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Research Article

Postoperative Pain Control in Femto-Lasik with the Use of Therapeutic Contact Lenses Soaked in Ketorolac Trometamol 0.45% TCL Soaked in Ketorolac for Pain After Femto-Lasik

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Abstract

Objective: To compare the postoperative pain between patient eyes submitted to femtosecond laser-assisted LASIK after placement of contact lens (TCL) soaked in 0.45% ketorolac trometamol in one eye and placement of a TCL not soaked in the drug solution in the contralateral eye.

Setting: Sadalla Amin Ghanem Eye Hospital in Joinville, SC, Brazil.

Design: A double-blind, randomized, contralateral, prospective clinical study.

Methods: Patients submitted to LASIK with femtosecond laser received the TCL soaked in ketorolac trometamol 0.45% (Acular® CMC, Allergan, Inc., Irvine, CA) in one eye and a TCL without any medication in the other eye. The laterality selection was done randomly through a drawing. Patients with ocular surface diseases or those on chronic pain medication were excluded. The pain sensation was registered by the patients during 3 postoperative periods. The Wong-Baker Faces pain rating scale (from 0 to 10) was used.

Results: The study involved 64 eyes from 32 patients. The average postoperative pain score 3 hours after surgery in the eyes with TCL + ketorolac was 1.47 ± 2.12, significantly lower than the score among the eyes that received just the TCL, which was 3.31 ± 2.73 (P = 0.004). No statistically significant difference for pain level was observed 6 hours after surgery (P =0.053) and upon awakening the next day (P = 0.081).

Conclusion: The use of TCL soaked in ketorolac trometamol 0.45% safely provides significant pain reduction three hours after femto-LASIK when the pain is most intense.

Keywords: Pain; LASIK; Femtosecond Laser; Ketorolac; Contact Lenses

Introduction

Ketorolac is a non-steroidal anti-inflammatory drug (NSAID) with analgesic properties that has been used in ophthalmological formulations to relieve postoperative pain and inflammation in cataract and refractive surgeries since 1997 [1,2]. The formulations of 0.5% (Acular; Allergan, Inc., Irvine, CA) and 0.4%(Acular LS; Allergan, Inc., Irvine, CA) are equivalent in potency and both have efficacy and safety well demonstrated by several studies [3-8]. The solution with 0.4%, which contains 20% less active ingredient, is used to reduce the burning and itching sensation after refractive surgery [1]. Still, complaints of burning after instillation of eye drops in both formulations are frequent because they contain the preservative benzalkonium chloride (BAK), the surfactant octoxynol – 40, the metal chelator, and sodium edetate, which are all substances that cause ocular discomfort [2,8,9].

Consequently, a new ketorolac formulation appeared at 0.45% (Acular CMC; Allergan, Inc., Irvine, CA), in which a viscosity agent, carboxymethylcellulose (CMC) was added, and which did not contain the preservative, the surfactant, nor the metal chelator while still maintaining a greater concentration of the active ingredient. This increases its ocular bioavailability and generates higher concentrations in the aqueous humor and iris-ciliary body, and as a result, leads to a reduction in pH and greater tolerability in postoperative complaints [10]. Because of its anti-inflammatory and analgesic properties, this solution has been used with the therapeutic contact lenses (TCL) being soaked in it to relieve postoperative pain in photorefractive keratectomy (PRK) surgeries [11-13].

Laser in situ keratomileuses (LASIK) has been a well-known refractive surgery technique since the 90s. And it is currently the most widely used technique for refractive error corrections because it presents a faster visual recovery and less postoperative pain when compared to PRK [14-16]. Despite the advantages described above, it has been observed that the postoperative pain in femto-LASIK cases may be intense for some patients. Searching to ease these symptoms, we conducted a study to evaluate the use of TCLs soaked in ketorolac trometamol 0.45% (Acular CMC; Allergan, Inc., Irvine, CA) compared to the TCL control group without the drug in pain reduction after femto-LASIK surgeries.

Materials and Methods

The present study was conducted between July and December of 2020 at the Sadalla Amin Ghanem Eye Hospital in Joinville, SC, Brazil. After being approved by the institution's ethics committee, a consent form was provided to all voluntary participants informing them, in detail, of the treatment, the study's aim, and its possible complications.

The inclusion criteria were patients 18 years of age or older who, after a complete ophthalmological evaluation, had the best indication for the LASIK technique and who opted for the femtosecond laser, following the institution's protocols.

Patients with ocular surface diseases, keratoconus, previous ocular surgery, or with systemic disease that compromised pain perception, or those on chronic pain medication were excluded from the study.

The preoperative ophthalmological examination included corrected distant visual acuity (CDVA), extrinsic ocular motility, subjective cycloplegic refraction, slit-lamp biomicroscopy, and retinal mapping. Corneal topography and tomography by Scheimpflug imaging were also evaluated.

The surgeries were performed by two experienced refractive surgeons (VCG and RCG), using the Amaris 1050RS excimer laser (Schwind, Kleinostheim, Germany) and the LDV Z8 femtosecond laser (Zeimer, Port, Switzerland). The femtosecond laser with the double docking technique was programmed to produce flaps with a thickness of 100 µm and a diameter of 9.5 mm in the 2D method, always with a temporal pedicle of 0.4 mm. The lens preparation consisted of asepsis of the TCL (Acuvue Oasys® contact lenses with base curve 8.4 mm) case with 70% alcohol, opening and aspiration of the internal liquid with a syringe and thin needle, with subsequent instillation of four drops of 0.45% ketorolac trometamol (Acular CMC, Allergan, Inc., Irvine, CA), and leaving the soaked solution separated on a sterile surgical field for a period of 20 to 25 minutes before use.

At the end of the surgery, the patients received a 0.45% ketorolac-soaked TCL in one of the operated eyes, and a TCL not soaked in ketorolac was placed in the contralateral eye. The eyes

that received the TCL soaked in ketorolac were randomly assigned through a drawing. The lenses were removed in the morning the following day. And at the same time the forms were returned with the Wong-Baker 17 face scale assessment (from 0-10) where the pain was recorded by the patient at three moments: 1) 3 hours after surgery, 2) 6 hours after surgery, and 3) upon waking up the next day.

Postoperatively, gatifloxacin 0.3% eye drops combined with prednisolone acetate 1% (Zypred, Allergan, Inc., Irvine, CA) were used every hour until bedtime and every 4 hours from the second day onward until seven days had passed, along with carmellose sodium (Optive, Allergan, Inc., Irvine CA) every 4 hours until the bottle was empty. The interval between eye drops was at least 5 minutes.

Results

The study evaluated 64 eyes of 32 patients; 17 were male (53.1%) and 15 were female (46.9%). The age of the patients ranged from 22 to 58 years, with a mean age of 36.41 ± 8.6 years.

In the eyes with TCL soaked in ketorolac, the average spherical equivalent (SE) was -1.61D ± 2.92D. The pain sensation 3 hours after surgery ranged from 0 to 7, with the average pain of 1.47 ± 2.12. At the 6-hour postoperative evaluation, the pain ranged from 0 to 4, with an average of 0.72 ± 1.17. Upon waking up the next day, the pain ranged from 0 to 5, with an average of 0.19 ± 0.90. There was a statistically significant difference between the pain 3 hours after surgery and the pain upon waking up (p=0.004). Three hours after surgery, 15.5% of the eyes with the TCL + ketorolac and 46.8% of the eyes with the TCL without ketorolac reported moderate or intense pain. Six hours after surgery, 6.2% of the eyes with TCL + ketorolac and 25% of the eyes with BCL without ketorolac reported moderate pain. None of the eyes with TCL + ketorolac and 21.9% of the eyes with non-ketorolac BCL reported mild pain. None of the patients from either group had intense pain. Upon waking up the next day, 3.1% of the eyes with BCL + ketorolac and 21.9% of the eyes with non-ketorolac BCL reported mild pain. None of the patients from either group had moderate or intense pain (Table 1).

Comparison of postoperative pain in 3 timepoints between groups.

		Groups			
		TCL soaked in ketorolac trometamol 0.45%		TCL without medication	
		n	%	n	%
Pain 3 hours after LASIK	No pain	17	53.1	8	25.0
	Mild pain	10	31.2	9	28.1
	Moderate pain	4	12.5	10	31.2
	Intense pain	1	3.1	5	15.6
	Maximum pain	0	0.0	0	0.0
	Total	32	100	32	100
Pain 6 hours after LASIK	No pain	20	62.5	13	40.6
	Mild pain	10	31.2	11	34.4
	Moderate pain	2	6.2	8	25.0
	Intense pain	0	0.0	0	0.0
	Maximum pain	0	0.0	0	0.0
	Total	32	100	32	100.0
Pain waking up the next day	No pain	30	93.8	25	78.1
	Mild pain	1	3.1	7	21.9
	Moderate pain	1	3.1	0	0.0
	Intense pain	0	0.0	0	0.0
	Maximum pain	0	0.0	0	0.0
	Total	32	100	32	100

Table 1

Of the patients who had no pain at any of the three periods evaluated, 46.8% received BCL + ketorolac and 21.9% received BCL without the drug.

In the eyes that received the TCL without ketorolac, the average SE was -1.46D ± 2.54D. The pain 3 hours after surgery ranged from 0 to 8 on the scale, and with an average pain of 3.31 ± 2.73. And 6 hours after the procedure, the pain ranged from 0 to 6 with an average of 1.62 ± 2.03. Upon waking the following day, there was a variation of 0 to 3 with an average of 0.41 ± 0.88. There was a statistically significant reduction in pain between 3 and 6 hours after surgery (P = 0.022) and between 6 hours and the following day (P = 0.037).

Comparing the eyes with and without medication, for a significance level = 5%, there was no significant difference in the mean spherical equivalent (P = 0.833). In relation to pain sensation, for a significance level of 5%, there was a statistically significant difference between the eyes with BCL + ketorolac and non-medication BCL for postoperative pain 3 hours after surgery (P = 0.004) (Figure 1).

No complications such as detachment, flap folds, or postoperative DLK were observed. Adverse effects were not reported by the patients.

Figure 1: Means and confidence interval (95%) of postoperative pain at 3 evaluated time periods.

Discussion

The administration of drugs through TCL has shown promising results *in vitro*, as it is very efficient because it presents a higher uptake and bioavailability [18-21]. In a recent 2019 study, Shetty., *et al*. [11] evaluated the modulation of postoperative pain in 35 patients submitted to the PRK technique with the use of TCL soaked in ketorolac trometamol 0.45% perioperatively, resulting in an average pain score of 2.76 ± 0.85, lower than the group which had not used the medication with the TCL (7.95 ± 2.12). In our study, in the first 3 postoperative hours, the average pain score of (1.47 ± 2.12) in patients who received the TCL + ketorolac was also significantly lower than in the group who had only received the TCL (3.31 ± 2.73). And this pattern was maintained in the subsequent evaluations.

The use of ketorolac trometamol before and after conventional LASIK surgery for pain reduction has been studied for years, as shown in Dougherty's [22] study in 2009. The average intraoperative pain was significantly greater ($p = 0.002$) in the group which received artificial tears (mean = 1.23), in comparison with the group that received instilled ketorolac trometamol 0.4 (mean = 0.53).

Evaluating the efficacy of another topical NSAID, bromfenac 0.07% in control of the pain after femto-LASIK in 64 patients, Cleaveland., *et al*. [23] demonstrated more significant results in reducing pain after two hours in patients who had used the topical NSAID before and after LASIK, and a greater reduction in the first hour in patients who had used the NSAID just before LASIK. These results are in agreement with our study results, reinforcing the benefit of incorporating an intraoperative NSAID for better pain management in the first postoperative hours.

In a prospective and randomized study that involved 45 patients, Zhao., *et al*. [24] observed that there was improved comfort and postoperative pain relief in patients who were treated with BCL after femto-LASIK, as well as a better response in flap edge healing. They associated these factors with the compressive effect of the contact lenses on the flap margin, which may help stabilize the flap and reduce the infiltration of inflammatory mediators present in the tear. In line with our study, pain relief was greater in the first hours after surgery, and there was no flap detachment or other complications.

The postoperative pain, the possible surgical complications, and the satisfaction of patients were also evaluated by Pahlitzch., *et al*. [25] in 2017 comparing the effect of two types of femtosecond laser (LensX and LDV Z4) with the photorefractive keratectomy technique (PRK). In this study, 61% of the patients submitted to LensX experienced mild to intense pain on the first postoperative day and just 4% ($p < 0.001$) of the patients submitted to LDV Z4 had mild pain. Although femto LDV had the lowest pain score on the first postoperative day ($p < 0.001$), there was no difference in refraction between the three techniques three months after surgery. In our study, using the LDV Z8 femtosecond laser, we observed that 53% of the patients who received the BCL + ketorolac did not have pain three hours after surgery, 62.5% after 6 hours, and 94% upon waking up. In patients who used just the BCL, 25% did not have pain in the first three hours, 40.5% after 6 hours, and 78% upon waking up.

Conclusion

The use of TCL soaked in ketorolac trometamol 0.45% safely provided significant pain reduction three hours after femto-LASIK when the pain is most intense.

"What Was Known"

- TCL soaked in ketorolac trometamol 0.45% reduces postoperative pain after PRK.
- TCL improves comfort and reduces postoperative pain after femto-LASIK.
- Ketorolac trometamol reduces postoperative pain after refractive surgery.

"What This Paper Adds"

TCL soaked in ketorolac trometamol 0.45% significantly reduces postoperative pain after femto-LASIK.

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