as the study group using dexpanthenol-sodium hyaluronate (Panthol Eye, Deva, Türkiye) and the control group using unpreserved single-dose sodium hyaluronate (Eyestil, Sifi, Italy).

OUTCOME MEASUREMENTS

Age, gender, and intraoperative phaco metrics, including cumulative dissipated energy (CDE), total ultrasound (US) time, and torsional amplitude were recorded.

All patients underwent comprehensive ophthalmologic examinations by the same ophthalmologist at baseline (before surgery) and on the postoperative first week, first month, and 4 months, including the following tests: best-corrected visual acuity (BCVA); TBUT; CFS (by Oxford 5-point scale); OSDI questionnaire.[7-9]

In addition, laser scanning IVCM (HRT-III, Rostock Cornea Module, Heidelberg, Germany) was performed on the central cornea to assess cell density changes in different layers of the cornea and OSI at baseline and in postoperative first and fourth months. Laser scanning IVCM requires direct contact of a confocal cap, and the field of view is 400*400 µm with a lateral resolution of 1 µm/pixel.[10]

While analyzing the IVCM images, 3 well-focused images were chosen and evaluated by two masked ophthalmologists. A frame with a size of 200x200 µm was positioned at the center of the images. The cells were then counted manually by using the manual counting feature of the instrument and the average of the results were used. The subbasal nerve plexus images were analyzed using the Image J plug-in Neuron J program, a semi-automated scanning software (http://www.imagescience.org/ meijering/software/neuronj/).[11,12] The number of total nerves was determined by counting the number of nerve trunks and branches seen in a frame. The degree of nerve tortuosity, and the nerve reflectivity were then rated from 0 to 4, as proposed by Oliveira-Soto and Efron.[13]

STATISTICAL ANALYSIS

SPSS version 28.0 (IBM Corporation, Armonk, NY, USA) was utilized. Independent samples t-test and Mann-Whitney U test were used to compare quantitative data. Wilcoxon test was used for the repeated measurements. The chi-square test was used for the comparison of the qualitative data.

RESULTS

Our study included a total of 63 eyes, as 30 eyes in the study group and 33 eyes in the control group. Only one eye per patient was selected. In terms of age, gender, and intraoperative phaco metrics, both groups were comparable (p>0.05) (Table 1).

BCVA increased significantly at one week postoperatively (p=0.000) and remained stable throughout follow-up in both groups, and the groups were similar in terms of BCVA at all visits (Table 2).

DED FINDINGS

TBUT showed a significant decrease at postoperative 1 week (p=0.000). However, the TBUT values were statistically higher in the study group (9.1±1.1, 11.2±1.1, respectively) compared to the control group (8.0±1.0, 8.9±1.1) at postoperative 1 and 4 months. The change in TBUT was shown in Table 2.

CFS showed a significant increase at the postoperative one week (p=0.000). However, CFS values were statistically lower in the study group (0.67±0.80, 0.13±0.43, respectively) compared to the control group (1.03±0.81, 0.48±0.76) at postoperative 1 and 4 months. The change in CFS was shown in Table 2.

TABLE 1: Demographic and intraoperative data.

Mean±sd (median)	Study group (n=30)	Control group (n=33)	p value
Age (years)	67.7±7.0 (68.0)	67.0±6.5 (68.0)	0.697[t]
Sex (male/female)	16/14	17/16	0.885[X²]
CDE (%-s)	10.2±3.2 (10.4)	10.9± 3.6 (10.7)	0.872[m]
Total U/S time (s)	48.4±12.6 (46.0)	46.71±11.1 (45.0)	0.686[m]
Torsional amplitude (%)	56.2±11.0 (57.0)	57.4±8.9 (57.0)	0.883[m]

CDE: Cumulative dissipated energy; [t]Independent Samples t test; [X²]Chi-square test; [m]Mann-Whitney U test.

TABLE 2: Comparison of preoperative and postoperative BCVA and DED measurements between groups.

Mean±sd (median)	Study group (n=30)	Control group (n=33)	p value
BCVA (logMAR)			
Preoperative	0.58±0.29 (0.50)	0.56±0.26 (0.50)	0.972[m]
Postoperative 1 week	0.04±0.06 (0.00)	0.04±0.05 (0.00)	0.796[m]
Postoperative 1 month	0.03±0.04 (0.00)	0.03±0.04 (0.00)	0.955[m]
Postoperative 4 months	0.02±0.04 (0.00)	0.02±0.04 (0.00)	0.842[m]
TBUT (sn)			
Preoperative	9.0±1.4 (9.0)	9.1±1.1 (9.0)	0.983[m]
Postoperative 1 week	6.1±1.0 (6.0)	6.1±0.9 (6.0)	0.960[m]
Postoperative 1 month	9.1±1.1 (9.0)	8.0±1.0 (8.0)	**0.000[m]**
Postoperative 4 months	11.2±1.1(11.0)	8.9±1.1 (9.0)	**0.000[m]**
CFS (0-5)			
Preoperative	0.37±0.61 (0.00)	0.39±0.70 (0.00)	0.938[m]
Postoperative 1 week	1.13±0.97 (1.00)	1.15±1.00 (1.00)	0.982[m]
Postoperative 1 month	0.67±0.80 (0.50)	1.03±0.81 (1.00)	**0.042[m]**
Postoperative 4 months	0.13±0.43 (0.00)	0.48±0.76 (0.00)	**0.026[m]**
OSDI (0-100)			
Preoperative	17.1±2.7 (16.5)	17.2±4.0 (15.0)	0.377[m]
Postoperative 1 week	26.2±4.6 (25.0)	26.1±5.0 (25.0)	0.703[m]
Postoperative 1 month	14.0±2.2 (14.0)	23.4±4.2 (22.0)	**0.000[m]**
Postoperative 4 months	10.8±1.7 (11.0)	17.1±3.9 (16.0)	**0.000[m]**

BCVA: Best-corrected visual acuity; DED: Dry eye disease; TBUT: Tear break-up time; CFS: Corneal florescein staining; OSDI: Ocular surface disease index; [m]Mann-Whitney U test; bold type: Statistically significant.

OSDI score showed a significant increase at postoperative 1 week (p=0.000). However, the OSDI score was significantly higher in the control group 23.4±4.2, 17.1±3.9, respectively) than in the study group (14.0±2.2, 10.8±1.7, respectively) at postoperative 1 and 4 months. The change in OSDI score was shown in Table 2.

IVCM FINDINGS

The basal epithelial cell density decreased significantly at postoperative 1 month in both groups (p=0.000). However, the study group had a higher density of basal epithelial cells (5730±637) than the control group (5663±504) at the postoperative 4 months, but this difference was not statistically significant. In preoperative and all postoperative controls, basal epithelial cell density was comparable between groups (Table 3).

While the number of dendritic cells and activated keratocytes increased in both groups in the first postoperative month (p=0.000), there was no difference between the groups. In the fourth postoperative month, the number of dendritic cells and activated keratocytes decreased in both groups. However, the

number of cells in the study group (40.8±16.8, 13.9±3.7, respectively) was significantly lower than in the control group (51.2±18.0, 18.0±4.3, respectively) (Table 3).

Endothelial cell density was found to be similar in both groups in preoperative and postoperative all controls (Table 3).

While the total number of nerves decreased in both groups at postoperative 1 month (p=0.000), nerve tortuosity significantly increased (p=0.000). In the fourth postoperative month, however, the total number of nerves was significantly greater in the study group (4.57±1.04) than in the control group (3.91±0.80), and the nerve tortuosity was significantly lower in the study group (1.57±0.68) compared to the control group (2.18±0.68).

Nerve reflectivity did not change in preoperative and postoperative all controls, and there was no significant difference between the groups. IVCM subbasal nerve plexus data was shown in Table 4.

Figure 1 shows the subbasal nerve plexus density and dendritic cells before and 4 months after treatment with dexpanthenol/sodium hyaluronate fixed combination eye drops.

TABLE 3: Comparison of IVCM cell densities between groups.

Mean±sd (median)	Study group (n=30)	Control group (n=33)	p value
Basal epithelial cell density (cells/mm²)			
Preoperative	5729±637 (5850)	5730±524 (5770)	0.912[m]
Postoperative 1 month	5447±634 (5550)	5325±987 (5470)	0.984[m]
Postoperative 4 month	5730±637 (5855)	5663±504 (5720)	0.596[m]
Dendritic cell (n)			
Preoperative	50.4±19.9 (45.0)	50.1±19.5 (45.0)	0.890[m]
Postoperative 1 month	70.2±19.8 (66.5)	74.5 ±17.3 (71.0)	0.311[m]
Postoperative 4 month	40.8±16.8 (33.5)	51.2±18.0 (48.0)	**0.021[m]**
Activated keratocyte (n)			
Preoperative	17.6 ±4.5 (16.5)	17.3±4.7 (16.0)	0.836[m]
Postoperative 1 month	24.2±4.3 (22.5)	25.2±4.9 (23.0)	0.445[m]
Postoperative 4 month	13.9±3.7 (13.5)	18.0±4.3 (17.0)	**0.047[m]**
Endothelial cell density (cells/mm²)			
Preoperative	2865± 221 (2850)	2852± 198	0.914[m]
Postoperative 1 month	2800±199 (2810)	2801±221	0.986[m]
Postoperative 4 month	2861±212 (2850)	2851±195	0.965[m]

[m]Mann-Whitney U test; bold type: Statistically significant; IVCM: In vivo confocal microscopy.

TABLE 4: Comparison of IVCM subbasal nerve plexus data between groups.

	Study group (n=30)	Control group (n=33)	p value
Subbasal total nerve (n)			
Preoperative	4.80±1.13 (5.00)	4.82±1.10 (5.00)	0.966[m]
Postoperative 1 month	3.17±1.05 (3.00)	3.09±0.95 (3.00)	0.677[m]
Postoperative 4 month	4.57±1.04 (5.00)	3.91±0.80 (4.00)	**0.008[m]**
Subbasal nerve tortuosity (0-4)			
Preoperative	1.37±0.56 (1.00)	1.39±0.70 (1.00)	0.804[m]
Postoperative 1 month	2.40±1.10 (2.00)	2.42±0.83 (2.00)	0.788[m]
Postoperative 4 month	1.57±0.68 (1.00)	2.18±0.68 (2.00)	**0.001[m]**
Subbasal nerve reflectivity (0-4)			
Preoperative	2.03±0.67 (2.00)	2.06±0.66 (2.00)	0.871[m]
Postoperative 1 month	2.07±0.64 (2.00)	2.09±0.68 (2.00)	0.871[m]
Postoperative 4 month	2.00±0.69 (2.00)	2.03±0.64 (2.00)	0.859[m]

[m]Mann-Whitney U test; bold type: Statistically significant; IVCM: In vivo confocal microscopy.

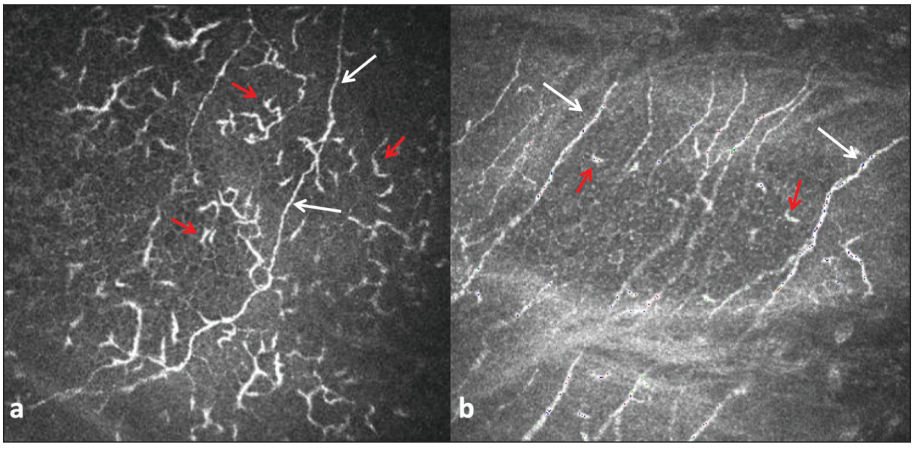

FIGURE 1: Subbasal nerves (white arrows) and dendritic cells (red arrows) before **(a)** and 4 months after **(b)** treatment with dexpanthenol/sodium hyaluronate fixed combination eye drops.

DISCUSSION

DED can cause ocular symptoms such as burning, stinging, foreign body sensation, sensitivity to light, and it is one of the leading cause of poor quality of life. Anxiety and depression are common among patients with DED, and even they have similar quality of life scores as patients with angina and those receiving dialysis.[14,15] It has been shown that cataract surgery induces or aggravates pre-existing DED, and disease symptoms and ocular surface findings continue after approximately three months.[1,16,17] Considering that cataract surgery is typically performed on elderly patients with a tendency to develop DED, it is crucial to manage DED before and after surgery.

Recently, dexpanthenol/sodium hyaluronate fixed combination eye drops were introduced to the market. Dexpanthenol is the precursor molecule that is converted into pantothenic acid intracellularly. It has an antioxidant effect by increasing glutathione and superoxide dismutase levels, as well as an anti-inflammatory effect by decreasing the pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin (IL)-6.[18] In an experimental rat model, dexpanthenol has also been shown to improve nerve regeneration.[19] On the other hand, sodium hyaluronate absorbs water, traps it in the aqueous layer, and binds to fibrin in order to form a protective film on the ocular surface.[20]

IVCM enables us to evaluate corneal micro structural changes using high-resolution en face images, currently, it is used in a number of fields, particularly in the differential diagnosis of keratitis and corneal dystrophies.[10,21] Since too many people suffer from DED, it is also a popular topic for IVCM studies. A decrease in subbasal nerve plexus density was observed in both evaporative and aqueous deficiency DED, suggesting that DED is associated with the neurosensory abnormalities.[22] In addition, it has been demonstrated that the density of dendritic cells is higher in all types of DED, indicating that OSI plays a crucial role in the pathophysiology of DED.[23] Furthermore, according to another study conducted in our country, subbasal nerve density decreased and the number of dendritic cells increased in Sjogren's syndrome-related DED.[24]

Our study included 63 eyes of 63 patients with no or mild preoperative DED symptoms without any ocular surface staining. Standard phacoemulsification was performed, and phaco metrics (CDE, total US time, torsional amplitude) were comparable between groups. After cataract surgery, in addition to changes in tear film stability and ocular surface staining, increased inflammatory cells and subbasal nerve plexus changes were observed at the microscopic level. While sodium hyaluronate eye drops provided a slight improvement in DED findings and OSI, dexpanthenol/sodium hyaluronate fixed combination eye drops were associated with a significant reduction in

OSI and a concurrent improvement in DED symptoms and findings.

Many agents have been used for the management of DED following cataract surgery. Sodium hyaluronate is one of the most preferred agents. A meta-analysis including 24 articles and 2,177 eyes found that sodium hyaluronate eye drops significantly improved DED symptom score and ocular surface findings.[19] In another study, 1% carboxymethylcellulose sodium improved TBUT, but ocular surface staining and OSDI scores were comparable to those of patients who did not receive tear film substitutes.[25] Diquafosol 3%, rebamipide, trehalose/sodium hyaluronate, and cyclosporine eye drops have also been associated with an improvement in DED symptoms and findings.[26-29]

The development of DED after cataract surgery is multifactorial. Damage to the corneal nerves is one of the most important causes. The corneal nerves maintain the sensation and neural arc for the tear film secretion and the control of blink reflex.[30] In addition, the precorneal tear film is essential for both the protection and the delivery of nutrients and oxygen to the cornea. The corneal nerves can be damaged directly by incisions or indirectly by inflammation after cataract surgery. In our study, the subbasal nerve plexus density decreased significantly in both groups 1 month after surgery. However, subbasal nerve plexus healing was faster in the dexpanthenol/sodium hyaluronate group than in the sodium hyaluronate group, leading to a more rapid improvement in DED symptoms and signs. A study evaluating dexpanthenol's efficacy after cataract surgery has also been recently published. In this study, dexpanthenol/alpha-glycerylphosphorylcholine (Oftassiale®, DMG, Italy) was applied to the study group, while sodium hyaluronate was applied to the control group for 1 month after cataract surgery; the dexpanthenol/alpha-glycerylphosphorylcholine group had higher postoperative subbasal nerve plexus density, with fewer bead-like formations.[31] Similarly, coenzyme Q10 and trehalose/sodium hyaluronate eye drops have provided rapid nerve healing after cataract surgery.[32,33]

Another leading cause of DED after cataract surgery is OSI. It was shown that cytokines such as IL-8, IL-6, IL-1, TNF-, MCP-1, and interferon-gamma were increased in the tear film following cataract surgery.[34] In addition, at the microscopic level, Langerhans cells, dendritic cells, and activated keratocytes were detected at the center of the cornea, and subbasal nerve plexus changes were also noted in IVCM after cataract surgery.[33,35] In a previous study using dexpanthenol/alpha-glycerylphosphorylcholine drops, activated keratocyte and langerhans cell infiltrations were observed, particularly at the incision sites 1 month after surgery, and no difference was reported between study and control groups.[31] In another study, Cagini et al. compared the efficacy of trehalose/sodium hyaluronate eye drops to a single dose of sodium hyaluronate in the treatment of postoperative DED and observed a statistically significant decrease in langerhans cell count, degree of keratocyte activation, nerve tortuosity, and reflectivity with trehalose/sodium hyaluronate eye drops.[33] In our study, we also observed a significant reduction in the number of dendritic cells, activated keratocytes, and the degree of nerve tortuosity, which are all indicators of OSI. But, they did not assess the phaco metrics and endothelial cell count between groups.

As far as we know, this is the first study to evaluate the efficacy of dexpanthenol/sodium hyaluronate fixed combination eye drops in the treatment of DED and OSI following cataract surgery. In addition, phaco metrics and endothelial cell count were assessed. However, our study has several limitations. The primary limitation was that the study was conducted retrospectively and included a relatively small sample size. The anti-inflammatory and nerve-regenerative effects of this new formulation cannot be determined clearly in such a small sample size and with a retrospective analysis. In addition, it is difficult to understand the effect of cataract surgery alone on iatrogenic dry eye in human studies because the influence of systemic diseases and external factors cannot be completely ruled out. In this regard, studies using an animal model of dry eye is needed for understanding the pathophysiology. In addition, it is difficult to examine the same area of the cornea on IVCM in repeated analyses. Furthermore, the corneal sensation was not assessed which is an important assessment for DED.

CONCLUSION

To summarize, multiple intraoperative and postoperative factors can cause DED after cataract surgery, and OSI is one of the most important factors. This study shows that dexpanthenol/sodium hyaluronate fixed combination eye drops could be preferred as an adjuvant for the treatment of DED and OSI following cataract surgery. However, additional animal studies and prospective clinical studies involving a large number of patients are required to verify our findings.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Huri Sabur, Mutlu Acar;* ***Design:*** *Huri Sabur, Mutlu Acar;* ***Control/Supervision:*** *Huri Sabur, Mutlu Acar, Neşe Arslan;* ***Data Collection and/or Processing:*** *Huri Sabur, Neşe Arslan;* ***Analysis and/or Interpretation:*** *Huri Sabur, Mutlu Acar;* ***Literature Review:*** *Huri Sabur, Neşe Arslan;* ***Writing the Article:*** *Huri Sabur, Mutlu Acar, Neşe Arslan;* ***Critical Review:*** *Huri Sabur, Mutlu Acar, Neşe Arslan;* ***References and Fundings:*** *Mutlu Acar, Neşe Arslan;* ***Materials:*** *Huri Sabur, Mutlu Acar, Neşe Arslan.*

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