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Use of an ointment based on sodium chloride and sodium hyaluronate (Edenight) in the postoperative period after cataract surgery

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Contents

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Keywords: Hyaluronic acid - Sodium hyaluronate - Sodium chloride - Ophthalmic ointment - Dry eye syndrome - Ocular discomfort - Corneal edema

Summary

The authors, who have been prescribing tear substitutes - mainly hyaluronic acid-based eye drops - after anterior segment surgical procedures for many years, have tested an ointment based on sodium chloride in hypertonic concentration and sodium hyaluronate (Edenight) for the night-time protection of the corneal and conjunctival surfaces following cataract surgery.

Use of the ointment showed excellent results in terms of attenuation or disappearance of corneal edema symptoms in the immediate postoperative period (first days after surgery) and of dry eye symptoms in the early postoperative period (1-2 months) in patients undergoing cataract surgery (phacoemulsification + intraocular lens implantation).

Introduction

Phacoemulsification is currently the most commonly performed cataract surgery. Recent advances in diagnostic methods and the management of cataracts through phacoemulsification have enabled most patients to achieve excellent visual outcomes. Corneal edema following phacoemulsification is a postoperative complication that may occur in the immediate postoperative period and often leads to patient dissatisfaction and worse outcomes[1].

The relative state of corneal dehydration is maintained at the endothelial level by an array of molecular pumps, chemical modulators, and cell junctional properties[2,3]. Post-phacoemulsification corneal edema may occur due to endothelial pump failure following surgery, which may in turn result from mechanical injury, chemical injury, subsequent infection/inflammation, or concurrent/pre-existing endothelial dysfunction[4]. The patients usually present with impaired vision in the immediate postoperative period with a lack of the expected gain in quality of vision. In addition, pain, photophobia, watering, and congestion may be present to variable degree as a result of the corneal edema and associated inflammation[1].

Medical management includes the use of hypertonic agents that are able to create a hypertonic tear film that draws water out

of the edematous cornea. Edenight is a hypertonic ophthalmic ointment containing 4.5% sodium chloride and 0.4% sodium hyaluronate formulated to provide temporary relief from the symptoms of corneal edema, such as altered vision and pain. The sodium hyaluronate contained in Edenight forms a protective shield on the corneal surface, providing protection and hydration; additionally, it makes the application of the hypertonic ointment more comfortable thanks to its lubricating and mechanical protection properties. Its viscous nature enables prolonged adhesion to the ocular surface, where it exerts its moisturizing and protective action even during the night hours. Ointment formulations are more effective than solution formulations: applying ointment at night may significantly reduce the early morning symptoms.

A further important aspect we have faced over the years is the problem of postoperative ocular discomfort in patients undergoing cataract surgery. In fact, a large part of these patients complain of foreign body sensation, ocular burning and redness in the early postoperative period (1-2 months) after cataract surgery in the absence of pathognomonic signs of corneal and conjunctival distress, especially in subjects aged over 70 years old.

Careful analysis of the tear film break-up time (BUT) and fluorescein, lissamine green and rose bengal staining led us to the conclusion that, in the postoperative period after cataract surgery, there was a quantitative and qualitative alteration of the corneal and conjunctival tear film that could justify the patients' symptoms. We therefore decided to prescribe, in our discharge protocols, tear substitute eye drops in addition to the traditional antibiotic-corticosteroid therapy, with the aim of alleviating the patients' dry eye symptoms.

In our opinion, dry eye syndrome, already present or at least latent in the vast majority of the patients undergoing cataract surgery (due to genetic, hormonal, iatrogenic or environmental factors), can be accentuated by topical therapy, by pre- and postoperative disinfection strategies (povidone-iodine is known to cause corneal and conjunctival epithelial cell distress and damage) and by the surgical wound healing process. We have not noticed significant differences in symptoms between populations of patients undergoing cataract surgery with a cut at 12 o'clock or with a lateral cut; frequently, the symptoms and signs of dry eye are also reported by patients undergoing intravitreal injections (a surgical procedure not addressed in the present study), where the surgical insult is minimal, which demonstrates that the type of surgery has very little influence on the postoperative course with regards to dry eye.

Objective of the study

By refining the observation of the dry eye symptoms most frequently reported by our patients, our attention focused on the symptoms experienced at night and on awaken-

ing that forced the patient to repeated tear substitute instillations to mitigate the ocular discomfort and alleviate the symptoms in the postoperative period. We therefore hypothesized that patients might benefit from the use of a protective ointment to be prescribed for night-time use, and the recent availability on the market of a hypertonic ointment has rekindled our interest in this strategy.

We considered that the combination of a hypertonic component (sodium chloride at 4.5%) and the traditional high concentration of sodium hyaluronate (0.4%), formulated as an ointment, would be suitable for improving corneal edema, if present, and dry eye syndrome in the postoperative period. Indeed, sodium chloride at this concentration, through an osmotic mechanism, is able to recall fluid from the cornea towards the tear film, resulting in two advantages: a reduction of the possible stromal edema resulting from the surgical insult, with improvement of image sharpness; hydration of the tear film by ensuring a greater presence of water molecules that improve the hydrosaline balance of the ocular surface.

Sodium hyaluronate, by binding the free water molecules in the tear film, may improve the protection of both the corneal and conjunctival surface.

Additionally, the ointment formulation of the product results in a prolonged residence time of the water molecules on the ocular surface and, because the ointment is administered shortly before bedtime, the visual clouding typically produced by ointments would not interfere with the patients' normal activities, thus greatly improving compliance with therapy.

We therefore evaluated the effectiveness of Edenight hypertonic ophthalmic ointment in improving corneal edema and dry eye syndrome in a cohort of patients undergoing cataract surgery.

Materials and methods

Procedure

We conducted a study (a clinical case series) on 100 patients operated on for cataract. Application of Edenight ointment was prescribed to 50 patients in the evening for night-time protection of the corneo-conjunctival surface, in addition to the usual antibiotic-corticosteroid, hyaluronic acid tear substitute eye drops and local NSAID therapy: netilmicin + dexamethasone + fluoroquinolone + hyaluronic acid tear substitute eye drops for the first 15 days, and then bromfenac and hyaluronic acid tear substitute eye drops with three instillations daily for an additional 15 days. The other 50 patients were prescribed the usual therapy with antibiotic-corticosteroid, hyaluronic acid tear substitute eye drops and NSAID without Edenight ointment application at night-time.

All the cataract procedures were performed by four surgeons of our Department following the same surgical technique and protocol: disinfection of the skin and conjunctival fornices through repeated pre- and post-

operative application of 5% povidone-iodine, lateral corneal cut of 2.2 / 2.4 mm, phacoemulsification with Alcon or Bausch and Lomb instruments, intraocular lens (IOL) implantation in the sac, hydrosuture and cefuroxime injection in the anterior chamber at the end of the operation.

Patients whose surgery presented intra- or postoperative complications (even if only in terms of lengthening of the procedure compared to the average of 10-12 minutes), undergoing cataract operations with premium IOL and patients with evident blepharitis were excluded, as were those undergoing anterior segment surgery involving the conjunctiva (filtering procedures for glaucoma). Within the planned study timeframe, no patients affected by lacrimal apparatus disease came to our attention. Enrolment was limited to the month of January 2020 (one of the periods of the year in which we had already encountered ocular discomfort symptoms in recent years), and no extension was foreseen to avoid seasonal differences that could compromise the homogeneity of the observation period.

We enrolled patients aged between 65 and 85 years, without excluding subjects with associated conditions and related ongoing treatments – although aware that some of them are able to slow down tear secretion (diabetes, hypertension, heart disease, use of systemic beta-blockers, selective serotonin reuptake inhibitors, benzodiazepines) – and with a numerical balance between male and female subjects.

The study population comprised:

- Patients treated with Edenight: 28 women aged 65 to 83 (mean age, 77 years) and 22 men aged 65 to 85 (mean age, 75 years) (Edenight group)
- Patients not treated with Edenight: 32 women aged 65 to 81 (mean age, 75 years) and 18 men aged 65 to 82 (mean age, 73 years) (control group).

Edenight was applied for 1 month after cataract surgery (30 bedtime applications), under constant supervision by the ophthalmologist.

Assessments

All the 100 subjects enrolled were evaluated by the same ophthalmologist to avoid discrepancy of judgment, given that one component of the evaluation of the postoperative course involved the ophthalmologist interviewing the patients about the presence and degree (on a 6-point scale from 0 = no symptoms to 5 = maximum discomfort) of the following five symptoms and signs:

- presence of burning
- periocular or orbital pain at night and/or upon awakening
- presence of eye redness
- foreign body sensation
- presence of paroxysmal tearing.

The ophthalmologist performing the evaluation was not involved in the surgery. He was provided with the list of patients treated but was blinded to those prescribed Edenight ointment.

The postoperative visits scheduled for these 100 patients reflected our usual follow-up protocol for patients undergoing cataract surgery. Visits took place at 2-3 days, 7-15 days and 30-40 days after surgery. For brevity, we report only the assessments aimed at

establishing the effectiveness of Edenight. During each of the three follow-up visits all patients were administered the oral questionnaire assessing their subjective symptoms based on the symptoms/signs and scores mentioned above. All patients reporting symptoms were able to give a very detailed description, which was always in line with the five categories used for the assessment.

Outcome measures

The following tests were also performed:

- an evaluation of corneal surface with vital fluorescein staining, in sterile disposable strips, with a BUT comparison between the two eyes at 7-15 days and 30-40 days after surgery
- a Schirmer I test comparison (3 minutes without anesthetic) between the two eyes at one of the two visits at 7-15 days or at 30-40 days after surgery
- a comparative BUT test analysis between the two eyes, using the Sirius CSO corneal topography program during the final visit (at 30-40 days after surgery). When envisaged, this test was performed before any other diagnostic evaluation.

Results

In this clinical case series, we considered the patient's subjective evaluation of the symptoms related to corneal edema (when present) and dry eye syndrome to be fundamental because the patient's comfort is our most important goal.

A poor correspondence was noted between the values obtained with the Schirmer I test and the patient-reported symptoms, indicating that this test offers a quantitative but not qualitative evaluation of the tear film. Indeed, in the event of discomfort affecting the operated eye, the Schirmer I test values were almost always very similar to those obtained in the contralateral eye and to those measured in patients without symptoms.

The fluorescein staining assessments of the corneo-conjunctival surfaces were more reliable in terms of correspondence between the patients' subjective evaluations and staining abnormalities, and premature tear film rupture (short BUT, shorter than in the contralateral eye) often accompanied the patients' subjective complaints.

The assessments based on the corneal maps produced by the BUT test Sirius CSO program were quite straightforward, showing a clear improvement in the corneo-conjunctival surfaces treated with Edenight compared with the ocular surfaces of the patients in the control group and of the patient's contralateral eye (**Figures 1** and **2** show the comparison of three patients in the control group and three patients in the treated group), with excellent correspondence between the patients' subjective evaluations and the objective data obtained with the test.

In some cases, the patients expressed a desire to use Edenight ointment also on the unoperated or recently operated-on contralateral eye since their eye disorders had

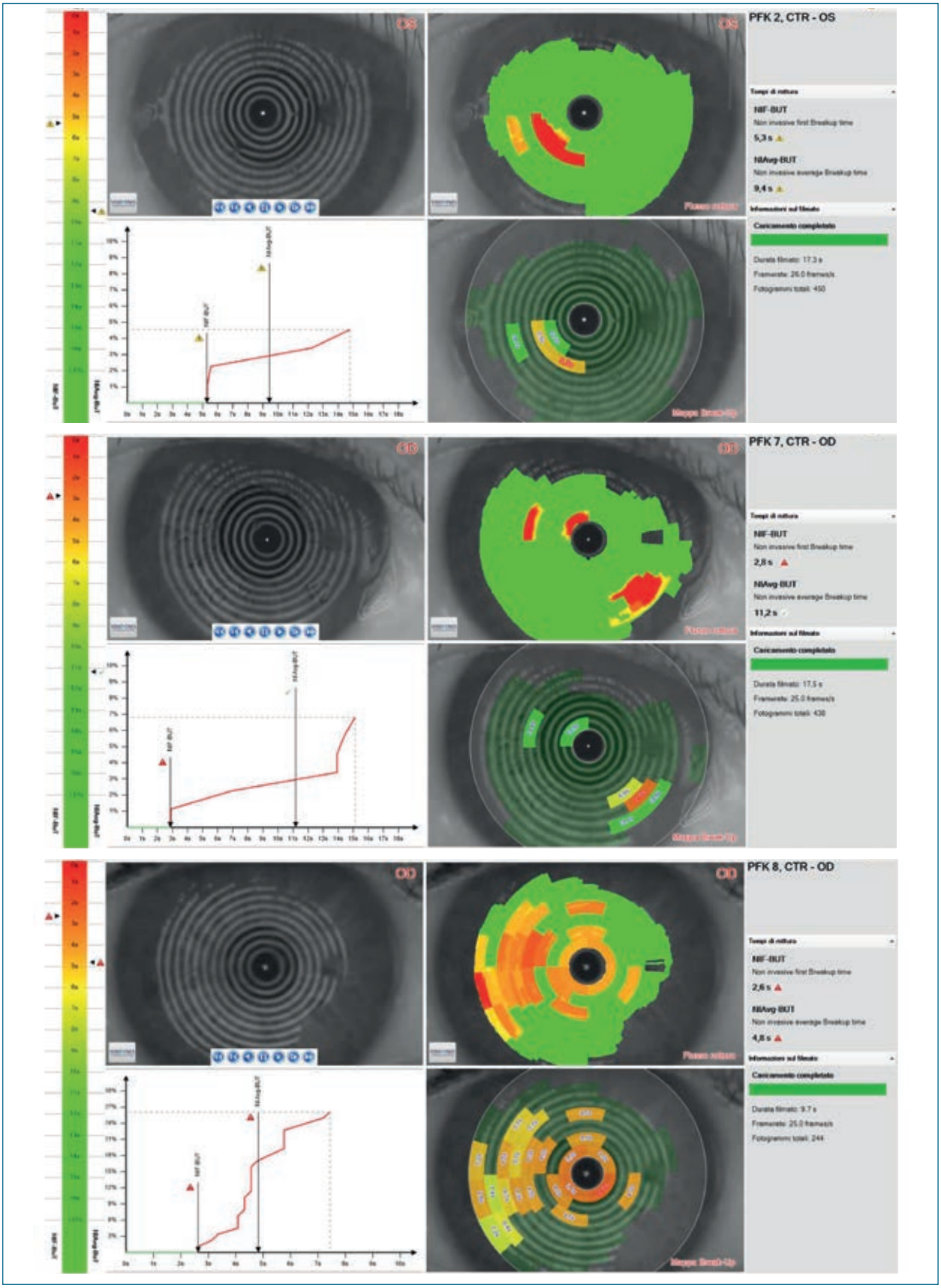

Figure 1. BUT test analysis with Sirius corneal topography program. Results obtained in three patients in the control group: the irregularities/alterations of the Placido disc rings are evident in both young and older patients. The subjects evaluated in the control group and Edenight group were of various ages and homogeneous between the two groups.

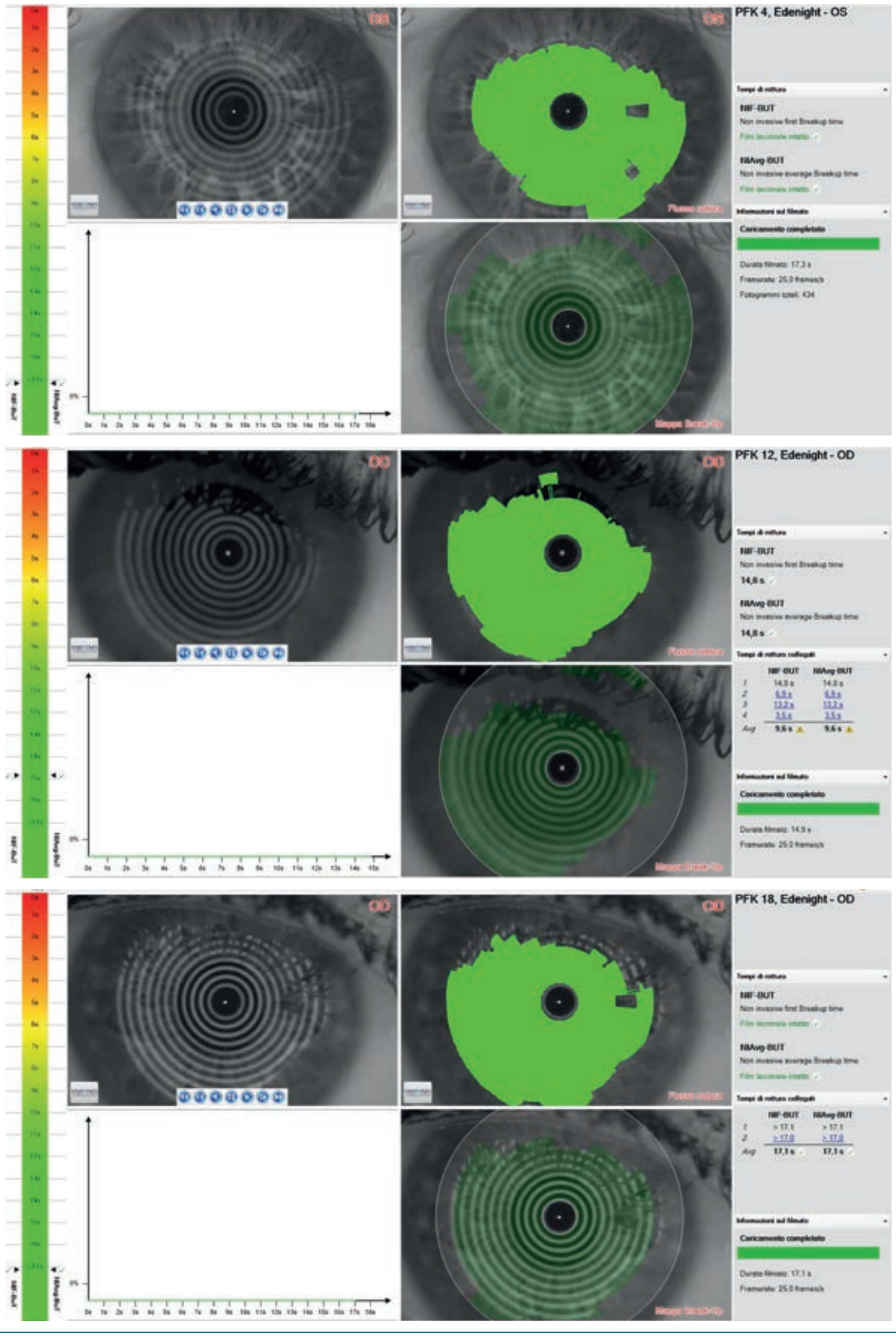

Figure 2. BUT test analysis with the Sirius corneal topography program. Results obtained in three patients in the Edenight group: there is greater regularity of the Placido disc rings regardless of age. The subjects evaluated in the control group and Edenight group were of various ages and homogeneous between the two groups.

TABLE 1. Percentage of patients reporting the five symptoms evaluated in the study **(burning, periocular and orbital pain, eye redness, foreign body sensation, and paroxysmal tearing)**, by visit and by group. 0 = no discomfort; 5 = maximum discomfort

Score	1st visit (2-3 days after surgery)		2nd visit (7-15 days after surgery)		3rd visit (30-40 days after surgery)	
	Group 1 Edenight	Group 2 Control	Group 1 Edenight	Group 2 Control	Group 1 Edenight	Group 2 Control
0	38%	19%	56%	27%	68%	32%
1	30%	15%	0%	10%	10%	5%
2	22%	17%	23%	10%	10%	10%
3	0%	0%	10%	33%	7%	30%
4	5%	29%	6%	7%	3%	13%
5	5%	20%	5%	13%	2%	10%

markedly improved after the use of the ointment during the night.

As for dry eye syndrome, based on the results collected by the ophthalmologist at the third visit, 68% of patients treated with Edenight had no symptoms, 27% had attenuated symptoms (between 1 and 3 out of the 5 symptoms listed above), and 5% had symptoms (between 4 and 5 out of the 5 listed above), versus 32%, 45%, and 23%, respectively, for the patients not using Edenight (**Table 1**).

There were no allergic reactions to the Edenight ointment.

Conclusions

The first recommendation that arises from our clinical practice is that it is very important to give patients clear instructions on how to instill the eye drops and apply the ointment as well as on the position of the head during instillation. They should also be told to keep the eyelids closed for one minute after instillation/application and wait at least 3-4 minutes between the use of different products. Being able to rely on a caregiver to administer the products, after careful and proper hand hygiene, is also important.

In the past, we noticed significant differences in clinical outcomes when we provided patients with clear written instructions illustrating how to apply the products compared to when this was not done. The patient discharge form must contain some simple written advice regarding personal

hygiene, recommended rest over 7 postoperative days and positioning of the protective eye shield during the night.

We also found a decrease in the orbital neuralgia often reported by elderly patients in association with the most typical manifestations of dry eye, a clear demonstration that the regularity of the corneal surface positively influences trigeminal neuralgia.

Considering the homogeneity of the population in terms of age, sex, and type of surgical procedure, we can state that we achieved an improvement of night-time eye comfort and a significant decrease in corneal edema and dry eye syndrome in the postoperative period after cataract surgery, with many patients also reporting complete disappearance of symptoms during the daytime. Based on these findings and the difference in symptoms between the patients treated with Edenight and the control group, we can state that we have fully achieved the goal of improving the patients' postoperative comfort, through the use of the hypertonic night ointment based on sodium hyaluronate and sodium chloride.

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